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Efficacy

VUR


Chandrasekharan VV. (2013)


Kim JW, Oh MM. (2013)


Bayne AP, Roth DR. (2010) 

Chen HC, Yeh CM, Chou CM. (2010) 

Hsieh MH, Madden-Fuentes RJ, Lindsay NE, Roth DR. (2010) 


Chung PH, Lan LC, Wong KK, Tam PK. (2009) 


Läckgren G. (2009) 

Cerwinka WH, Scherz HC, Kirsch AJ. (2008) 
Dave S, Bägli DJ. (2008)  
*A review of the effect of injected dextranomer/hyaluronic Acid copolymer volume on reflux correction following endoscopic injection* Adv Urol. 2008:579370


*The treatment of vesicoureteral reflux* Arch Esp Urol. 2008 Mar;61(2):244-7


*Endoscopic Treatment of Vesicoureteral Reflux with Dextranomer/Hyaluronic Acid in Children* Advances in Urology Volume 2008, Article ID 513854


*Endoscopic treatment with Deflux for primary vesicoureteral reflux* Actas Urol Esp. 2007 Sep;31(8):880-4


McMann LP, Scherz HC and Kirsch AJ. (2007)  

*New contralateral vesicoureteral reflux after endoscopic correction of unilateral reflux--is routine contralateral injection indicated at initial treatment?* J Urol. 2007 Oct;178(4 Pt 2):1711-3

Menezes MN, Puri P. (2007)  
*The role of endoscopic treatment in the management of grade v primary vesicoureteral reflux.* Eur Urol. 2007 Nov;52(5):1505-9

Wadie GM, Tirabassi MV, Courtney RA, Moriarty KP. (2007)


Elmore JM, Scherz HC, Kirsch AJ. (2006)


*Single center experience with endoscopic management of vesicoureteral reflux in children.* J Urol. 2006 May;175(5):1889-92


Yu RN, Roth DR. (2006)


VUR - Comparison of Therapies


Ngo TC, Wong IY, Kennedy WA 2nd. (2013)


Aguiar A, Cardoso A, Prisco R, Cruz ME. (2011)
Surgical treatment of vesicourethral reflux in paediatric population Acta Med Port. 2011 Dec;24 Suppl 2:59-64


Stredele RJ, Dietz HG, Stehr M. (2011)

Bae YD, Park MG, Oh MM, Moon du G. (2010)
*Endoscopic Subureteral Injection for the Treatment of Vesicoureteral Reflux in Children: Polydimethylsiloxane (Macroplastique(R)) versus Dextranomer/Hyaluronic Acid Copolymer (Deflux(R)).* Korean J Urol. 2010 Feb;51(2):128-31


Molitierno JA, Scherz HC, Kirsch AJ. (2008)


Terry W, Hensle MD, Grace Hyun, MD, Amy L. Grogg, PharmD, Manan B. Shah, PhD, PharmD (2006)
*Assessing the effectiveness of endoscopic injection in treating patients with Vesicoureteral reflux for the reduction of urinary tract infections.* Presented at the 2006 Annual Meeting of the American Academy of Pediatrics, Atlanta, GA. October 7-10,2006

*Critical appraisal: antibiotic prophylaxis and endoscopic injection for VUR Issues in Urology May / June 2006; 18 (3)*


The effect of location of the ureteric orifice on the efficacy of endoscopic injection to correct vesico-ureteric reflux. BJU Int. 2005 Jun;95(9):1314-8


Endoscopic treatment of vesicoureteral reflux Harefuah. 2004 Sep;143(9):664-8, 694, 693.

Long-term outcome of the endoscopic correction of vesico-ureteric reflux: a comparison of injected substances. BJU Int. 2004 Aug;94(3):381-3


Prospective comparison and 1-year follow-up of a single endoscopic subureteral polydimethylsiloxane versus dextranomer/hyaluronic acid copolymer injection for treatment of vesicoureteral reflux in children Urology. 2002 Nov;60(5):894-7;

VUR - Complicated Cases


Lambropoulos V, Mouravas V, Papageorgiou I, Spyridakis I, Marakis G. (2014)
A novel use of dextranomer/hyaluronic acid copolymer. Urologia. 2014 May 14;0(0):0.


*The outcome of initial endoscopic treatment in the management of concomitant vesicoureteral reflux and ureteropelvic junction obstruction.* Urology. 2013 May;81(5):1040-5.


Polackwich AS, Skoog SJ, Austin JC. (2012) 


Kraft KH, Molitierno JA Jr, Dewhurst L, Geers C, Gunderson K, Scherz HC, Kirsch AJ. (2011) 
*Is endoscopic injection therapy a reasonable treatment option for low-grade vesicoureteral reflux in association with overactive bladder?* Urology. 2011 Sep;78(3):675-8


Romero NP, Romo MI, Vegas AG, Izquierdo JB, Varela JC, Arteche AH, Moyano AS. (2010) 


Rossini CJ, Mariarty KP, Courtney RA, Tashjian DB. (2009) 


Molitierno JA Jr, Scherz HC, Kirsch AJ. (2008)


Williams MA, Giel DW, Colleen Hastings M. (2008)

Cerwinka WH, Scherz HC, Kirsch AJ. (2007)


Endoscopic Treatment With Stabilized Nonanimal Hyaluronic Acid/Dextranomer Gel is Effective in Vesicoureteral Reflux Associated With Bladder Dysfunction J Urol. 2007 Mar;177(3):1124-8


**VUR - Cost Analysis**


**VUR - Diagnostic**


VUR - Quality of Life


VUR - Technique

Kirsch AJ1, Arlen AM2, Lackgren G3. (2014)


Watters ST, Sung J, Skoog SJ. (2013)

Usefulness of concomitant autologous blood and dextranomer/hyaluronic acid copolymer injection to correct vesicoureteral reflux. J Urol. 2012 Sep;188(3):948-52

Kalivsart JF, Scherz HC, Cuda S, Kaye JD, Kirsch AJ. (2012)


Tamarkina E, El-Sherbiny M, Jednak R, Capolicchio JP. (2009)


Cerwinka WH, Scherz HC, Kirsch AJ. (2008)


Injection of Deflux®/ Zuidex using a new injection device - Magnetic Resonance Imaging confirms the periurethral location of deposits HUDDINGE-UNIVERSITETSSJUKHUS
Safety

Calcification

Palagiri AV, Dangle PP. (2011)

Cerwinka WH, Kaye JD, Scherz HC, Kirsch AJ, Grattan-Smith JD. (2010)

Cerwinka WH, Qian J, Easley KA, Scherz HC, Kirsch AJ. (2009)

Malpositioning


Migration


New Contralateral Vesicoureteral Reflux - NCVUR

Cerwinka WH, Kaye JD, Leong TL, Elmore JM, Scherz HC, Kirsch AJ. (2013)

*New contralateral vesicoureteral reflux following dextranomer/hyaluronic Acid implantation: incidence and identification of a high risk group. J Urol.* 2006 Mar;175(3 Pt 1):1097-100

Obstruction

Zemple RP, Potretzke AM, Kryger JV (2012)

Postoperative ureteral obstruction after endoscopic antireflux therapy Arch Esp Urol. 2008 Mar;61(2):328-34.


Snodgrass WT. (2004)

**Tissue Changes**


Endoscopic treatment of vesicoureteral reflux: histologic findings Arch Esp Urol. 2008 Mar;61(2):112-6


**Urinary Tract Infection**

Fotso Kamdem A, Galli G, Aubert D. (2014)


Urinary Tract Infection

Antibiotic Prophylaxis


Diagnostic


Management

Ristola MT, Hurme T. (2014)

Kenneth B. Roberts, MD, Chairperson, Stephen M. Downs, MD, MS, Stanley Hellerstein, MD, Michael J. Holmes, MD, PhD, Robert L. Lebowitz, MD, Jacob A. Lohr, MD, Linda D. Shortliffe, MD Russell W. Steele, MD (1999)
*Committee on Quality Improvement, Subcommittee on Urinary Tract Infection - Practice Parameter: The Diagnosis, Treatment, and Evaluation of the Initial Urinary Tract Infection in Febrile Infants and Young Children* Pediatrics 1999;103;843
VUR

Antibiotic Prophylaxis


Comparison of Therapies


Cost Analysis


Diagnostic


Management


Tekgül S, Riedmiller H, Hoebeka P, Kočvara R, Nijman RJ, Radmayr C, Stein R, Dogan HS; European 
Association of Urology. (2012) 

*Is availability of endoscopy changing initial management of vesicoureteral reflux?* J Urol. 2009 Sep;182(3):1152-7

Hensle TW, Grogg AL. (2007) 


**Spontaneous Reflux Resolution**


Teixeira CB, Cançado MA, Carvalhaes JT. (2014) 


Abstracts

Efficacy

VUR

Retrospective study of endoscopic treatment in children with primary vesicoureteral reflux and multivariate analysis of factors for failure.

Akin Y, Gulmez H, Güntekin E, Baykara M, Yucel S.

Abstract Objective. The aim of this study was to investigate endoscopic treatment in children with primary vesicoureteral reflux (VUR) and conduct a multivariate analysis of factors for failure.

Material and methods. Between August 2006 and January 2012, 216 children (32 boys and 184 girls) with primary VUR (grades I-IV) who underwent endoscopic treatment were analysed. Patients with grade V VUR were excluded. Hydrodistension tests and intraureteral injection techniques were performed, if applicable. Urinary ultrasound and voiding cystourethrography were studied 3-6 months after surgery. Univariate and multivariate logistic regression were used for statistical analyses.

Results. In total, 172 children (21 boys and 151 girls) were enrolled, and 280 ureters were treated (108 bilateral, 64 unilateral; three with grade I, 34 with grade II, 214 with grade III and 29 with grade IV VUR). The median (± SD) age was 7.8 ± 3.1 years (boys 7 ± 3.1 years, girls 7.9 ± 3.1 years). The mean (± SD) follow-up was 24.4 ± 4.1 months (boys 28.2 ± 8.1 months, girls 21.4 ± 4.1 months). Mean injected volume per ureter was 1.8 ± 0.5 ml. A single injection resolved the reflux in 79.6% and a second injection resolved it in 90.4% of ureters. Eight children (4.6%) had postoperative febrile urinary tract infections (fUTIs). Postoperative fUTIs were significantly associated with failures in injection (p < 0.001). Renal scars were significantly associated with postoperative fUTI (p = 0.006). Haematuria occurred in three children (minor complication); a non-functional kidney was observed in one child (major complication) and a laparoscopic nephrectomy was performed. Fourteen children underwent ureteroneocystostomy owing to unsuccessful VUR treatment.

Conclusions. Endoscopic injection of small-diameter microsphere (80-120 μm) non-animal dextranomer-hyaluronic acid copolymer seems to be an effective treatment for VUR. Only postoperative fUTI and the presence of a renal scar were correlated with failed endoscopic treatment of VUR.

Effective endoscopic diagnosis and treatment of pediatric occult vesicoureteral reflux with intermediate to long-term follow-up.


PURPOSE: Recurrent febrile urinary tract infections (fUTIs) in children with non-diagnostic voiding cystourethrogram (VCUG) are challenging, as misdiagnosis can lead to renal damage and increased morbidity. We compared fUTI rates before and after endoscopic treatment of patients with suspected occult VUR.

METHODS: Between January 2009 and December 2012, children with history of fUTI and non-diagnostic VCUG(s) underwent endoscopic ureteral hydrodistention (HD) and injection of dextranomer hyaluronic acid co-polymer (Dx/HA). fUTI rates before and after intervention were evaluated. Demographics, imaging and endoscopic findings were assessed.

RESULTS: Thirty-four children (mean age 5.4 ± 2.8 years) underwent bilateral Dx/HA injection for occult VUR. Average follow-up was 28.8 months. Seventeen children had renal scarring. Mean ureteral HD grade was 2.2/3. HD grade for ureters associated with renal scarring was significantly (p < 0.05) higher (2.6/3) than those without scarring (2.0/3). Mean injected volume was 1.2 mL. Ureters associated with renal scarring (n = 21) required significantly (p < 0.05) higher volumes (1.4 mL) than those without scarring (n = 47; 1.1 mL). Prior to intervention, the fUTI rate was 0.15/patient/month compared to just 0.02 after treatment (p < 0.0001).

CONCLUSIONS: Incidence of fUTIs significantly decreased following treatment, supporting the use of Dx/HA injection in carefully selected children when the suspicion for occult VUR is high.

Endoscopic management of vesicoureteral reflux in children in kosova.

Berisha M, Hyseni N, Statovci S, Grajqevci S, Xhiha B.

INTRODUCTION: Vesicoureteral reflux (VUR) in children has been treated with subureteric deflux injection of Deflux (dextranomer hyaluronic acid copolymer) since 2009. The aim of this study was to analyze the results of endoscopic treatment of VUR in our clinic.

METHODS: Between March 2009 and December 2013, fifty-five children underwent endoscopic subureteral injection of Deflux in 78 ureters. Two months postoperatively voiding cystourethrogram (VCUG) was performed. This study examined the disappearance of VUR and urinary tract infection (UTI) as well as the quality of life during long-term follow-up.

RESULTS: The study included 55 patients (40 females and 15 males) with 78 refluxing ureters. There were 22 refluxed ureters altogether and 33 children had a unilateral reflux (two duplicated systems). All patients were treated, from the age 6 months up to 12 years old. The mean age of patients was 5.2 years. There has been no complications, but with few recurrences. In 6 patients (16.6%), endoscopic treatment with deflux was done twice, while in three patients (8.5%), the endoscopic treatment with deflux was performed three times, because of recurrence.

We recommend the use of endoscopic Deflux injection as first line treatment for children with VUR. Endoscopic subureteral injection of Deflux is a minimally invasive method for VUR treatment in pediatric patients and is associated with low morbidity.

Endoscopic Treatment with Dextranomer/Hyaluronic Acid for Persistent Incontinence After Continent Urinary Reconstruction.


Abstract Purpose: To determine the applicability and long-term outcome of endoscopic injection of dextranomer/hyaluronic acid (Dx/HA) to correct incontinence in patients who had previously undergone continent urinary reconstruction.

Patients and Methods: A retrospective cohort study was performed of all patients who underwent Dx/HA injection at our institution from January 2001 to June 2011. All patients had adequate bladder capacity and compliance on maximized medical therapy before injection. “Success” was defined as either “continence” (daytime dry interval >3 hours) or “improvement” (daytime dry interval >2 hours).

Results: A total of 22 children (16 females and 6 males) had Dx/HA injections for persistent incontinence from either bladder neck (7), Mitrofanoff (10), or both (5). Median age at injection was 13 years (range 4-21). Children underwent an average of 1.6 injection sessions per patient with an average of 2.6 mL of Dx/HA per session. At a median follow-up of 72 months (range 4-104), 19 (86.4%) patients had successful results (16 continent, 3 improved). For those incontinent from bladder neck, 42% became continent after 1, 75% after 2, and 83% after 3 injections, with a success rate of 91% (10 continent, 1 improved). For those incontinent from Mitrofanoff, 20% became continent after 1, and 73% after 2 injections, with a success rate of 86% (11 continent, 2 improved).

Conclusions: Endoscopic injection of Dx/HA to correct residual incontinence in selected children after urinary reconstruction appears to be safe and effective, achieving a dry interval in more than two-thirds of patients.

Clinical value of persistent but downgraded vesicoureteral reflux after dextranomer/hyaluronic acid injection in children.

Baek M, Kang MY, Lee HE, Park K, Choi H.

We aimed to investigate the clinical value of persistent but downgraded vesicoureteral reflux (VUR) after dextranomer/hyaluronic acid (Dx/HA) injection in children.

The medical records of 128 children (195 ureters) who underwent Dx/HA injections for VUR were reviewed. The incidences of pre- and post-operative febrile urinary tract infections (UTIs) were analyzed in children with or without persistent VUR on voiding cystourethrography (VCUG) 3 months postoperatively. The surgical results of VUR persistent children who underwent a single additional injection were assessed.

The VUR resolved completely in 100 ureters (51.3%), was persistent in 95 ureters, and newly developed in 2 ureters. The incidence of pre/post-operative febrile UTIs were 0.35 ± 0.39 per year and 0.07 ± 0.32 per year in VUR resolved children (P < 0.001), and 0.76 ± 1.18 per year and 0.20 ± 0.61 per year in VUR persistent children (P < 0.001). A single additional Dx/HA injection (44 ureters) resolved VUR in 29 ureters (65.9%), and also reduced the VUR to grade I in 7 ureters (15.9%), II in 4 (9.1%), and III in 4 (9.1%).

Even in children with persistent VUR after Dx/HA injection, the incidence of febrile UTIs decreased markedly. The VUR grade significantly decreases after single additional Dx/HA injection.


Bajpai M, Verma A, Panda SS.

AIMS: To study the outcome of endoscopic hyaluronic acid/dextranomer injection in patients with vesico-ureteric reflux (VUR)

MATERIALS AND METHODS: Sixty-three children were evaluated with a median follow up of 18 months (12-55 months) before injecting hyaluronic acid/dextranomer in a total of 99 ureteric moieties. Median age at presentation was 24 months (6-72 months). Primary VUR was the main presenting diagnosis in 60%. Patients were monitored for urinary tract infection (UTI), glomerular filtration rate (GFR), renal scarring, persistence, or appearance of contra-lateral reflux.

RESULTS: Grade III VUR was the most common (38%) followed by Grade IV (24%), Grade V (17%), Grade II (14%), and Grade I (7%). Most common cause for VUR was Primary (60%), followed by posterior urethral valve (PUV) (19%), bladder extrophy (5%), anorectal malformation (ARM), epispadias, and duplex system. Analysis of patients characteristics at presentation revealed renal scarring (40%), split renal functions <35% (35%), recurrent UTI (15%), GFR <50 ml/min/1.73 m² (15%), serum creatinine >1.4 mg/dL (10%). Complete resolution (100%) of Grade I and Grade II VUR was achieved after single injection. For Grade III VUR, single injection resolved reflux in 85.5% ureters, 100% resolution was seen after 2(nd) injection. In Grade IV VUR, 1(st) injection resolved VUR in 83.3% ureters, 95.8% ureters were reflux free after 2(nd) injection, and 100% resolution was seen after 3(rd) injection. In Grade V VUR, 94% ureters showed absent reflux after three injections.

CONCLUSION: Hyaluronic acid/dextranomer injection holds promise even in higher grades of VUR.


Chandrasekham VV.

PURPOSE: VUR is a common urologic problem in children. Cystoscopic injection of bulking agents (most commonly Deflux) has gained popularity as the first line treatment in the west. However, primarily due to cost factors, it has not gained much popularity in our country. We present our initial experience with cystoscopic Deflux injection for VUR.

MATERIALS AND METHODS: We reviewed our 3-yr experience with the use of Dx/HA (Deflux) for correction of VUR in children and adolescents. All children were evaluated with Ultrasound, MCUG and DMSA renal cortical scan. The indications for surgical correction of VUR included breakthrough infections while on antibiotic prophylaxis, persistent high-grade VUR beyond 3 yrs of age, and presence of significant renal damage on DMSA at diagnosis (in those children presenting with UTI). All children underwent cystoscopic Deflux injection using the standard technique of subureteral injection (0.4-1 ml per ureter). All children received antibiotic prophylaxis for 3-6 months after the injection. USG was done at 1 month and MCUG at 3-6 months after the injection.

RESULTS: 33 patients (48 ureters) underwent cystoscopic Deflux injection for correction of VUR. Mean age was 4.5 yrs (1-17 yrs); there were 12 boys and 21 girls. Thirteen children had antenatally diagnosed HDN, while 20 children presented with febrile UTI. All children had primary VUR except one child with persistent VUR 4 yrs after PUV fulguration. The VUR was grade 1-2 in 8, grade 3-4 in 37, and grade 5 in 3 ureters. Every child had at least one ureter with dilating reflux (grades 3,4 or 5). When present, low grade VUR (grade 1or 2) was always on the contralateral side. Only one child received a 2(nd) injection after 6 months. Follow-up MCUG was done in 28 children (41 ureters). Complete reflux resolution was achieved in 27 ureters (65%), and the reflux was downgraded in 2 (5%). There were no complications of Deflux injection.

CONCLUSIONS: Endoscopic correction of VUR in children is a safe and effective minimally invasive treatment for VUR. It stops or downgrades VUR in 70% of ureters. At present, we recommend it as a first-line treatment for grades 1-4 VUR requiring surgical management. Cost is the major factor limiting its use in our country.

Dextranomer/hyaluronic acid endoscopic injection is effective in the treatment of intermediate and high grade vesicoureteral reflux in patients with complete duplex systems.

Hunziker M, Mohanan N, Puri P.

PURPOSE: Endoscopic subureteral injection of dextranomer/hyaluronic acid has become an established alternative to long-term antibiotic prophylaxis or surgical treatment for vesicoureteral reflux. We evaluated the effectiveness of endoscopic injection of dextranomer/hyaluronic acid in intermediate and high grade vesicoureteral reflux in patients with complete duplex collecting systems.

MATERIALS AND METHODS: A total of 123 children underwent endoscopic correction of intermediate or high grade vesicoureteral reflux using injection of dextranomer/hyaluronic acid into complete duplex systems between 2001 and 2010. Vesicoureteral reflux was diagnosed by voiding cystourethrogram, and dimercapto-succinic acid scan was performed to evaluate the presence of renal scarring. Followup ultrasound and voiding cystourethrogram were performed 3 months after the outpatient procedure and renal ultrasound thereafter every 2 years. Mean followup was 6.7 years.

RESULTS: Complete duplex systems were unilateral in 110 patients and bilateral in 13. Reflux severity in the 136 refluxing units was grade II in 1 (0.7%), III in 52 (38.2%), IV in 61 (44.9%) and V in 22 (16.2%). Dimercapto-succinic acid scan revealed renal functional abnormalities in 63 children (51.2%). Vesicoureteral reflux resolved after the first endoscopic injection of dextranomer/hyaluronic acid in 93 ureters (68.4%), after a second injection in 35 (25.7%) and after a third injection in 8 (5.9%). Febrile urinary tract infection developed in 5 patients (4.1%) during followup. No patient required ureteral reimplantation or experienced significant complications.

CONCLUSIONS: Our results confirm the safety and efficacy of endoscopic injection of dextranomer/hyaluronic acid in eradicating intermediate and high grade vesicoureteral reflux in patients with complete duplex systems. We recommend this minimally invasive, 15-minute outpatient procedure as a viable option for treating intermediate and high grade vesicoureteral reflux in patients with complete duplex collecting systems.

Endoscopic treatment of vesicoureteral reflux in pediatric patients.

Kim JW, Oh MM.

Endoscopic treatment is a minimally invasive treatment for managing patients with vesicoureteral reflux (VUR). Although several bulking agents have been used for endoscopic treatment, dextranomer/hyaluronic acid is the only bulking agent currently approved by the U.S. Food and Drug Administration for treating VUR. Endoscopic treatment of VUR has gained great popularity owing to several obvious benefits, including short operative time, short hospital stay, minimal invasiveness, high efficacy, low complication rate, and reduced cost. Initially, the success rates of endoscopic treatment have been lower than that of open antireflux surgery. However, because injection techniques have been developed, a recent study showed higher success rates of endoscopic treatment than open surgery in the treatment of patients with intermediate- and high-grade VUR. Despite the controversy surrounding its effectiveness, endoscopic treatment is considered a valuable treatment option and viable alternative to long-term antibiotic prophylaxis.


BACKGROUND: The goals of medical intervention in patients with vesicoureteral reflux are to allow normal renal growth, prevent infections and pyelonephritis, and prevent renal failure. We present our experience with endoscopic treatment of vesicoureteral reflux in children by subureteral dextranomer/hyaluronic acid copolymer injection.

METHODS: Under cystoscopic guidance, dextranomer/hyaluronic acid copolymer underneath the intravesical portion of the ureter in a subureteral or submucosal location was injected in patients undergoing endoscopic correction of vesicoureteral reflux.

RESULTS: A total of 282 patients (120 boys and 162 girls) underwent the procedure. There were 396 refluxed ureters altogether. The mean age of patients was 4.9 years. The mean overall follow-up period was 44 months. Among the 396 ureters treated, 76% were cured with a single injection. A second and third injection raised the cure rate to 93% and 94%, respectively. Twenty-two (6%) ureters failed all 3 injections, and were converted to open surgery.

CONCLUSION: Endoscopic treatment of vesicoureteral reflux can be recommended as a first-line therapy for most cases of vesicoureteral reflux, because of the short hospital stay, absence of complications and the high success rate.


OBJECTIVE: To evaluate the incidence of febrile urinary tract infection (UTI) after successful endoscopic correction of intermediate and high-grade vesicoureteral reflux (VUR).

STUDY DESIGN: Medical records of 1271 consecutive children (male, 411; female, 903) who underwent successful endoscopic correction of VUR were reviewed. Factors potentially influencing postoperative UTIs, such as history of presentation, age, sex, grade of VUR, renal scarring, and agent used for the endoscopic injection, were analyzed.

RESULTS: Febrile UTI developed in 73 children (5.7%) after successful endoscopic correction of VUR. Thirty-nine children had a single episode of UTI, and 34 children had two or more episodes at 1 month to 5.9 years (median, 1 year) after correction of VUR. With multivariate analysis, female sex (P < .001), history of preoperative bladder/bowel dysfunction (BBD; P = .005), and BBD after endoscopic correction (P = .001) were revealed to be the most important independent risk factors for a febrile UTI after successful correction of VUR.

CONCLUSIONS: The incidence of febrile UTIs after successful correction of intermediate and high grade VUR is low. Female sex and BBD were the most important risk factors in the development of febrile UTI. Our data supports the importance of assessing bladder and bowel habits in older children with febrile UTIs after endoscopic correction of VUR.

Clinical and radiographic results of endoscopic injection for vesicoureteral reflux: defining measures of success.


OBJECTIVE: Criteria for success following endoscopic vesicoureteral reflux (VUR) surgery vary greatly. We sought to define outcomes based on radiographic and long-term clinical follow up.

METHODS: We reviewed the charts and interviewed parents of children who underwent endoscopic treatment for primary VUR (grades I-IV). All patients had a postoperative voiding cystourethrogram (VCUG) at mean of 3 months (1-21 months) and all cases of postoperative febrile urinary tract infection (FUTI) prompted repeat VCUG. Radiographic success was defined as no VUR on postoperative VCUG and clinical success as no FUTIs during follow up of 12-36 months. To demonstrate how criteria for success can affect outcomes, we calculated the success rates using different definitions.

RESULTS: In 2004-2008, 336 patients (296 female and 40 male, mean age 4 years) were treated with dextranomer/hyaluronic acid via the Double-HIT method. Initial radiographic success was 90% (302/336). Of these, 19 (6%) developed FUTIs, 12 (4%) of whom had recurrent VUR, and 5 (2%) went on to open surgery. Of the radiographic failures, 18% were observed with no further treatment. Success defined clinically was 94% (281/300), and as ‘radiographic cure and no clinical evidence of FUTIs’ it was 82% (275/336).

CONCLUSIONS: It is important to agree on a universal definition of success for VUR interventions to compare across studies and across therapies. Clinical success is more meaningful to the patient, and initial radiographic success could be followed by UTI necessitating further intervention. We question the need for routine postoperative VCUG.

Intraureteral injection of NASHA/Dx gel under direct ureteroscopic visualization for the treatment of primary high-grade vesicoureteral reflux.

Mattioli G, Guida E, Rossi V, Podestà E, Jasonni V, Ghiggeri GM.

OBJECTIVE: To present a preliminary experience with the modified technique of extravesical intraureteral injection of non-animal-stabilized hyaluronic acid/dextranomer (NASHA/Dx) gel under direct ureteroscopic visualization for the treatment of primary high-grade vesicoureteral reflux (VUR).

PATIENTS AND METHODS: The medical records of all pediatric patients (age range, 0-14 years) who underwent intraureteral injection of NASHA/Dx gel under direct ureteroscopic visualization for the treatment of primary high-grade VUR during the period June 2006-June 2010 were reviewed.

RESULTS: Eighty-nine children (61 boys, 28 girls; M:F ratio, 2.1) underwent intraureteral injection of NASHA/Dx gel under direct ureteroscopic visualization for the treatment of primary high-grade VUR during the study period. VUR completely disappeared after the injection of NASHA/Dx gel into 105 (73%) of 144 ureters, with no further treatment required. Thirty-five (24.3%) required a second injection, and 2 (1.4%) required a third injection for resolution of their VUR. No intraoperative complications were observed. No ureteral obstruction during follow-up was observed using ultrasound or micturition studies.

CONCLUSIONS: Intraureteral injection of NASHA/Dx gel under direct ureteroscopic visualization is safe and effective in the treatment of primary high-grade VUR, including cases with ureteral duplication, if the ureteral meatus is easy to pass through without mechanical dilation. This approach represents an effective and safe alternative to antibiotic prophylaxis alone and open surgery.

Endoscopic correction of vesicoureteric reflux: 10-year experience of a tertiary care center.

Neel KF.

Endoscopic treatment (ET) of vesicoureteric reflux (VUR) is becoming the new gold standard for surgical correction. ET for VUR using newly available bulking agents is a reliable and safe alternative procedure to open ureteral reimplantation for the treatment of VUR in children.

We retrospectively reviewed our experience over 10 years of patients with primary VUR who underwent ET and had at least one year of follow-up at our center from 1998 to 2008. We looked at laterality, success rate, need for a second procedure and complication rate. We observed 321 patients with ET for VUR during this period; 115 (35.8%) of them were males and the total intervened ureters were 480. Correction of VUR was defined as either the resolution of reflux or a downgrading to grade 1 revealed with a follow-up voiding cystourethrogram and no ipsilateral renal or ureteric dilatation detected on renal ultrasound.

At two to three months of follow-up, VUR was corrected in 393/480 (81.8%) refluxing ureters after a single endoscopic injection. With a second, repeated injection in the failed cases, VUR was corrected in a total of 418 (87.1%) refluxing ureters. Only three patients had post-operative complications (<1%).

We conclude that our study suggests that the majority of patients will be cured after undergoing, as out-patients, this endoscopic procedure. We believe that the widely reported safety of bulking agents and the short learning curve will make ET the standard treatment for VUR once surgical correction is warranted.

http://www.ncbi.nlm.nih.gov/pubmed/22237218
Single center experience with endoscopic subureteral dextranomer/hyaluronic acid injection as first line treatment in 1,551 children with intermediate and high grade vesicoureteral reflux

Puri P, Kutasy B, Colhoun E, Hunziker M.

PURPOSE: In recent years the endoscopic injection of dextranomer/hyaluronic acid has become an established alternative to long-term antibiotic prophylaxis and the surgical management of vesicoureteral reflux. We determined the safety and effectiveness of the endoscopic injection of dextranomer/hyaluronic acid as first line treatment for high grade vesicoureteral reflux.

MATERIALS AND METHODS: Between 2001 and 2010, 1,551 children (496 male, 1,055 female, median age 1.6 years) underwent endoscopic correction of intermediate and high grade vesicoureteral reflux using dextranomer/hyaluronic acid soon after the diagnosis of vesicoureteral reflux on initial voiding cystourethrogram. Vesicoureteral reflux was unilateral in 761 children and bilateral in 790. Renal scarring was detected in 369 (26.7%) of the 1,384 patients who underwent dimercapto-succinic acid imaging. Reflux grade in the 2,341 ureters was II in 98 (4.2%), III in 1,340 (57.3%), IV in 818 (34.9%) and V in 85 (3.6%). Followup ultrasound and voiding cystourethrogram were performed 3 months after the outpatient procedure, and renal ultrasound was performed annually thereafter. Patients were followed for 3 months to 10 years (median 5.6 years).

RESULTS: Vesicoureteral reflux resolved after the first, second and third endoscopic injection of dextranomer/hyaluronic acid in 2,039 (87.1%), 264 (11.3%) and 38 (1.6%) ureters, respectively. Febrile urinary tract infections developed during followup in 69 (4.6%) patients. None of the patients in the series needed reimplantation of ureters or experienced any significant complications.

CONCLUSIONS: Our results confirm the safety and efficacy of the endoscopic injection of dextranomer/hyaluronic acid in the eradication of high grade vesicoureteral reflux. We recommend this 15-minute outpatient procedure as the first line of treatment for high grade vesicoureteral reflux.

Endoscopic hyaluronic acid/dextranomer gel implantation is effective as first-line treatment of vesicoureteral reflux (VUR) in children: a single centre experience.

Häcker FM, Frech-Dörfler M, von Rotz M, Rudin C.

PURPOSE: Aim of the study was to analyse the success rate of endoscopic treatment (ET) using Dx/HA for primary vesicoureteral reflux (VUR) in children and to assess the incidence of postoperative urinary tract infections (UTIs).

METHODS: We retrospectively reviewed the charts of 103 children with VUR grade II-V who underwent ET, including children with additional urogenital malformations. Outcomes were verified with voiding cystourethrography (VCUG) and periodical urinalysis.

RESULTS: 103 children with a total of 174 ureters underwent ET. 71 patients presented with bilateral VUR. Additional malformations were: duplex ureters (19 patients), posterior urethral valves (PUV) (12 patients), diverticulum (4 patients), neurogenic bladder and ectopic orifice. VUR grade was II in 52, III in 74, IV in 41 and V in 7 ureters, respectively. Postoperative VCUG demonstrated no VUR in 140 ureters (80%) and diminished VUR grade in an additional 18 ureters (total 91%). After a second ET, VCUG was negative in 28 ureters. The overall success rate was 98%. 30 patients had had more than 3 febrile and 67 patients had had 1-3 febrile UTIs before ET. 4 out of 103 patients (3.9%) had 1 febrile UTI within the first year of follow-up. Serious complications after ET were not noted.

CONCLUSION: ET is effective at eliminating VUR in children, even in patients with high-grade reflux, as well as in patients with VUR and additional malformations. Early intervention may reduce the incidence of UTIs and prevent long-term renal damage.

Endoscopic treatment of vesicoureteral reflux in children

Ionescu S, Tîrllea S.

INTRODUCTION: Although vesicoureteral reflux (VUR) is a relatively common disease, in present there are different opinions regarding its approach by paediatric urologist, nephrologist and paediatrician. European Society for Paediatric Urology, European Association of Perinatal Medicine in collaboration with paediatric nephrologists developed--based on multicentric studies--a consensus approach for this disease. An efficient alternative is represented by endoscopic treatment.

MATERIALS AND METHODS: From January 2002 to December 2008 a number of 58 children, confirmed after mictional cistography with the diagnosis of VUR grade II - V, went endoscopic subureteral injection of dextranomer/ hyaluronic acid (Deflux). The reflux was unilateral in 21 cases and bilateral for the rest of 37. From 95 ureters, VUR was considered grade II - V in 15(15,79%), 45(47,37%), 28(29,47%) and 7(7,37%) cases. Follow-up and evaluation were based on mictional cistography and ultrasound examination.

RESULTS AND CONCLUSIONS: Reflux remitted after the first, the second or the third injection in 63(66,31%), 13(13,68%) and 1(1,05%) of the ureters.

These results confirm the fact that endoscopic subureteral injection of an adequate material confers semnificative advantages. High rate of success, absence of postoperative complications, reduced period of hospitalization sustain this kind of treatment that is indicated in all grades of reflux.

Does compliance status predict clinical status in patients undergoing endoscopic management of vesico-ureteral reflux?

Kalisvaart JF, Scherz HC, Cuda S, Kaye JD, Kirsch AJ.

Objective: Previous studies of endoscopic management of vesico-ureteral reflux (VUR) have had non-compliance rates around 50%. We examined success rates of patients non-compliant with a delayed follow up protocol after endoscopic injection for VUR.

Materials and methods: Patients undergoing Double HIT, dextranomer/hyaluronic acid copolymer endoscopic injection for VUR were enrolled in a 1-year, delayed voiding cystourethrogram (VCUG) study. All patients non-compliant with the VCUG were contacted and information on their clinical status was collected. Non-compliant patients were re-scheduled for a VCUG.

Results: 49/54 (91%) patients underwent endoscopic injection for VUR and completed the 6-week ultrasound. At 1-year 49% (24/49) were non-compliant with a VCUG; 75% (18/24) were contacted and provided clinical information. All but one patient agreed to the VCUG. Patients compliant with the 1-year VCUG showed 96% (24/25) clinical and 92% (23/25) radiologic success rates. Non-compliant patients had an 89% (16/18) clinical success rate; 5 (21%) non-compliant patients underwent VCUGs with a 100% success rate.

Conclusions: Long-term compliance remains an issue for patients treated endoscopically for VUR, but compliance does not predict clinical status as both groups have favorable clinical outcomes. The repeat VCUG is a barrier to long-term follow up as only 21% of patients underwent the study.

Is a third endoscopic treatment for vesicoureteral reflux indicated if previous attempts have failed?

Luján S, Serrano A, Domínguez C, Estornell F, García-Ibarra F.

OBJECTIVE: To evaluate the efficacy of a third endoscopic injection to correct vesicoureteral reflux (VUR).

PATIENTS AND METHODS: This was a prospective study of 605 patients, of whom 42 (6.4%), involving 44 (4%) ureteral units, received a third injection. The results were analysed regarding VUR grade and aetiology, substance used, volume, location and morphology of the mound, presence of poor prognostic factors, the urologist’s experience, and complications.

RESULTS: The treatment resolved the VUR in 38 (86.4%) units, 22 of primary cause (91.6%) and 16 with anatomical/functional abnormalities (80%) (no significant difference; P = 0.26). There was also no significant difference in success rate with regard to the substance injected (P = 0.23), the degree of VUR (P = 0.76) or the volume injected (P = 0.17). The success rate was higher (96.9%) if a less experienced urologist had performed the previous procedure versus a more experienced urologist (54.5%), and this difference was significant (P < 0.005). There was one complication (haematuria) (2.3%).

CONCLUSION: Third treatment presents a similar efficacy to first and second treatments, with a very low rate of complications, and could be indicated before open surgery.

Endoscopic treatment of vesicoureteral reflux in a paediatric surgery ambulatory unit.

Rivilla F.

BACKGROUND: Vesicoureteral reflux (VUR) is a major urological problem in children. Its incidence ranges from 1 to 3% in healthy children.

MATERIALS AND METHODS: We treated 38 children and analysed their data on age, sex, reflux grade, laterality, and results of endoscopic treatment (ET), at the different grades of reflux. All children were operated on an Ambulatory Surgery basis, studying the complications and post-operative course.

RESULTS: Thirty-eight patients were operated during a period of six years, of age between one and twelve years. VUR was bilateral in 24 (63%) patients, unilateral in 14 (34%), with a collection of a total of 62 renal units or ureters. In 29 children (76%), 46 refluxing ureters (70%) completely disappeared after just 1 ET. Nine patients (24%) with 16 ureteral units (30%) received a second ET, with the reflux disappearing successfully in seven children (12 ureteral units), changing the success rate in the disappearance of VUR, after two injections of Deflux, to 90% of the total group of ureters (58 of 62).

CONCLUSION: The endoscopic treatment of VUR has become the first choice of treatment to control the primary reflux, not just because of the good results, but because of the low post-operative morbidity and the direct relationship with the Ambulatory Surgery Unit.


Scarpa AA, Del Rossi C, Casolari E, Gatti C, Scarpa AG. 

BACKGROUND AND AIM OF THE WORK: Vesicoureteric reflux is the most common uropathy in paediatric age. It may be treated with open surgery, antibiotic therapy or endoscopic injection. The purpose of this work is to determine outcomes and experiences of parents with children who underwent endoscopic treatment for VUR.

MATERIALS AND METHODS: In a period of 5 years (from 2004 to 2009) 48 patients (20 boys and 28 girls, mean age 5,5, range 1-17) underwent endoscopic treatment for VUR. Sample included 31 cases of primary reflux (64,6%), 11 complex cases of VUR (6 duplex system, 3 duplex system with ureterocele, 2 bladder exstrophy) and 6 children (12,5%) with VUR secondary to neurogenic bladder. All procedures were performed by the same surgeon. A questionnaire assessing experiences with endoscopic treatment was administered to all families.

RESULTS: Follow-up lasted from a minimum of 6 months to 5 years. Overall cure rate was 68,7% (33/48) per child after a single injection, a second injection performed in cases with VUR recurrence raised it to 81,2% (39/48 patients). Overall cure rate per grade of VUR was 60% (3/5) for grade I, 94,1% (16/17) for grade II, 86,9% (20/23) for grade III, 64,7% (11/17) for grade IV and 85,7% (6/7) for grade V. Minimal postoperative complications were recorded: 2,1% urinary tract obstruction, 12,5% macro-haematuria, 6,2% lumbar pain, 4,1% urinary retention or strangury. The results of the survey given to families were encouraging.

CONCLUSIONS: Endoscopic treatment for VUR seems to be a feasible procedure as primary intervention.


BACKGROUND: A number of bulking agents have been used for the endoscopic correction of vesicoureteral reflux in children. We present our long-term results of endoscopic use of dextranomer/hyaluronic acid copolymer (Deflux®) for VUR treatment in children.

PATIENTS AND METHODS: Between 2004 and 2008, 21 children underwent endoscopic subureteral injection of Deflux® in 30 ureters as an outpatient procedure. Twelve children had unilateral reflux (2 duplicated systems) and nine had bilateral reflux. Median age was 5-years (6-months to 14.9-years). Six weeks postoperatively, a voiding cystourethrogram was performed. This study examined the disappearance of VUR and urinary tract infection (UTI) in the long-term follow-up as well as QoL (questionnaire of the parents).

RESULTS: No intra- or postoperative complications had been noticed. In 25 ureters (83%), VCUG showed no VUR 6-weeks postoperatively. Three children received a 2nd injection (two successful). After a median follow-up of 2.5 years, 27 ureters in 17 children (90%) had no urinary tract infection and VUR. The questionnaire results in regard to quality of life (QoL) were very good in the successfully treated children and the parents would choose the same treatment option again.

CONCLUSION: Subureteral injection of Deflux® for children with VUR is an effective treatment option with a low complication rate.

Salvage ureteral reimplantation after failure of dextranomer/hyaluronic acid injection.


PURPOSE: Ureteroneocystostomy after dextranomer/hyaluronic acid injection is reportedly associated with significantly more morbidity, and increased operative time, length of stay and postoperative obstruction. To evaluate our experience, we reviewed results of patients who underwent salvage ureteral reimplantation following failed dextranomer/hyaluronic acid injection.

MATERIALS AND METHODS: We retrospectively reviewed charts of patients at a single institution who underwent intravesical ureteral reimplantation as salvage treatment following failed dextranomer/hyaluronic acid injection. Data points such as operative time, blood loss and length of stay were compared to those of controls undergoing de novo reimplantation by the same surgeons. Statistical analysis was performed using Student’s t test and chi-square test.

RESULTS: We identified 18 patients who underwent salvage reimplant. We compared data to an equal number of controls. Mean age (4.28 years in patients vs 3.34 years in controls, p = 0.62) and mean reflux grade at reimplant (3.15 vs 3.40, p = 0.97) were comparable between the groups. Operative time (128 vs 141.9 minutes, p = 0.14), blood loss (12.9 vs 11.9 ml, p = 0.71) and length of hospital stay (1.68 vs 1.3 days, p = 0.25) were not significantly different. No statistically significant differences were found regarding any of the compared variables.

CONCLUSIONS: Ureteral reimplantation after dextranomer/hyaluronic acid injection is no more difficult than primary ureteral reimplantation regarding operative time, blood loss and length of hospital stay. These results support dextranomer/hyaluronic acid as initial operative treatment of vesicoureteral reflux when deemed appropriate and may further shift the paradigm of treatment away from prolonged medical management.

Dextranomer/hyaluronic injection for the management of vesicoureteric reflux in complete ureteral duplication: should age and gender be factors in decision making?

Bayne AP, Roth DR.

BACKGROUND AND PURPOSE: The injection of dextranomer/hyaluronic acid (DHA) has become an accepted treatment for children with vesicoureteral reflux (VUR). Complete ureteral duplication has been considered by some practitioners as counterindication for its use. We reviewed the Texas Children’s Hospital (TCH) records for children with complete ureteral duplication who were treated with DHA for VUR.

METHODS: We searched medical records at TCH for patients with a preoperative diagnosis of complete ureteral duplication who had undergone DHA injection between January 1, 2001, and October 15, 2008. Operative notes, imaging studies, and clinic notes were reviewed.

RESULTS: In this period, 28 kidneys in 24 children were treated. The average grade of reflux before injection was 3.44 (range 1-5). First injection resolution of reflux was 57% with an increase to 73% after a second injection with an average volume of DHA of 1.05 mL. New contralateral VUR developed postinjection in three (15%) children with unilateral VUR. There were no perioperative complications. The average age of the children who were treated was 41.4 months. Mean follow-up was 45.94 months. Success of DHA injection tended to be higher in girls (65%) and older children.

CONCLUSIONS: High levels of success can be achieved with DHA injection in children with complete ureteral duplication. DHA injection is more likely to be successful for older girls with VUR and complete ureteral duplication. If initial injection does not result in VUR resolution, a second injection offers an opportunity for improved success. For physicians and families who are seeking an alternative to open surgical management, DHA represents an attractive option for selected children with complete ureteral duplication.

Endoscopic Treatment of Vesicoureteral Reflux in Children with Dextranomer/Hyaluronic Acid-A Single Surgeon’s 6-Year Experience

Chen HC, Yeh CM, Chou CM.
Diagn Ther Endosc. 2010;2010. pii: 278012

Endoscopic treatment for vesicoureteral reflux (VUR) has become an established alternative to long-term antibiotic prophylaxis and ureteral reimplantation. We present the outcome of endoscopic treatment with dextranomer/hyaluronic acid copolymer (Deflux) for VUR in children by a single surgeon at our institute from October 2003 to October 2009.

We reviewed the cases of 150 patients (total 239 ureters), 56 girls (37%) and 94 boys (63%), with a mean age of 2.2 years and a median followup of 2.5 years (range 3-68 months).

Among the 239 ureters treated, 67.4% (161/239) were cured with a single injection, and a second and third injection raised the cure rate to 86.6% (207/239) and 88.3% (211/239), respectively. None had postoperative ureteral obstruction.

Endoscopic correction is a safe, effective, and minimally invasive outpatient procedure for VUR in children. It demonstrated a cure rate of approximately 92% (138/150) of patients and 88% (211/239) of the ureters by using the bulking agent, Deflux by an experienced surgeon. Even high grade VUR, complex VUR, and failed open ureteroneocystostomy do not seem to adversely affect results.

Treatment of Pediatric Vesicoureteral Reflux Using Endoscopic Injection of Hyaluronic Acid/Dextranomer Gel: Intermediate-term Experience by a Single Surgeon

Hsieh MH, Madden-Fuentes RJ, Lindsay NE, Roth DR.

Endoscopic injection of non-animal-stabilized hyaluronic acid/dextranomer gel is an increasingly recognized treatment option for vesicoureteral reflux. The procedure is minor compared with open surgery and, when successful, avoids the need for long-term antibiotic prophylaxis. We present data from 3 years of using non-animal-stabilized hyaluronic acid/dextranomer gel to treat children with vesicoureteral reflux.

Pediatric patients aged 16 years with uncomplicated primary vesicoureteral reflux were recruited for endoscopic treatment with non-animal-stabilized hyaluronic acid/dextranomer gel. A follow-up voiding cystourethrogram was scheduled at 2 weeks after treatment, and vesicoureteral reflux resolution was defined as grade 0. Repeat non-animal-stabilized hyaluronic acid/dextranomer gel treatment was offered to patients with persistent vesicoureteral reflux.

Of 178 patients treated, 12 were lost to follow-up or yet to undergo post-treatment voiding cystourethrogram. The 166 remaining patients (efficacy population) had a mean age of 4.21 years (range: 0-16), and the median reflux grade was 3 (range: 1-5). Vesicoureteral reflux was resolved in 81.9% of patients and 86.4% of ureters after initial endoscopic treatment with non-animal-stabilized hyaluronic acid/dextranomer gel. The overall reflux resolution rate for patients increased to 89.6% after a second treatment in 19 patients, and 90.2% after a third treatment in 1 patient. No adverse events were reported. Five patients underwent open ureteral reimplantation after failed endoscopic injections.

Endoscopic treatment with non-animal-stabilized hyaluronic acid/dextranomer gel is effective in a high proportion of children with vesicoureteral reflux and, in our opinion, should be considered as a first-line treatment option

Endoscopic treatment of primary grade V vesicoureteral reflux using hyaluronic acid copolymer (DX/HA).


PURPOSE: Since DX/HA was approved by the Food and Drug Administration in 2001 as an acceptable tissue-augmenting substance for subureteral injection, endoscopic treatment has become increasingly popular for treating vesicoureteral reflux (VUR). However, most paediatric urologists still continue to recommend ureteral reimplantation as the treatment of choice in the management of grade V VUR. The purpose of this study was to prospectively evaluate the effectiveness of endoscopic subureteral injection of DX/HA in the treatment of grade V reflux.

MATERIALS AND METHODS: During 2001-2009, 56 children (35 males, 21 females) with primary grade V VUR underwent endoscopic treatment using DX/HA. Their ages ranged from 4 months to 11 years. Forty-nine patients had unilateral grade V VUR, and seven had bilateral grade V (63 refluxing ureters including 17 duplex systems). Renal scarring on dimercaptosuccinic acid was observed in 39 kidneys (mild scarring 13, moderate scarring 14 and severe scarring 12). In all patients, endoscopic injection was made after inserting the needle within the wide ureteral orifice. Renal ultrasound and voiding cystourethrogram was performed 3 months after the endoscopic treatment. If VUR had not resolved, the patient was considered for further endoscopic treatment. After the VUR was resolved, children were followed with renal ultrasound at 1 year and every 2 years thereafter.

RESULTS: The VUR completely resolved after first injection of DX/HA in 33 (52.4%) ureters and downgraded to grade I VUR in 7 (11.1%) ureters. 19 (30.2%) ureters required a second injection, and 4 (6.3%) ureters required a third injection to resolve VUR. No children in this series needed reimplantation of ureters or presented with ureteral obstruction during follow-up.

CONCLUSION: Endoscopic treatment with DX/HA is effective in eradicating grade V primary reflux. This simple and minimally invasive treatment should be offered to all parents of children with grade V VUR as an alternative to ureteral reimplantation.

Endoscopic treatment of primary grade V vesicoureteral reflux using hyaluronic acid copolymer (DX/HA).

Hunziker M, Mohanan N, D'Asta F, Puri P.

PURPOSE: Since DX/HA was approved by the Food and Drug Administration in 2001 as an acceptable tissue-augmenting substance for subureteral injection, endoscopic treatment has become increasingly popular for treating vesicoureteral reflux (VUR). However, most paediatric urologists still continue to recommend ureteral reimplantation as the treatment of choice in the management of grade V VUR. The purpose of this study was to prospectively evaluate the effectiveness of endoscopic subureteral injection of DX/HA in the treatment of grade V reflux.

MATERIALS AND METHODS: During 2001-2009, 56 children (35 males, 21 females) with primary grade V VUR underwent endoscopic treatment using DX/HA. Their ages ranged from 4 months to 11 years. Forty-nine patients had unilateral grade V VUR, and seven had bilateral grade V (63 refluxing ureters including 17 duplex systems). Renal scarring on dimercaptosuccinic acid was observed in 39 kidneys (mild scarring 13, moderate scarring 14 and severe scarring 12). In all patients, endoscopic injection was made after inserting the needle within the wide ureteral orifice. Renal ultrasound and voiding cystourethrogram was performed 3 months after the endoscopic treatment. If VUR had not resolved, the patient was considered for further endoscopic treatment. After the VUR was resolved, children were followed with renal ultrasound at 1 year and every 2 years thereafter.

RESULTS: The VUR completely resolved after first injection of DX/HA in 33 (52.4%) ureters and downgraded to grade I VUR in 7 (11.1%) ureters. 19 (30.2%) ureters required a second injection, and 4 (6.3%) ureters required a third injection to resolve VUR. No children in this series needed reimplantation of ureters or presented with ureteral obstruction during follow-up.

CONCLUSION: Endoscopic treatment with DX/HA is effective in eradicating grade V primary reflux. This simple and minimally invasive treatment should be offered to all parents of children with grade V VUR as an alternative to ureteral reimplantation.

Dextranomer/Hyaluronic Acid for Pediatric Vesicoureteral Reflux: Systematic Review

OBJECTIVE: Published success rates of dextranomer/hyaluronic acid (Dx/HA) injection for pediatric vesicoureteral reflux (VUR) vary widely. Our objective of this study was to assess whether underlying patient or study factors could explain the heterogeneity in reported Dx/HA success rates.

METHODS: We searched the Cochrane Controlled Trials Register and Medline, Embase, and Scopus databases from 1990 to 2008 for reports in any language, along with a hand search of included study bibliographies. Articles were assessed and data abstracted in duplicate, and differences were resolved by consensus. Conflict of interest (COI) was determined by published disclosure. Meta-regression was performed to adjust for patient as well as study-level factors.

RESULTS: We identified 1157 reports, 89 of which were reviewed in full with 47 included in the pooled analysis. Of 7303 ureters that were injected with Dx/HA, 5633 (77%) were successfully treated according to the authors’ definition. Injection success seemed to vary primarily on the basis of the preoperative reflux grade. After adjustment for VUR grade, other factors, such as the presence or absence of COI disclosure, were not significant. Studies were markedly heterogeneous overall.

CONCLUSIONS: The overall per-ureter Dx/HA success rate was 77% after 3 months, although success rates varied widely among studies. Increased VUR grade negatively affected success rates, whereas COI, patient age, and injected Dx/HA volume were not significantly associated with treatment outcome after adjustment for VUR grade. There is a significant need for improved reporting of VUR treatments, including comparative studies of Dx/HA and other VUR treatments.

Long-term results after endoscopic subureteral injection for VUR using dextranomer/hyaluronic acid copolymer: a five years experience


BACKGROUND: A number of bulking agents have been used for the endoscopic correction of vesicoureteral reflux in children. We present the long-term results of endoscopic use of dextranomer/hyaluronic acid copolymer (Deflux) for VUR grade I-IV in children.

PATIENTS AND METHODS: Between 2004 and 2008, 21 children underwent endoscopic subureteral injection of Deflux in 30 ureters as an outpatient procedure. Twelve children had a unilateral reflux (two duplicated systems) and nine had a bilateral reflux. The median age was 5 years (6 months to 14.9 years). Six weeks postoperatively a voiding cystourethrogram (VCUG) was performed. This study examined the disappearance of VUR and urinary tract infection (UTI) as well as the quality of life (parents’ questionnaire) during long-term follow-up.

RESULTS: No intra- and postoperative complications were noticed. In 25 ureters (83%) VCUG showed no VUR 6 weeks postoperatively. In three children a second injection was done (two were successful). After a median follow-up of 2.5 years 27 ureters in 17 children (90%) had no UTI and VUR. The results of the questionnaire regarding quality of life were very good in the successfully treated children and the parents would choose the same treatment option again.

CONCLUSION: Subureteral injection of Deflux for children with VUR is an effective treatment option for VUR with a low complication rate.

The Swedish Reflux Trial in Children: V. Bladder Dysfunction
J Urol. 2010 Jul;184(1):298-304

Purpose: We investigated the prevalence and types of lower urinary tract dysfunction in children with vesicoureteral reflux grades III and IV, and related improved dilating reflux, renal damage and recurrent urinary tract infection to dysfunction.

Materials and Methods: A total of 203 children between ages 1 to less than 2 years with reflux grades III and IV were recruited into this open, randomized, controlled, multicenter study. Voiding cystourethrography and dimercapto-succinic acid scintigraphy were done at study entry and 2-year followup. Lower urinary tract function was investigated by noninvasive methods, at study entry with 4-hour voiding observation in 148 patients and at 2 years by structured questionnaire and post-void residual flow measurement in 161.

Results: At study entry 20% of patients had lower urinary tract dysfunction, characterized by high bladder capacity and increased post-void residual urine. At 2 years there was dysfunction in 34% of patients. Subdivision into groups characteristic of children after toilet training revealed that 9% had isolated overactive bladder and 24% had voiding phase dysfunction. There was a negative correlation between dysfunction at 2 years and improved dilating reflux (p = 0.002). Renal damage at study entry and followup was associated with lower urinary tract dysfunction at 2 years (p = 0.001). Recurrent urinary tract infections were seen in 33% of children with and in 20% without dysfunction (p = 0.084).

Conclusions: After toilet training a third of these children with dilating reflux had lower urinary tract dysfunction, mainly voiding phase problems. Dysfunction was associated with persistent reflux and renal damage while dysfunction at study entry did not predict the 2-year outcome.

Dextranomer beads in stabilized non-animal sodium hyaluronate gel (NASHA/Dx gel) for vesicoureteral reflux: multi-center study in Japanese patients


PURPOSE: To investigate the efficacy and safety of endoscopic treatment with the injectable gel of dextranomer beads in stabilized non-animal sodium hyaluronate (NASHA/Dx gel) administered submucosally close to the proximity of ureteral orifice, we performed the multi-center open study of Japanese patients with vesicoureteral reflux (VUR). We herein report the results of the study.

SUBJECTS AND METHODS: Patients aged > or = 1 year with grade II-IV VUR underwent endoscopic injection with NASHA/Dx gel. Post-treatment assessment was done by voiding cystourethrography (VCUG) at 3 and 12 months. Patients with VUR grade II-IV at 3 months underwent re-treatment, with VCUG assessment 3 and 12 months after retreatment. Positive response to treatment was defined as reflux grade 0 or 1.

RESULTS: The initial treatment was conducted to 116 ureters in 73 patients. The per-protocol efficacy population included 97 ureters in 71 patients. On a per-ureter basis, the positive response rate at 12 months after the last endoscopic treatment was 69.1%, compared with 62.0% on a per-patient basis. Improvement in reflux grade was shown to be statistically significant at both 3 months post initial treatment and 12 months post last treatment. Positive response rate decreased with increasing baseline reflux grade. There were only two mild adverse events (AEs) and one moderate laboratory fluctuation which were potentially relating to NASHA/Dx gel.

CONCLUSIONS: This study has shown that endoscopic injection of NASHA/Dx gel is effective and well tolerated in Japanese patients with VUR. First-line use of this treatment for VUR could potentially be considered for Japan also.

Deflux injection for the treatment of vesicoureteric reflux in children—a single centre’s experience


BACKGROUND: Vesicoureteric reflux (VUR) is a common condition that may lead to end-staged renal failure. Treatment options include long term prophylactic antibiotics or surgical intervention. Recently, endoscopic treatment by a subureteral injection of Deflux has gained popularity. Our centre has introduced this treatment modality since 2002.

METHODS: The medical records of 42 patients (15 male and 27 female) who received Deflux injections for treatment of VUR from 2002 to 2007 were reviewed. All the patients were followed up with voiding cystourethrograms at 3 months after the procedure.

RESULTS: The median age at operation was 72.59 months (range, 8 to 216 months). Unilateral involvement was found in 20 patients while 22 patients had bilateral involvement. Of the 64 ureters, VUR were grade II to V in six (9.4%), 31 (48.4%), 20 (31.2%) and seven (10.9%) patients respectively. Resolution of reflux, defined as grade 0 to I, after one injection was seen in six (100%), 20 (64.5%), and 16 (80%) ureters from grade II to IV respectively. Only one patient with grade V reflux achieved complete resolution after a single injection. Of the 21 ureters which had residual reflux, three were lost from follow up and 18 (ten grade III, two grade IV and six grade V) received a second injection and eventually 12 ureters achieved resolution. Thus, the overall success rate was 67.2% after a single injection and 85.9% after two injections. No procedure-related complications was reported.

CONCLUSION: Injections of Deflux is an effective treatment for VUR. A significant reduction in disease severity was seen in patients with grade II to IV disease after a single injection. Most patients with grade V disease needed more than one injection before achieving complete resolution. With this high success rate, we recommend the use of endoscopic Deflux injection as the first line treatment for children with vesicoureteric reflux disease.

Treatment of vesicouretheral reflux in pediatric patients

Grebeldinger S, Radojčić B, Meljnikov I, Balj S.

BACKGROUND/AIM: Vesicourethral reflux (VUR) is an inherited abnormality of the urinary tract caused by dysfunction of vesicourethral junction frequently accompanied by recurrent urinary infection. The optimal treatment method of VUR is still controversial. The aim of the study was to analyze medical charts of children with VUR with special focus on the results of endoscopic treatment with Deflux.

METHODS: This retrospective study analyzed the medical charts of all children diagnosed with VUR at the Institute for Children and Youth Health Care of Vojvodina, in five years period. The analyzed data were: age, gender, grade, bilateral or unilateral presence of reflux, distribution to the sides of the body, urinary tract infections, associated anomalies and complications of VUR, treatment methods and the success rate of endoscopic correction with Deflux. Data processing was

RESULTS: The study included 167 patients (101 females and 66 males) with 231 refluxing ureters. The patients age at diagnosis was 1 month to 18 years (mean 4.6 years). Frequencies of different grades of VUR at initial investigation were: 17%, 27%, 22%, 21% and 13% for grades I to V, respectively. VUR was unilateral in 103 patients (left in 65 and right in 38), and bilateral in 64. Urinary tract infections were present in 78.4% of patients, reflux nephropathy in 38.3%, hypertension in 3.0%, chronic renal insufficiency in 4.8%, associated anomalies in 39.5% of patients. The treatment method was recorded in 154 cases. Medically were treated 80 patients, and surgically 74. Endoscopic injection of Deflux was carried out in 59 patients. From 79 ureters treated, five had grade I reflux, 11 grade II, 23 grade III, 27 grade IV, and 13 grade V. In 46 patients Deflux injection was carried out once. A second injection was required in eight, and third injection in five patients. Reflux was absent in 42 of the treated patients (71.2%) and 15 patients (25.4%) had a decreased grade of reflux after the treatment Overall success rate was 96.6%.

CONCLUSION: Endoscopic subureteral injection of Deflux is a minimally invasive method for VUR treatment in pediatric patients.

Endoscopic treatment of vesicoureteral reflux: current practice and the need for multifactorial assessment.

Läckgren G, Stenberg A.
Ther Adv Urol. 2009 Aug;1(3):131-41

Vesicoureteral reflux (VUR) affects around 1% of all children. It carries an increased risk of febrile urinary-tract infections (UTIs) and is associated with impaired renal function. Antibiotic prophylaxis is an established approach to managing the condition, but it does not protect against UTI and encourages bacterial resistance. Ureteral re-implantation (open surgery) is a relatively traumatic procedure typically requiring hospitalization, and there is a risk of significant post-treatment complications. Endoscopic treatment with NASHA/Dx gel (Deflux®) is minimally invasive, well tolerated and provides cure rates approaching those of open surgery: 80-90% in several studies. It has also been shown to be effective in a variety of ‘complicated’ cases. Thus, endoscopic treatment is generally preferable to open surgery and long-term antibiotic prophylaxis. Non-treatment of VUR is being discussed as an alternative option, although this mainly appears suitable for children with low-grade reflux and normal kidneys. A new approach to managing VUR may be considered, with treatment decisions based not only on the grade of reflux but also on factors such as age, sex, renal scarring and bladder dysfunction. Open surgery would be reserved only for use in the 10-15% of children not responding to endoscopic treatment and those with severe ureteral anomalies.

VUR is associated with recurrent and febrile UTI as well as renal damage. The optimum approach to managing the condition remains controversial, but non-treatment appears inappropriate for most patients except those with reflux grade I II and normal kidneys. Long-term antibiotic prophylaxis should not be considered viable as it does not protect against UTI and it encourages resistance among bacteria of the urinary tract. In contrast, endoscopic treatment provides a convenient means of curing the condition through a single procedure, without the need for major surgery. The cure rates with NASHA/Dx gel approach those seen with open surgery, and the post-treatment incidence of UTI is lower. Open surgery need only be undertaken in patients failing to respond to endoscopic treatment and in those with refluxing primary megaureter. A revised approach to the management of VUR may now be considered, with patients classified according to several factors in addition to reflux grade. Further randomized, prospective studies are required to confirm the optimal management approach for VUR.

Endoscopic treatment of vesicoureteral reflux: Current status.

Läckgren G.

Vesicoureteral reflux (VUR) affects around 1% of all children. It carries an increased risk of febrile urinary tract infections (UTIs) and is associated with impaired renal function. Endoscopic treatment with NASHA/Dx gel (dextranomer microspheres in a stabilized hyaluronic acid-based gel of nonanimal origin) is minimally invasive, well tolerated and provides cure rates approaching those of open surgery: approximately 90% in several studies. It has also been shown to be effective in a variety of ‘complicated’ cases. Endoscopic treatment is therefore considered preferable to open surgery and long-term antibiotic prophylaxis. Nontreatment of VUR is being discussed as an alternative option, whereby children are treated with antibiotics only when UTIs occur.

Considering all the available evidence, however, active intervention with endoscopic treatment remains preferable. A new approach to managing VUR may nevertheless be considered, with treatment decisions based not only on the grade of reflux, but also factors such as age, sex, renal scarring, and bladder dysfunction. Open surgery would be reserved for use only in the (approximately) 10% of children not responding to endoscopic treatment, and patients with refluxing primary megaureter.

Endoscopic treatment is clearly beneficial for patients with VUR: it provides a convenient means of curing the condition through a single procedure, without the need for major surgery. The cure rates with NASHA/Dx gel approach those seen with open surgery, but with a lower incidence of posttreatment UTI. As a result, the need for open surgery is now limited (although, importantly, endoscopic treatment with NASHA/Dx gel does not preclude subsequent open surgery). The use of endoscopic treatment is consistent with minimizing chronic use of antibiotics, and minimizing children’s exposure to radiation. A revised approach to the management of VUR may now be considered, with patients classified according to several factors in addition to reflux grade. Further randomized, prospective studies are required to confirm the optimal management approach for VUR.

Endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid in children.
Cerwinka WH, Scherz HC, Kirsch AJ.
Adv Urol. 2008:513854

PURPOSE: The goal of this review is to present current indications, injectable agents, techniques, success rates, complications, and potential future applications of endoscopic treatment for vesicoureteral reflux (VUR) in children.

MATERIALS AND METHODS: The endoscopic method currently achieving one of the highest success rates is the double hydrodistention-implantation technique (HIT). This method employs dextranomer/hyaluronic acid copolymer, which has been used in pediatric urology for over 10 years and may be at present the first choice injectable agent due to its safety and efficacy.

RESULTS: While most contemporary series report cure rates of greater than 85% for primary VUR, success rates of complicated cases of VUR may be, depending on the case, significantly lower. Endoscopic treatment offers major advantages to patients while avoiding potentially complicated open surgery. As the HIT method continues to be applied to complex cases of VUR and more outcome data become available, the indication for endoscopic treatment may exceed the scope of primary VUR

CONCLUSIONS: Endoscopic injection is emerging as the treatment of choice for VUR in children.

A review of the effect of injected dextranomer/hyaluronic Acid copolymer volume on reflux correction following endoscopic injection

Dave S, Bägli DJ.
Adv Urol. 2008:579370

The current literature suggests that multiple variables affect vesicoureteric reflux (VUR) resolution rates following dextranomer/hyaluronic acid copolymer (Dx/HA) injection. This article reviews the evidence pertaining to the effect of injected Dx/HA volume on success rates following endoscopic correction.

Lack of prospective studies which use injected volume as a continuous variable coupled with a nonstandardized injection technique and endpoint hinders the ability to reach a definite conclusion.

Learning from the learning curve: factors associated with successful endoscopic correction of vesicoureteral reflux using dextranomer/hyaluronic acid copolymer.


PURPOSE: Conflicting reports exist regarding the parameters guiding successful correction of vesicoureteral reflux using dextranomer/hyaluronic acid copolymer. We performed logistic regression analysis to evaluate the effect of injected volume while adjusting for other factors potentially associated with success following dextranomer/hyaluronic acid copolymer injection.

MATERIALS AND METHODS: Between July 2003 and June 2006, 126 consecutive patients (34 boys and 92 girls) with a mean +/- SD age of 6.5 +/- 3.7 years with primary vesicoureteral reflux (196 refluxing ureters) underwent injection for febrile urinary tract infections. Success was defined as complete reflux resolution. Age, gender, laterality, preoperative vesicoureteral reflux grade, surgeon experience, dextranomer/hyaluronic acid copolymer volume, time to surgery from initial presentation and preoperative treatment for lower urinary tract symptoms were analyzed.

RESULTS: Vesicoureteral reflux grade was I to V in 7 (3.5%), 53 (27%), 91 (46.4%), 30 (15.3%) and 15 renal units (7.6%), respectively. The success rate after 1 injection was 50% by patient and 59.2% by ureter. Mean injected volume was 0.9 +/- 0.27 ml in those who had a successful injection vs 0.67 +/- 0.24 ml in those in whom injection failed (p <0.001). The success rate after 1 injection was 78.9% using 0.8 ml or greater dextranomer/hyaluronic acid copolymer compared to 31.7% with less than 0.8 ml. Multivariate analysis confirmed that higher dextranomer/hyaluronic acid copolymer volume (p = 0.001), lower preoperative grade (p = 0.013), surgeon experience (p = 0.025) and treatment for lower urinary tract symptoms (p = 0.009) were associated with successful correction of vesicoureteral reflux.

CONCLUSIONS: Our analysis strengthens the previously reported association of surgeon experience and vesicoureteral reflux grade with successful endoscopic vesicoureteral reflux correction. The data also revealed an association between injected volume and vesicoureteral reflux correction even while controlling for other variables, highlighting its importance as a true success modifier.

The treatment of vesicoureteral reflux

de Castro R, Massó P, Reis A.
Arch Esp Urol. 2008 Mar;61(2):244-7

OBJECTIVES: Vesicoureteral reflux (VUR) is a frequent pathology, with an incidence of 29/50% in children studied for urinary tract infection (UTI) and 20% of newborns with the diagnosis of prenatal hydronephrosis. Over the years, the treatment has been the subject of many meetings, many research studies, and continues being a topic under discussion. The number of candidates for surgical treatment increased with the development of minimally invasive endoscopic techniques by subureteral injection of bulking agents. We present the results of the surgical treatment of VUR between 2001 and 2006.

METHODS: We performed a retrospective study of the endoscopic treatment of VUR by subureteral injection of Dextranomer and hyaluronic acid copolymer (Copol-Dx/AH). All children undergoing treatment between July 1st 2001 and December 30th 2006 were included in this study. Treatment was performed in children with VUR grade II or greater. All patients presenting no reflux or grade I VUR on control VCUG were considered cured; stopping antibiotic prophylaxis was proposed in these cases.

RESULTS: 661 children underwent treatment, 607 endoscopic and 54 with the Cohen technique. Among children treated endoscopically, 437 where females and 170 males. VUR was bilateral in 37.7% of the cases, with grade II being the most frequent (40% in males and 57% in females). Overall success rate was 70% after first treatment, 75% after second treatment and increased to 78% after the third.

CONCLUSIONS: Subureteral injection of dextranomer and hyaluronic acid copolymer is an effective treatment in children with VUR, independently of the grade. It is a simple, safe, well tolerated procedure with low associated morbidity. Currently, it is the surgical treatment of choice in most patients with VUR.

Endoscopic treatment of complicated vesicoureteral reflux grades III-V in infants under the age of one year

Miguélez Lago C, Moreno Román J, García Mérida M, Galiano Duro E, Mieles Cerchar M, Ibáñez Cerrato F.

OBJECTIVES: Our aim is to know the results of Endoscopic Treatment (ET) in infants with recurrent pyelonephritis and high grade (G) Vesicoureteral Reflux (VUR).

METHODS: Inclusion criteria: infants 2-12 months old with G III-V VUR and at least 2 pyelonephritis, one of them during antibiotic prophylaxis (AP). N = 27 infants: 19 males (70%) and 8 females. VUR was primary in 17 (63%) and secondary in 10. VUR Grade was III in 12 ureters (U) (32%), IV 16 (42%) and V 10 (26%). Polydimethylsiloxane, Hydroxiapatite and Dextranomer/ Hyaluronic Acid (DAH) were the bulking agents employed. Results Classification: Solved: G 0-I; Improved: G II (control without AP); Persistence: III-V Open Surgery (OS) or repeated ET (1-2) was done depending on cystoscopic findings.

RESULTS: 34 ureters are available for final results; 1 G III, 2 G IV and 1 G V are waiting for a new injection. G III 11 U: 11 first and 4 second injections (1.36 Injections / ureter): Solved 9 (81.8%), Improved 1, OS 1 (9%). G IV 14 U: 14 first 3 second and 1 third injection (1.28 injections / ureter): Solved 10 (71.4%), Improved 4. No OS. G V 9 U: 9 first, 4 second and 1 third injections (1.55 injections / ureter): Solved 5 (55.6%), Improved 1, OS 3 (33.3%). Overall results: Solved: 24 U (70.58%), Improved: 6 (17.6%), OS 4 (11.8%). OS avoided 30 (88.2%): G III 91%, IV 100% and V 66.7%. Results of G III are better than G V. The only complication was 1 ureteral obstruction treated successfully with open surgery.

CONCLUSIONS: ET can be considered the first therapeutic option in infants with G III-V VUR and pyelonephritis in spite of PA, because ET has solved VUR in 70.58% and avoided OS in 88.2% with a minimally invasive procedure and low incidence of complications.

Endoscopic treatment of primary vesicoureteral reflux in childhood. Review of 989 cases in a 9 years period

Nortes Cano L, Zambudio Carmona G, Guirao Piñera MJ, Ruiz Jiménez JI.
Cir Pediatr. 2008 Jul;21(3):173-80

PURPOSE: The primary vesicoureteral reflux (PVUR) is the most common urologic pathology during childhood and affects from 1 to 3% of newborn. It causes acute pyelonephritis (APN) and renal damage in addition to hospital visits with high economic and social costs. Nowadays the endoscopic treatment (ETR) seems to be the most suitable one for the reflux, due to its lower biological cost and its good results. We report our experience in the endoscopic treatment of the primary vesicoureteral reflux (ETR) in Murcia Pediatric Hospital from 1998 to 2007.

PATIENTS AND METHODS: We present a retrospective study describing 989 patients (1498 ureters) treated by means of ETR. All patients were treated with chemoprophylaxis since the moment of the diagnosis. ETR was fulfilled by the surgeon in an ambulatory way and with Sevofluorano. Deflux, Macroplastique and Coaptite were used. Age, stade, number of ETR, material, chemoprophylaxis, ureterocistoneostomy and ETR costs were evaluated.

RESULTS: One-thousand four-hundred and ninty-eight ureteral units, corresponding to 989 patients, (51,2% males), at ages from 4 months to 21-years-old, have been treated by means of ETR. The average age was 4-years-old. Grade III reflux was the most common of all, with 801 ureters affected. Deflux was used in 777 patients, Macroplastique in 203 and Coaptite in 9. No problems in early post-operation happened and the average length was shorter than 2 hours. Forty-eight hours after, 7 patients had to be treated due to APN. Four patients showed late litiasis related to ETR. Two suffered litotomy. The 89.9% of the patients were cured at first ETR. The 11.2% needed a second ETR, with 2.12% of failure (21 patients). Six cured with the third injection and 2 needed a fourth ETR. Thirteen children were treated with ureterocistoneostomy. Radiological correction have not relation with PVUR level and does not show significant differences. Failure regarding the used material was around 9% for Deflux, 11.8% for Macroplastique and 66.6% for Coaptite. The cost of ETR was 1.400 euros, the cost of ureterocistoneostomy 4.822 euros and of the chemoprophylaxis 4.158,7 euros per year.

CONCLUSIONS: From our experience, ETR is a method as safe as surgery and with less morbidity. It is, furthermore, much more predictable than chemoprophylaxis and implies lower economical, biological and social costs than those other methods. In case of failure, ETR does not prevent any other kind of treatment. We regard ETR as a first order therapeutic gesture when dealing with PVUR.

Endoscopic Treatment of Vesicoureteral Reflux with Dextranomer/Hyaluronic Acid in Children

Wolfgang H. Cerwinka, Hal C. Scherz, and Andrew J. Kirsch
Advances in Urology Volume 2008, Article ID 513854

Purpose. The goal of this review is to present current indications, injectable agents, techniques, success rates, complications, and potential future applications of endoscopic treatment for vesicoureteral reflux (VUR) in children.

Materials and Methods. The endoscopic method currently achieving one of the highest success rates is the double hydrodistention-implantation technique (HIT). This method employs dextranomer/hyaluronic acid copolymer, which has been used in pediatric urology for over 10 years and may be at present the first choice injectable agent due to its safety and efficacy.

Results. While most contemporary series report cure rates of greater than 85% for primary VUR, success rates of complicated cases of VUR may be, depending on the case, significantly lower. Endoscopic treatment offers major advantages to patients while avoiding potentially complicated open surgery. As the HIT method continues to be applied to complex cases of VUR and more outcome data become available, the indication for endoscopic treatment may exceed the scope of primary VUR.

Conclusions. Endoscopic injection is emerging as the treatment of choice for VUR in children.

http://www.hindawi.com/journals/au/2008/513854/
Are there predictive factors for the outcome of endoscopic treatment of grade III-V vesicoureteral reflux with dextranomer/hyaluronic acid in children?


Dextranomer/hyaluronic acid (Dx/HA) copolymer has been used widely for the treatment of vesicoureteral reflux (VUR) in children since 2001. However, the factors that influence the outcome of injection therapy with Dx/HA have remained unclear. In this study, we retrospectively evaluated the outcomes in 101 consecutive children to determine the cure and to identify the factors that can impact treatment outcomes of Dx/HA injection.

Endoscopic treatment with Dx/HA was performed in 133 ureters, in 101 patients with grade III-V VUR. Of the patients, 68 (67.3%) were girls and the mean age was 6.5 years. Before and after the treatment, the presence and grades of VUR were determined by voiding cystourethograms. The patients’ age, gender, laterality, preoperative reflux grade, ureteral duplication, morphology of ureteral orifice, renal hypoplasia and experience with surgery were assessed as predictive factors related to the success rates of Dx/HA injection therapy.

The cure rates were 54.8% after the first injection, 66.9% after the second and 73.6% after the third injection. Patients with a high grade (grade IV or V), duplicated system, golf hole-shaped orifice and renal hypoplasia had significantly lower cure rates (P<0.05). Experience with the technique also correlated with the positive outcome of the procedure. New contralateral vesicoureteral reflux developed in five (7.2%) patients with unilateral VUR, and all of them resolved spontaneously during the first year of followup. No treatment-related significant complication was encountered.

Although, endoscopic treatment of VUR with Dx/HA provides a high rate of success in children with medium or high grade VUR, treatment failure may be seen in some patients. However, we showed that endoscopic treatment with Dx/HA was effective in selected patients with grade V VUR, and we emphasize the need for further large-scale studies to confirm our findings.

Endoscopic treatment with Deflux for primary vesicoureteral reflux

Escala Aguirre JM, Retamal Pinto G, Cadena González Y, López Egaña PJ, Letelier Cancino N, Zubieta Acuña R.
Actas Urol Esp. 2007 Sep;31(8):880-4

PURPOSE: Effectivety for endoscopic treatment for primary reflux has been under discussion as a single procedure. In the last 3 years our unit have been used Deflux, (dextranomer copolymer in hialuronic acid) for this pathology. The aim of this study is to analyze the results of our experience.

MATERIAL AND METHODS: Since 2002, a prospective protocol for VUR has been applied. We reviewed the last 25 cases treated with Deflux per thousand injection who had ultrasound and cistography.

RESULTS:  86% (n = 21) were females and with a mean age of 6.1 years (range 2-14) the success rate with a single injection was 73.6% (n = 28). The amount of deflux injected was irrelevant in the result. The results in the low grades reflux (I-II) reaching the 100% (n = 15). The worse result was in the double system cases with just one successful case out of 6 injected. The procedure was in outpatient bases. There were no peri-procedures complications.

CONCLUSIONS: The endoscopic treatment for VUR with Deflux, is a good alternative to medical treatment especially in single ureter with low grade. Therefore the authors recommend this technique at the time of counseling parents.

Endoscopic treatment of vesicoureteric reflux with Deflux: a Canadian experience.

Guerra LA, Khanna P, Levasseur M, Pike JG, Leonard MP.

INTRODUCTION: Vesicoureteric reflux is a common problem encountered in urological practice. Traditionally, if medical management with low-dose antibiotic prophylaxis failed, the only alternative was ureteroneocystostomy. Recently, promising results with subureteric injection of dextranomer/hyaluronic acid copolymer (Deflux) have renewed interest in the endoscopic treatment of vesicoureteric reflux (VUR).

OBJECTIVE: We reviewed the outcome of the subtrigonal injection (STING) procedure with Deflux at a single pediatric hospital and included the rate of VUR resolution and complications.

METHODS: An Institutional Review Board approved the retrospective review of all cases of STING performed with Deflux at the Children’s Hospital of Eastern Ontario, from April 2003 to October 2005. We used voiding cystourethrogram (VCUG) or radionuclide cystogram (RNC) for diagnosis of VUR. The most common indications for surgery were breakthrough infection, progression of renal scars and parental preference. A subureteral or intra-ureteral injection, at the 6 o’clock position, delivered the material to support the ureter and correct VUR.

RESULTS: We reviewed the cases of 64 patients, 47 girls (73%) and 17 boys (27%), with a mean age of 6 years (range 1-17 yr) and a mean follow-up of 8 months (range 2-23 mo). A total of 26 patients (41%) had bilateral VUR and 38 (59%) had unilateral VUR (90 renal units were treated). Overall cure rate was 79.7% (51/64) per child and 74% (67/90) per renal unit. Among the 64 patients treated, 62.5% (40/64) were cured with a single injection, and a second and third injection raised the cure rate to 78% (50/64) and 79.7% (51/64), respectively. Contralateral low-grade de novo VUR was present in 7.9% (3/38) of the 38 unilateral cases. Postoperatively, de novo hydronephrosis developed in 3.3% (3/90) of the ureters, in 2 patients.

CONCLUSIONS: The endoscopic treatment of VUR with Deflux is a feasible outpatient procedure, requires minimal operating room time and is associated with low morbidity. In our study, it demonstrated a cure rate of 80% of patients and 74% of renal units. Dysfunctional voiding and neurogenic bladder (NB) do not seem to adversely affect results. STING should be considered for failed open reimplants, because it is much less morbid than redo reimplants. Further experience with the material and increased use of intraureteral injection may improve our cure rates.

McMann LP, Scherz HC and Kirsch AJ.
J Urol. 2007 Jan;177(1):316-20;

PURPOSE: We compared injected volume of dextranomer/hyaluronic acid with sonographic volumes obtained 2 weeks to 36 months postoperatively to evaluate the amount of volume retention with time and to correlate volume retention with voiding cystourethrogram results.

MATERIALS AND METHODS: We retrospectively reviewed sonographic volume measurements of dextranomer/hyaluronic acid implants in children at 2 weeks to 36 months postoperatively. Hydronephrosis and percentage of dextranomer/hyaluronic acid retained at each interval were recorded. Average change in volume at each interval was used to compare volume retention with time. The fraction of dextranomer/hyaluronic acid retained was compared to voiding cystourethrogram at 3 months.

RESULTS: No patient had new or worsened hydronephrosis. Volumetric data were available for 296, 150, 42, 23 and 20 ureters at 2, 3, 6 and 12 weeks, and 24 to 36 months postoperatively, respectively. Percentage of dextranomer/hyaluronic acid retained was 79% at 2, 74% at 3, 70% at 6 and 78% at 12 weeks, and 65% at 24 to 36 months (p >0.05). While there was no significant difference in mean volume retained between cures (74%) and treatment failures (67%), the 94% cure rate with mega-implants (greater than anticipated volume retention) was higher than that with micro-implants (75%) or nonvisualized implants (70%).

CONCLUSIONS: After the initial volume reduction at 2 weeks dextranomer/hyaluronic acid implants remained durable with insignificant volume reduction for up to 36 months postoperatively. Although mega-implants were associated with high cure rates and may justify elimination of postoperative voiding cystourethrography.

New contralateral vesicoureteral reflux after endoscopic correction of unilateral reflux—is routine contralateral injection indicated at initial treatment?


PURPOSE: As more and more pediatric urologists use endoscopic therapy as a primary treatment option for vesicoureteral reflux, newer indications for this procedure are being considered. Recently it was suggested that contralateral nonrefluxing ureters should be treated prophylactically in patients undergoing unilateral endoscopic correction of vesicoureteral reflux. We analyzed the incidence of newly diagnosed contralateral reflux after endoscopic correction of unilateral reflux and identified possible risk factors for its development.

MATERIALS AND METHODS: Between 1996 and 2004, 662 patients underwent endoscopic correction of unilateral grades II to V vesicoureteral reflux. Of the ureters 97% had grades III to V reflux. The tissue augmenting substance used for endoscopic treatment was polytetrafluoroethylene from 1996 to 2000 and dextranomer/hyaluronic acid from 2001 to 2004. There were 203 males (30.7%) and 459 females (69.3%) with an age at endoscopic treatment of 2 months to 11 years. Voiding cystourethograms performed 3 months after endoscopic treatment of unilateral vesicoureteral reflux were analyzed in all patients to document newly diagnosed contralateral reflux.

RESULTS: A total of 67 children (10.1%), including 18 boys and 49 girls, showed new contralateral reflux on voiding cystourethrogram after endoscopic correction of unilateral reflux. Contralateral VUR was grades I to IV in 16 (23.9%), 17 (25.4%), 27 (40.3%) and 7 patients (10.5%), respectively. There was no correlation between the severity of ipsilateral reflux and the development of contralateral reflux. Patient age and gender did not influence the development of new contralateral reflux.

CONCLUSIONS: The low incidence and lower grade of newly diagnosed contralateral vesicoureteral reflux after endoscopic correction of unilateral reflux does not support prophylactic treatment of nonrefluxing contralateral ureters.

The role of endoscopic treatment in the management of grade V primary vesicoureteral reflux.

Menezes MN, Puri P.
Eur Urol. 2007 Nov;52(5):1505-9

OBJECTIVES: Although endoscopic treatment provides a high rate of success in children with grades II-IV vesicoureteral reflux (VUR), its role in the management of grade V reflux has been questioned. In this study we reviewed our 21-yr experience of endoscopic treatment in children with grade V primary VUR

METHODS: We retrospectively reviewed the medical records of 132 children who underwent endoscopic treatment for primary grade V reflux from 1984 to 2004. VUR was unilateral in 39 patients and bilateral in 34, and 59 patients had ipsilateral grade V reflux with a lower grade of VUR on the contralateral side. Endoscopic treatment was performed in a total of 166 grade V ureters; polytetrafluoroethylene was used from 1984 to 2000 and dextranomer/hyaluronic acid from 2001 to 2004. Median follow-up was 12.2 yr and mean follow-up was 13.4 yr.

RESULTS: VUR was completely resolved after first injection in 88 (53%) ureters and downgraded to grade I or II in 26 (15.7%). VUR resolved after a second and third injection in 36 (21.7%) and 10 (6%) of ureters, respectively. Endoscopic treatment failed to correct VUR in 6 (3.6%) ureters, requiring ureteral reimplantation in 5 and nephrectomy in 1. Thirteen patients developed urinary tract infections during the follow-up period, and on investigation 9 ureters (5.4%) had recurrence of VUR. No injection or morbidity related to tissue-augmenting substances was noted in any patient

CONCLUSION: Endoscopic treatment should be the first-line of treatment in management of grade V vesicoureteral reflux.

Endoscopic treatment of moderate and high grade vesicoureteral reflux in infants using dextranomer/hyaluronic acid.

Puri P, Mohanan N, Menezes M, Colhoun E.

PURPOSE: Renal parenchymal injury in vesicoureteral reflux occurs early, in most patients before age 3 years. It is generally believed that early prevention of urinary tract infections may decrease the amount of renal parenchymal damage. Endoscopic treatment for vesicoureteral reflux has become an established alternative to long-term antibiotic prophylaxis and ureteral reimplantation. We prospectively evaluated the effectiveness and safety of dextranomer/hyaluronic acid copolymer for high grade vesicoureteral reflux in infants.

MATERIALS AND METHODS: A total of 276 infants, including 124 boys and 152 girls, with a median age of 7 months (range 2 to 12) underwent endoscopic treatment for vesicoureteral reflux with dextranomer/hyaluronic acid. Reflux was detected in 225 infants following investigation for urinary tract infection, in 46 following screening for sibling vesicoureteral reflux and in 5 for prenatally diagnosed hydronephrosis. Vesicoureteral reflux was unilateral in 85 infants and bilateral in 191 (467 refluxing ureters). Reflux was grade II in 14 ureters, grade III in 188, grade IV in 248 and grade V in 17. Dimercapto-succinic acid scan was performed in 250 infants and it demonstrated renal scarring in 43 (17.2%).

RESULTS: Vesicoureteral reflux completely resolved in 373 ureters (79.9%) after a single injection of dextranomer/hyaluronic acid and it was downgraded to grade I in 21 (4.4%). Of the ureters 65 (14%) required a second injection and 8 (1.7%) required a third injection to resolve reflux. All patients underwent endoscopic treatment on an outpatient basis. There were no complications except in 1 patient, who was readmitted to the hospital the next day with acute pyelonephritis. Three children had urinary tract infections during followup, of whom 1 was found to have recurrent reflux on investigation.

CONCLUSIONS: Endoscopic treatment with dextranomer/hyaluronic acid is safe and highly effective for eradicating high grade vesicoureteral reflux in infants. Early intervention in infants with high grade reflux may change its natural history and protect against renal scarring.

The deflux procedure reduces the incidence of urinary tract infections in patients with vesicoureteral reflux.


PURPOSE: The aim of this study was to review the experience of a single institution with the Deflux (Q-Med Scandinavia; Uppsala, Sweden) procedure and assess its effectiveness in reducing the incidence of urinary tract infections (UTIs) in children with vesicoureteric reflux (VUR).

MATERIALS AND METHODS: After institutional review board approval, the charts of 100 patients with VUR, who presented between June 2003 and June 2005, were prospectively reviewed. Data collected included: demographics, the number of preoperative and postoperative UTIs, a radiologic grade of VUR on a voiding cystourethrogram (VCUG) and the presence of VUR on a radionuclide VCUG 3 months after the procedure. Patients were continued on oral antibiotics until urine culture at 3 months was negative and no reflux was demonstrated on VCUG. The student’s t test was used for data analysis.

RESULTS: The mean age was 3.8 +/- 0.3 years, and 76% were girls. From 155 ureters treated, 10 had Grade I reflux, 42 Grade II, 76 Grade III, 25 Grade IV, and 2 Grade V. A second injection was required in 22 ureters (14.2%). The overall success rate of the procedure (Grade 0 reflux at 3 months) was 77.4% after the first injection and 83.9% after a second injection. The success rate per grade was: 100% for Grade I, 88.1% for Grade II, 86.8% for Grade III, 64% for Grade IV, and 50% for Grade V. The mean follow-up was 446 +/- 20 days. The mean volume injected/ureter was 0.6 +/- 0.03 mL. Thirteen (13) patients had UTIs after the procedure, compared to 75 before. There was a 5-fold reduction in the incidence of UTIs/year, from a mean of 0.68 +/- 0.09 pre- to 0.12 +/- 0.04 postinjection (P = 0.001). The majority of UTIs were caused by Escherichia coli (74% pre- and 82% postinjection).

CONCLUSIONS: We conclude that the Deflux procedure is effective not only in eliminating VUR on radiologic studies, but also in reducing the incidence of UTIs and antibiotic use in children with VUR.

Multivariate analysis of factors predicting success with dextranomer/hyaluronic acid injection for vesicoureteral reflux.

Yucel S, Gupta A, Snodgrass W.


PURPOSE: Factors influencing outcomes of dextranomer/hyaluronic acid injection for vesicoureteral reflux remain poorly defined. We performed multivariate analysis of the experience of 1 surgeon (WS).

MATERIALS AND METHODS: The study group contained 168 patients and 259 refluxing units. Goal of injection was coaptation of the orifice with creation of a volcanic mound. Outcomes were determined by cystography obtained 12 weeks following injection. Intraoperative photographs of mounds were independently reviewed by 2 authors (WS, SY) without knowledge of results, and classified as “satisfactory” or “other.” Univariate and multivariate logistic regression analysis was done evaluating influence of gender, age, voiding dysfunction, reflux grade, unilateral vs bilateral reflux, ureteral duplication, orifice laterality, subureteral vs intranureteral injection, volume injected and mound appearance.

RESULTS: A single injection resolved reflux in 70% of patients and 78% of ureters. Additional injection resulted in overall success in 82% of patients and 86% of ureters. Multivariate analysis demonstrated that reflux grade, volume of dextranomer/hyaluronic acid injected and mound appearance correlated with outcomes. A satisfactory mound was achieved in 81% of ureters, of which 87% no longer refluxed.

CONCLUSIONS: The ability to create a satisfactory mound was the most important factor determining success of dextranomer/hyaluronic acid injection. Increasing reflux grade was associated with a decreased likelihood of achieving a volcanic mound, and increasing volume injected suggested difficulty in creating a mound.

Endoscopic treatment for high grade vesicoureteral reflux in infants.


PURPOSE: Minimally invasive endoscopic treatment for vesicoureteral reflux has become an established alternative to long-term antibiotic prophylaxis and surgical intervention in children. We determined the long-term efficacy and safety of this treatment for high grade reflux in infants.

MATERIALS AND METHODS: We retrospectively reviewed the medical records of 411 consecutive infants who underwent endoscopic treatment of grade III to V vesicoureteral reflux between June 1985 and October 2004. A total of 29 patients (7%) were excluded from study because they were lost to followup or the medical records were incomplete. Of the remaining 382 infants, including 203 males, 274 had bilateral and 108 had unilateral vesicoureteral reflux. This represented 642 high grade reflexing units with grade III to V disease in 232, 339 and 71, respectively. A dimercapto-succinic acid scan performed in 312 infants revealed renal scarring in 88 (28%). The tissue augmenting substance used for endoscopic injection was polytetrafluoroethylene and dextranomer/hyaluronic acid copolymer in 432 and 210 ureters, respectively. Endoscopic treatment was done at a median age of 7 months (range 2 months to 1 year). Median followup in these patients was 7 years (range 6 months to 20 years).

RESULTS: Complete resolution of vesicoureteral reflux after a single injection occurred in 443 ureters (69%), including 73% with dextranomer/hyaluronic acid copolymer and 65% with polytetrafluoroethylene. Of the 642 ureters 127 (20%) required more than 1 injection to correct vesicoureteral reflux. In 60 ureters vesicoureteral reflux was downgraded to grade I or II and no further treatment was given, while 12 ureters that failed to respond to endoscopic treatment required open surgical intervention. Only 1 ureter required reimplantation to treat vesicoureteral obstruction.

CONCLUSIONS: Endoscopic correction is a safe, effective, minimally invasive outpatient procedure for high grade vesicoureteral reflux in infants. Early correction of vesicoureteral reflux may provide protection from reflux associated renal damage and prolonged antibiotic use.

Endoscopic Therapy for Vesicoureteral Reflux: A Meta-Analysis. I. Reflux Resolution and Urinary Tract Infection


PURPOSE: Current American Urological Association treatment guidelines for vesicoureteral reflux do not include any recommendations pertaining to endoscopic therapy (subureteral injection of bulking agent). We performed a meta-analysis of the existing literature pertaining to endoscopic treatment to allow comparison with reports of open surgical correction.

MATERIALS AND METHODS: We searched all peer reviewed articles published through 2003 pertaining to endoscopic treatment of vesicoureteral reflux. A total of 63 articles were double reviewed by 9 pediatric urologists, and the data were tabulated on data retrieval sheets. A mixed effects logistic regression model was used to obtain overall estimates of event probabilities (eg reflux resolution, ureteral obstruction) together with their 95% confidence intervals. Individual study estimates were obtained with overall estimate and observation characteristics using empirical Bayes calculations. Differences between or among specific groups were assessed using the F-test.

RESULTS: The database included 5,527 patients and 8,101 renal units. Following 1 treatment the reflux resolution rate (by ureter) for grades I and II reflux was 78.5%, grade III 72%, grade IV 63% and grade V 51%. If the first injection was unsuccessful, the second treatment had a success rate of 68%, and the third treatment 34%. The aggregate success rate with 1 or more injections was 85%. The success rate was significantly lower for duplicated (50%) vs single systems (73%), and neuropathic (62%) vs normal bladders (74%). The success rate was similar among children and adults. Following a previous failed open reimplantation endoscopic treatment was successful in 65% of patients. After endoscopic treatment with variable followup pyelonephritis developed in 0.75% of patients and cystitis in 6%. There were few reports of renal scarring following treatment.

CONCLUSIONS: Endoscopic treatment provides a high rate of success in children with reflux that decreases with increasing grade, although multiple treatments may be necessary. Future reports of endoscopic therapy should include rates of urinary tract infection and renal scarring.

Dextranomer/hyaluronic acid for vesicoureteral reflux: success rates after initial treatment failure.


PURPOSE: Following Food and Drug Administration approval of Dx/HA there has been increasing interest in the endoscopic management of VUR. Currently, there are few data regarding the success rates of repeat injection. We recently published our success rates for a group of children following initial Dx/HA treatment, and herein report the success rate of a subgroup of children undergoing repeat injection.

MATERIALS AND METHODS: We queried our database to identify all children undergoing a second Dx/HA injection for the treatment of VUR at our institution. VUR grades as determined by VCUG before and after the second treatment were specifically noted. Success was defined as the complete absence of VUR by VCUG.

RESULTS: A total of 42 children (37 girls and 5 boys) with a mean age of 5 years underwent a second Dx/HA treatment for VUR after initial treatment failure. Complete followup was available for 39 patients (53 ureters). Before the second injection 14 patients had bilateral and 25 had unilateral VUR, with a mean grade of 2.2. A second Dx/HA injection resolved VUR in 35 of 39 patients (90%) and in 47 of 53 ureters (89%). A second injection resolved reflux in 7 of 8 ureters (88%) with grade I, 24 of 26 (92%) with grade II and 16 of 19 (84%) with grade III VUR.

CONCLUSIONS: A second Dx/HA injection for the treatment of VUR persisting after initial endoscopic treatment has a high success rate. This information is useful when counseling parents after initial treatment failure.

Injection therapy: advancing the treatment of vesicoureteral reflux

Kirsch A, Hensle T, Scherz H, Koyle M.

Vesicoureteral reflux (VUR) is a common urological anomaly among children, and is usually diagnosed following the occurrence of urinary tract infection(s). Treatment options are observation (non-treatment), antibiotic prophylaxis, ureteral reimplantation (open surgery) and endoscopic injection. The need for treatment of VUR is considered in light of the likelihood of spontaneous resolution and practical issues regarding management of the condition. The available evidence relating to the treatment options is reviewed alongside our experience in the clinic.

Endoscopic injection, particularly when non-animal stabilized hyaluronic acid/dextranomer (NASHA/Dx) gel is used, has an excellent safety profile and fewer disadvantages than either open surgery or antibiotic prophylaxis. Post-treatment success rates approaching those with open surgery have been reported with NASHA/Dx gel.

We conclude that endoscopic injection may be routinely recommended as a first-line treatment for VUR following a short period of antibiotic treatment.

Endoscopic treatment of reflux: management pros and cons

Lorenzo AJ, Khoury AE.
Curr Opin Urol. 2006 Jul;16(4):299-304

PURPOSE OF REVIEW: The goal of this review is to contrast the issues in favor of and against the use of endoscopic injection therapy in an attempt to highlight the current state of flux and draw attention to areas that merit further research.

RECENT FINDINGS: Current publications have mostly addressed the expanding use of endoscopic injection therapy for vesicoureteral reflux treatment, generally reporting short-term success rates and endpoints. This growing body of literature is presented in the context of perceived benefits vs. disadvantages in comparison with other available treatment modalities.

SUMMARY: The management of vesicoureteral reflux has changed dramatically in the past decade, mostly because of the increasing acceptance of endoscopic injection therapy as an adequate, minimally invasive, and effective form of therapy. Recent advances in the composition of injectable materials have allowed for easier placement with a perceived favorable safety profile. In particular, dextranomer/hyaluronic acid has become the injectable material of choice, with quick acceptance and widespread use soon after its introduction in different countries. As we critically evaluate the evolving treatment options, the presented literature helps draw attention to some of the challenges we face and the need for long-term and carefully planned prospective studies to support our interventions.

Subureteral dextranomer/hyaluronic acid injection as first line treatment in the management of high grade vesicoureteral reflux.

Puri P, Pirker M, Mohanan N, Dawrant M, Dass L, Colhoun E.

PURPOSE: Endoscopic correction of vesicoureteral reflux has become an established alternative to long-term antibiotic prophylaxis and ureteral reimplantation. A number of tissue augmenting substances have been used for the endoscopic correction of vesicoureteral reflux. We prospectively evaluated the effectiveness of dextranomer/hyaluronic acid copolymer (Deflux) as first line treatment for high grade vesicoureteral reflux.

MATERIALS AND METHODS: Between 2001 and 2004, 692 children with a median age of 2.1 years (3 months to 13.7 years) with high grade vesicoureteral reflux underwent endoscopic subureteral injection of Deflux soon after the diagnosis of vesicoureteral reflux was made on the initial voiding cystourethrogram. Vesicoureteral reflux was unilateral in 283 patients and bilateral in 409. Of the 1,101 ureters vesicoureteral reflux was grade II to V in 35 (3.2%), 580 (52.7%), 457 (41.5%) and 29 (2.6%), respectively. The procedure was performed on an outpatient basis. Followup ultrasound and voiding cystourethrogram were performed 3 months after the procedure, and renal and bladder ultrasound was done annually.

RESULTS: Reflux resolved after first, second and third endoscopic Deflux injections in 952 (86.5%), 130 (11.8%) and 19 ureters (1.7%), respectively. Followup ultrasound revealed no evidence of delayed vesicoureteral junction obstruction. Of the patients 18 (2.6%) had urinary tract infection during followup after successful vesicoureteral reflux correction.

CONCLUSIONS: Endoscopic subureteral injection of Deflux is excellent first line treatment in children with high grade vesicoureteral reflux. This 15-minute outpatient procedure is safe and simple to perform, and it can be easily repeated in failed cases.

Single center experience with endoscopic management of vesicoureteral reflux in children.
Routh JC, Vandersteen DR, Pfefferle H, Wolpert JJ, Reinberg Y.
J Urol. 2006 May;175(5):1889-92;

PURPOSE: Dx/HA copolymer was approved by the Food and Drug Administration in 2001 for the treatment of VUR in children. Published results have varied widely, prompting us to report our single center experience with 300 consecutive patients.

MATERIALS AND METHODS: All patients undergoing Dx/HA injection (300 children, median age 5.4 years) at our institution were eligible for this study. We examined several parameters to determine which variables influence the success of Dx/HA injection, including preoperative reflux grade, bladder diverticula, neurogenic bladder, ureteral duplication, perioperative urinary tract infection, dysfunctional voiding, laterality of reflux and amount of Dx/HA injected.

RESULTS: A total of 225 patients (75%) underwent postoperative studies, and, thus, were eligible for study inclusion. Reflux was cured in 144 patients (64%) and improved in 44 (20%). A total of 20 patients had ureteral duplication anomalies. Cure rates in this subgroup were significantly decreased compared to nonduplicated cases (40% vs 66%). Injection in low grade (I to II) reflux was significantly more successful than in high grade (III to IV) reflux (72% vs 54%). A total of 10 patients (8.3%) with unilateral reflux had development of de novo contralateral reflux. Of the patients who failed initial injection 10 (4%) underwent repeat injection, of whom 5 (50%) were cured after the second injection. Two patients (0.9%) had development of temporary ureteral obstruction.

CONCLUSIONS: We report a large short-term single center experience with endoscopically injected Dx/HA. Although our cure rate of 64% was less than published rates for open surgery, the minimal morbidity and low complication rate of endoscopic treatment make it an attractive first line therapy for patients with VUR. Longer followup is required to better evaluate this technique.

Treatment of vesicoureteral reflux in children using stabilized non-animal hyaluronic acid/dextranomer gel (NASHA/OX): A long-term observational study

Stenberg A, Läckgren G.

Objective: Vesicoureteral reflux (VUR) can be treated with open surgery, antibiotic therapy or endoscopic injection. A goal in children is to reduce the incidence of febrile urinary tract infections (UTIs). The present long-term observational study investigated outcomes and experiences of endoscopic treatment with stabilized non-animal hyaluronic acid/dextranomer, NASHATM/Dx.

Patients and methods: Children treated with NASHA/Dx between 1993 and 1998 were sent a questionnaire by mail in 2005. Patients included in the study (n = 231) had VUR grade III-V before treatment and grade 0-11 afterwards. Patients completed 21 questions, with parental assistance if required. The questionnaire assessed clinical outcome, and the attitudes of both patients and their parents to their experiences of treatment with NASHA/Dx gel. Patients reporting UTI after treatment were contacted and their records analyzed.

Results: Questionnaires were completed by 179 eligible patients. Most (72%) received a single injection of NASHA/Dx gel, and all experienced febrile UTI before treatment. After treatment, 45 patients (25%) experienced UTI; 25 of these reported fever. Patient records and telephone interviews revealed no evidence of febrile UTI in 19 cases; febrile UTI was confirmed in six cases, an incidence of 3.4%. When asked about the worst aspect of VUR treatment, 9% indicated treatment with NASHA/Dx compared to 19% for medication and 72% for voiding cystourethrogram (VCUG); parent-rated responses were 19%, 24% and 57%, respectively.

Conclusions: Endoscopic treatment with NASHA/Dx gel was associated with a low number of febrile UTIs following treatment, viewed positively and considered less bothersome than medication or VCUG. These findings support this treatment as a primary intervention for VUR.

Treatment of Vesicoureteral Reflux Using Endoscopic Injection of Nonanimal Stabilized Hyaluronic Acid/Dextranomer Gel: Initial Experience in Pediatric Patients by a Single Surgeon

Yu RN, Roth DR.

OBJECTIVE. Endoscopic injection of nonanimal stabilized hyaluronic acid/dextranomer gel is an increasingly recognized treatment option for vesicoureteral reflux. The procedure is minor compared with open surgery and, when successful, avoids the need for long-term antibiotic prophylaxis. We present data from our first 18 months using nonanimal stabilized hyaluronic acid/dextranomer gel to treat children with vesicoureteral reflux.

PATIENTS AND METHODS. Pediatric patients aged 15 years with uncomplicated primary vesicoureteral reflux were recruited for endoscopic treatment with nonanimal stabilized hyaluronic acid/dextranomer gel. A follow-up voiding cystourethrogram was scheduled at 2 weeks after treatment, and vesicoureteral reflux resolution was defined as grade 0. Repeat nonanimal stabilized hyaluronic acid/dextranomer gel treatment was offered to patients with persistent vesicoureteral reflux.

RESULTS. Of 120 patients treated, 6 were lost to follow-up, and 7 were yet to undergo posttreatment voiding cystourethrogram. The 107 remaining patients (efficacy population) had a mean age of 4.1 years (range: 0.5-15.0), and the median reflux grade was 2 (range: 1-5). The mean time to follow-up voiding cystourethrogram was 9.7 weeks (range: 2-26). Vesicoureteral reflux was resolved in 82.2% of patients and 86.9% of ureters after initial endoscopic treatment with nonanimal stabilized hyaluronic acid/dextranomer gel. The overall reflux resolution rate for patients increased to 90.7% after a second treatment in 14 patients. Two patients reported postoperative flank pain, although this was mild and transient in nature. No other adverse events were reported. No patients underwent open surgery for vesicoureteral reflux.

Endoscopic treatment with nonanimal stabilized hyaluronic acid/dextranomer gel is effective in a high proportion of children with vesicoureteral reflux and, in our opinion, may be considered as a first-line treatment option.

Endoscopic correction of vesicoureteric reflux--our thirteen years’ experience.

Zivkovic D, Varga J.

AIM OF THE STUDY: We review our thirteen years’ experience with the endoscopic treatment of primary vesicoureteric reflux (VUR).

METHODS: We retrospectively reviewed the charts of 81 patients with primary vesicoureteric reflux who were treated endoscopically. The study included 61 girls and 20 boys aged 3 - 15 years. Twenty-eight patients had unilateral reflux, and 53 patients had bilateral reflux. Endoscopic correction with Teflon paste was done in 64 patients, and endoscopic treatment with Deflux was done in 17 patients. A total of 134 ureters were treated.

RESULTS AND CONCLUSION: Reflux was corrected in 87 ureters (64.9 %) after the first injection. The second injection resolved reflux in an additional 20 ureters (14.9 %). Reimplantation was necessary in 4 patients (4.9 %). Overall success rate of the endoscopic treatment was 85.0 %.

Reflex was completely absent in 79.8 % of the treated patients, and 5.2 % of the patients had a decreased grade of reflux after the procedure. Treatment was unsuccessful in 3.0 % of the patients. In seven patients spontaneous resolution of the persisting reflux occurred.

Endoscopic correction should be performed in all patients with grade two, three and four reflux. Grade one reflux should be treated conservatively, and grade five reflux should be treated surgically. Since Deflux is a biodegradable material, most of the patients should be treated bilaterally, even if they have only grade one reflux. Endoscopic correction of primary vesicoureteric reflux is an easy, simple, fast and safe procedure that, in most cases, prevents regurgitation of urine from the bladder to the upper parts of the urinary system.

Endoscopic injection of dextranomer/hyaluronic acid for vesico-ureteral reflux--preliminary results

Bar-Yosef Y, Binyamini J, Sofer M, Matzkin H, Ben-Chaim J.
Harefuah. 2005 Sep;144(9):613-5, 679, 678.

BACKGROUND: Endoscopic injection is a minimal invasive treatment for vesico-ureteral reflux, an alternative for prophylactic antibiotics or open surgery. Concerns of safety were raised regarding traditional injectable materials used in the past. The recently introduced dextranomer/hyaluronic acid is a new biocompatible substance. Its safety and efficacy has been investigated and demonstrated. OBJECTIVES: To report our preliminary results with the endoscopic injection of dextranomer/hyaluronic acid.

METHODS: Twenty nine pediatric patients of mean age 58 months (range 6-144) underwent endoscopic treatment. A total of 42 refluxing ureteral units were treated. Reflux grade was 2, 3, and 4 in 10, 24, and 8, respectively. The procedure was performed under general anesthesia, using a 9.5FR pediatric cystoscope and a semi-rigid needle. The substance was injected submucosally at the 6-o’clock position of the ureteral orifice. A mean of 0.87 ml of the substance was injected (range: 0.6-1.2). In the latter part of the series we injected a minimum of 1 ml for each ureter. During follow-up, ultrasonography and a voiding cystography were performed after 1 and 3 months respectively.

RESULTS: Vesico-ureteral reflux resolved in 32/42 (76%) of the ureters. The rate of success was 10/10 (100%), 19/24 (79%) and 4/8 (50%) in reflux grades 2, 3, and 4, respectively. De-novo contralateral reflux was noted in 5 patients. A single complication occurred: acute venous bleeding originating in the injection site, which was managed endoscopically.

CONCLUSIONS: Endoscopic injection of dextranomer/hyaluronic acid is a safe and effective treatment. We recommend the injection of 1 ml, the entire volume available for each ureter.

Endoscopic treatment of vesicoureteral reflux.

Harrell WB, Snow BW

PURPOSE OF REVIEW: The treatment of vesicoureteral reflux in children has seen a shift from invasive surgery to endoscopic management in recent years. Early studies demonstrate favorable outcomes but do not reach the success of surgery. Subspecialization also may play a role in the successful outcomes of all reflux management. This review focuses on the recent literature regarding endoscopic treatment of reflux and the role of subspecialization in treatment of children.

RECENT FINDINGS: Dextranomer/hyaluronic acid copolymer has emerged as the favored bulking agent since its Food and Drug Administration approval in the United States. Although success is defined somewhat differently than surgery, overall success rates range from 82-89% with initial injection of dextranomer/hyaluronic acid. The outpatient nature of the procedure and its high success rate have led to a shift in treatment strategies especially in Europe, where endoscopic management is often considered first-line therapy. Extravesical reimplants can be performed on an outpatient basis safely. Subspecialization leads to improved outcomes with no difference in cost.

SUMMARY: Endoscopic treatment of reflux is promising, but long-term results are not available to ascertain the efficacy of treatment into adulthood. Open surgery remains the gold standard.

Subureteral injection of Deflux for correction of reflux: analysis of factors predicting success.
Lavelle MT, Conlin MJ, Skoog SJ.

OBJECTIVES: To review, prospectively, our experience with endoscopic Deflux injection and evaluate the volume injected, grade, endoscopic appearance after injection, and presence or absence of voiding dysfunction as predictors of success. Subureteral injection of dextranomer/hyaluronic acid copolymer (Deflux) has become an effective treatment of vesicoureteral reflux.

METHODS: A total of 52 patients (50 females and 2 males; 80 ureters) were treated with a single subureteral injection of Deflux. The mean patient age was 7.6 years (range 14 months to 22 years). The presence or absence of voiding dysfunction was evaluated with a preoperative questionnaire and patient history. The volume of Deflux injected in each ureter was recorded. The endoscopic appearance after injection was recorded as “volcano” or “other.” Success was defined as no reflux on postoperative voiding cystourethrography.

RESULTS: The success rate by grade of reflux in individual ureters was 82%, 84%, 78%, and 73% for grade 1, 2, 3, and 4 vesicoureteral reflux, respectively. No statistically significant difference was found in the cure rate by grade (P = 0.76). The overall cure rate by ureter was 80% and by patient was 71%. New contralateral reflux developed in 12.5% of patients. No statistically significant difference was found in the cure rate with respect to the volume injected or the presence or absence of voiding dysfunction. The ureteral cure rate with volcano and alternate morphology was 87% and 53%, respectively (P = 0.004).

CONCLUSIONS: Mound morphology was the only statistically significant predictor of a successful outcome, with an associated cure rate of 87%. Concomitant voiding dysfunction did not have an adverse effect on the cure rate. In our experience, no statistically significant difference was found in the cure rate for grades 1 through 4 vesicoureteral reflux after a single injection of Deflux.

Initial results of Deflux injection for vesicoureteral reflux: the Dallas experience

Elmore JM, Ewalt DH and Snodgrass WT. Program and abstracts of the American Urological Association 98th Annual Meeting; April 26-May 1, 2003; Chicago, Illinois. Abstract 487.

Elmore and colleagues presented their results of the recently FDA-approved agent Deflux. Thirty-five patients completed follow-up evaluation, with voiding cystourethrogram at 3 months, including 54 infected ureters. Results were analyzed following a single Deflux injection. Preoperatively, there was a wide range of grade of reflux, the majority being Society for Fetal Urology (SFU) Grade 2 or 3.

Overall, the authors reported that 63% (22 out of 35 ureters) of the patients had a successful outcome. With respect to number of ureters successfully managed, there was a 70% success rate (38 out of 54), which seems to be the recurring number in most of the literature following a single injection of Deflux.

The interesting finding in this study was that de novo contralateral reflux was identified in 2 of 35 patients. This is a commonly described finding with unilateral open ureteral reimplantation. The cited risk of contralateral reflux typically ranges between 7% and 20%, depending on how many previous voiding cystourethromgrams had been performed that demonstrated unilateral vesicoureteral reflux only. In addition, 1 patient of the 35 developed asymptomatic ureteral obstruction. This is the first patient described in any United States series and stresses the importance of follow-up radiograph evaluation of the upper tracts following ureteral surgery.
Minimally invasive treatment of vesicoureteral reflux with endoscopic injection of dextranomer/hyaluronic acid copolymer: the Children’s Hospitals of Atlanta experience.
Kirsch AJ, Perez-Brayfield MR, Scherz HC.

PURPOSE: Emerging data demonstrate that injection of dextranomer/hyaluronic acid (Dx/HA) copolymer (Deflux, Q-Med Scandinavia, Uppsala, Sweden) is a safe and effective treatment for most patients with vesicoureteral reflux (VUR). We sought to determine the efficacy and factors predictive of outcome in patients treated with Dx/HA.

MATERIALS AND METHODS: A total of 180 children 7 months to 15 years old (mean age 4.6 years) underwent subureteral injection of Dx/HA for VUR between October 2001 and February 2003. Dx/HA was injected submucosally within or beneath the intramural ureter. The average volume of injected material was measured for each ureter. At 2 weeks and 3 months postoperatively bladder ultrasounds were performed to measure the volume of Dx/HA (mm3) in the trigone using the volume of an ellipsoid (V = 4/3pir(1)r(2)r(3)). Renal sonography was performed to determine whether hydronephrosis was present. At 3 months fluoroscopic voiding cystourethrograms were used to evaluate for the presence of VUR.

RESULTS: A total of 292 ureters in 180 children were treated (112 bilateral cases). There were 141 girls and 39 boys. Mean maximum grade per patient was 2.6 (out of 5). Average injected volume per ureter was 0.83 +/- 0.03 ml (830 +/- 30 mm3). At 2 weeks the average measured volume was 663 +/- 70 mm3 (18% decrease from original volume), which decreased an additional 1% by 3 months to 656 +/- 103 mm3. There were no cases of hydronephrosis at up to 12 months postoperatively. There were 134 patients with at least 3 months of followup. After 1 treatment 72% (96) were cured (grade 0), while 55% of the failures (21 of 38) were improved. New contralateral VUR was seen in 6 patients (4.5%) who had neither a history of VUR nor an abnormal appearing ureteral orifice at cystoscopy. A lower success rate (60%) was seen in the first 20 patients compared with the last 20 patients (80%). The cure rate per grade was 90% for grade I, 82% for grade II, 73% for grade III and 65% for grade IV reflux. Local migration of material caudal to the ureteral orifice was seen in 61% of patients (11 of 18) at the time of reinjection of Dx/HA after initial treatment failure. There was no statistically significant difference in age, grade, volume injected, bilaterality or gender when successes were compared with failures.

CONCLUSIONS: The majority of patients (72%) undergoing minimally invasive treatment of VUR with Dx/HA are cured after 1 treatment. Contralateral treatment of nonrefluxing ureters should be considered in view of the increased incidence of new reflux (4.5%) and absence of morbidity with Dx/HA injection. There is a definite learning curve with injection therapy. The location of injected material and experience with the technique appear to correlate with the outcome of the procedure.

Endoscopic treatment of vesicoureteral reflux and urinary incontinence in children.

Läckgren G, Lottmann H, Hensle T, Stenburg A
AUA Update Series 2003; Volume XXII, Lesson 37: 294-9

Recent developments in the materials available for endoscopic injection, and data to support their use in pediatric patients, warrant a reappraisal of management strategies for both VUR and UL. Utilization of endoscopic injection as primary treatment could be a means of reducing the number of children referred for open surgery. Surgery could then become a second-line option for patients in whom endoscopic treatment is unsuccessful. It would provide greater patient convenience, more rapid recovery, and potential for fewer complications than open surgery.

Literature Review

Studies in both animals and humans have found PTFE particles in distant organs. Silicone like PTFE particles, carry a risk of distant migration. There is also a likely risk of phagocytosis. Silicone is also non-biodegradable so will remain permanently within the body. In vitro and in vivo studies have shown that bovine collagen provokes invasion of human fibroblasts, forming a matrix for endogenous collagen deposition and neovascularization. Allergic reactions may occur following injection even in patients with a negative skin testing result. The autologous nature of chondrocytes means that this method of treatment is non-immunogenic. However, the procedure involved in acquiring the cells is arduous, involving a complicated harvesting method.

Unlike PTFE and silicone, DxlHA copolymer is biodegradable. In addition, the lack of free dextran removes any potential for anaphylactic reactions. Fibroblast migration and collagen ingrowth between the dextranomer microspheres result in infiltration of the implant by endogenous connective tissue, thus, stabilizing its volume as the hyaluronate component is degraded the first 12 weeks after implantation. Long-term (three year) persistence of implanted dextranomer microspheres has been demonstrated in animal studies with no granuloma formation or calcification. These results are borne out in clinical practice: implanted DxlHA copolymer has been observed to remain effective after five years in patients with VUR. The larger particle size of DxlHA copolymer, compared with PTFE and silicone, prevents migration from the injection site to distant organs.
Treatment of vesicoureteral reflux by endoscopic injection of dextranomer/hyaluronic Acid copolymer: preliminary results.

Puri P, Chertin B, Velayudham M, Dass L, Colhoun E.

PURPOSE: Endoscopic subureteral injection of tissue augmenting substances has become an established alternative to long-term antibiotic prophylaxis and open surgery for the management of vesicoureteral reflux (VUR) in children. Recently, dextranomer/hyaluronic acid copolymer (Deflux, Q-Med AB, Uppsala, Sweden) a biodegradable injectable material has been reported to be a promising alternative to other tissue augmenting substances. However, the experience with dextranomer/hyaluronic acid copolymer is limited. We prospectively evaluate the effectiveness of dextranomer/hyaluronic acid copolymer in the endoscopic treatment of VUR.

MATERIALS AND METHODS: A total of 32 males and 81 females with a median age of 1 year (range 3 months to 10 years) underwent endoscopic correction of primary VUR with dextranomer/hyaluronic acid copolymer. Reflux was unilateral in 58 cases and bilateral in 54, affecting 166 ureters. Reflux was grades II to V in 7 (4.2%) cases, 91 (54.8%), 63 (38%) and 5 (3%), respectively. All patients underwent endoscopic correction as a day procedure and have been followed for 3 months to 1 year.

RESULTS: The reflux was corrected in 143 (86%) of the 166 ureters after a single injection, and resolved after a second and third injection in 22 (13%) and 1 (1%) ureter, respectively. No untoward effects were seen in any of these patients with the use of dextranomer/hyaluronic acid copolymer as an injectable material.

CONCLUSIONS: Dextranomer/hyaluronic acid copolymer is an effective tissue augmenting substance in the endoscopic treatment of all grades of VUR.

Influence of voiding dysfunction on the outcome of endoscopic treatment for vesicoureteral reflux.


PURPOSE: Some patients with vesicoureteral reflux also experience voiding dysfunction. Dextranomer/hyaluronic acid copolymer (Deflux, Q-MED AB, Uppsala, Sweden) is an effective endoscopic treatment for vesicoureteral reflux. In an open label study we investigated the effect of voiding dysfunction on the efficacy of endoscopic treatment with dextranomer/hyaluronic acid copolymer in patients with vesicoureteral reflux.

MATERIALS AND METHODS: A total of 320 children 3 to 11 years old with grade II to IV vesicoureteral reflux confirmed by voiding cystourethrography underwent endoscopic treatment with dextranomer/hyaluronic acid copolymer. Of the patients 50 were re-treated with dextranomer/hyaluronic acid copolymer because of persistent reflux (grade II or greater). The first implantation technique was recorded on videotape. Voiding cystourethrography and micturition details were recorded at the 3 to 6-month followup visit and compared with baseline measurements.

RESULTS: At baseline 13 patients had known voiding dysfunction and 18 were misdiagnosed as not having voiding dysfunction. Of the 50 patients who required re-treatment, the initial implant was correctly positioned in 45 according to the videotape. Endoscopic observation at the time of re-treatment revealed no evidence of the implant in 15 patients. The implant was displaced in 27 patients and remained correctly positioned in 3. A total of 27 patients had voiding dysfunction, the majority of whom had urgency and frequency incontinence, had not received any anticholinergic therapy and had a displaced implant.

CONCLUSIONS: Uncontrolled voiding dysfunction contributed to endoscopic treatment failure with dextranomer/hyaluronic acid copolymer in our series. Therefore, we suggest that patients with voiding dysfunction be treated at least 6 months before endoscopic therapy with anticholinergics and/or micturition rehabilitation.
Dextranomer/Hyaluronic Acid Copolymer Implantation for Vesico-Ureteral Reflux: A Randomized Comparison with Antibiotic Prophylaxis

Cappoza N, Caoine P

Objectives: Dextranomer/hyaluronic acid (Dx/HA) copolymer has favorable properties for endoscopic treatment of vesico-ureteral reflux (VUR). This open, randomized study was performed to compare the efficacy and safety of Dx/HA copolymer with antibiotic prophylaxis in children with VUR.

Methods: Children >1 year of age with VUR grade II to IV (confirmed by voiding cysto-urethrogram) received endoscopic treatment with Dx/HA copolymer (n = 40) or 12 months of antibiotic prophylaxis (n = 21). Patients in the latter group with reflux grade ≥ II at month 3 received a second implantation. All patients were reassessed by voiding cysto-urethrogram at month 12. Scintigraphy and ultrasound were performed to investigate renal status.

Results: At month 12, 69% of patients in the Dx/HA copolymer group had reflux grade ≤ I bilaterally, compared with 38% in the antibiotic group (P = .029). Of patients with reflux grade ≤ I at month 3, 89% showed a sustained response at month 12. One serious adverse event was reported in the antibiotic prophylaxis group, but this was not attributed to study treatment. No other adverse events occurred.

Conclusions: Endoscopic treatment with Dx/HA copolymer was more effective than antibiotic prophylaxis in alleviating childhood VUR, and there were no safety concerns with either treatment.

Endoscopic treatment of vesico-ureteral reflux: twelve years’ experience.

Capozza N, Patricolo M, Lais A, Matarazzo E, Caione P.

INTRODUCTION: Over the past 12 years, endoscopic treatment of vesico-ureteral reflux (VUR) has gained in popularity and has proved successful in a high percentage of cases. With improvements in injectable materials and more experience with the technique, the indications for endoscopic treatment have broadened. In the present paper we report our experience on 679 patients and 953 refluxing ureters, treated over the past 12 years.

MATERIALS AND METHODS: Reflux ranged from grade II to grade IV. In the first 14 cases Teflon was injected. After 1989, bovine dermal collagen was used in 442 children and, more recently, the Deflux system, a nonallergenic, biodegradable dextranomer in sodium hyaluronan in 223 children. All patients were clinically investigated for voiding dysfunctions and all completed a 1-year follow-up.

RESULTS: After 1 or 2 injections the 1-year cystogram showed no VUR in 686 ureters (72%). In grade II, III and IV success rates were, respectively, 83, 69 and 41%. Complications were minimal (1%).

CONCLUSIONS: Our results confirm endoscopic treatment of VUR is a valid alternative to long-term antibiotic prophylaxis and to open surgery in selected patients. The treatment often failed because of injected material displacement possibly due to voiding dysfunction. The short hospital stay, absence of significant postoperative complications, safety of the available injectable materials and high success rate suggest that endoscopic treatment should be offered to all children with grade II and III VUR, whereas it is questionable in patients with grade IV VUR. In patients with voiding dysfunction, appropriate therapy and voiding rehabilitation should precede treatment of VUR.

Long-term followup of children treated with dextranomer/hyaluronic acid copolymer for vesicoureteral reflux.

Läckgren G, Wåhlin N, Sköldenberg E, Stenberg A.

PURPOSE: Dextranomer/hyaluronic acid copolymer is a novel substance that has favorable properties for endoscopic treatment of vesicoureteral reflux. We assess the long-term efficacy and safety of this treatment of children.

MATERIALS AND METHODS: Children 1 to 15 years old with grade III or greater vesicoureteral reflux were eligible for enrollment in our study. All patients received endoscopic treatment with dextranomer/hyaluronic acid copolymer and were scheduled to have a voiding cystourethrogram 3 and 12 months after implantation. Children with reflux grade III or greater after treatment received up to 2 more implantations, and those with persistent reflux were referred for open surgery. In some cases long-term clinical followup was accompanied by a late voiding cystourethrogram.

RESULTS: A total of 228 patients received endoscopic treatment. The efficacy population was comprised of 221 children, including 67 who received 2 and 8 who received 3 implantations. Endoscopic treatment was performed without complications in all cases. Patients were followed clinically for 2 to 7.5 years (mean 5). On the last voiding cystourethrogram 68% of patients had a positive response (grade I or less) and 81% had no dilating reflux. The corresponding results for treated ureters were 75% and 85%, respectively. Only 27 (12%) patients were referred for open surgery. A late voiding cystourethrogram was performed in 49 patients 2 to 5 years after treatment. Of the ureters free of reflux (grade 0) 3 to 12 months after treatment 96% remained free of dilating reflux. Adverse events occurred in association with implantation in only 2% of patients, although urinary tract infection subsequently developed in 8%.

CONCLUSIONS: Endoscopic treatment with dextranomer/hyaluronic acid copolymer was effective and well tolerated in children with vesicoureteral reflux. Long-term followup indicated that there was no deterioration in patients responding positively to treatment.

Endoscopic treatment of children with vesico-ureteric reflux.
Läckgren G, Wåhlin N, Stenberg A.

Endoscopic subureteric injection of tissue-augmenting substances has become an alternative to long-term antibiotic prophylaxis and open surgery in the treatment of children with vesico-ureteric reflux. Successful elimination of reflux in about 80% of patients after a single injection (and in 90% after a repeat) has been achieved using the foreign-body non-degradable substances Teflon and silicone. Few patients have required open surgery and recurrence of reflux after initial successful treatment has occurred in only 5-10%. Concern has arisen, however, about possible distant migration and granuloma formation after injection of particulate plastic materials. Cross-linked bovine collagen is a biodegradable alternative substance, but with a lower response rate of 60% after the first treatment and a recurrence rate of 10-20%. Dextranomer in sodium hyaluronan is a new biological substance with microparticles with a response rate of 69% after the first injection. Biological substances have caused few complications.

Present literature on injection treatment unfortunately focuses on elimination of reflux, with little attention to subsequent frequency of pyelonephritis or to the long-term development of the kidneys. Furthermore, there are no controlled, randomized studies with subureteric injection as one of the treatment alternatives. Thus, although having the advantage of being a minimally invasive procedure that can be performed on an outpatient basis, this technique needs to be tested in a large prospective study with the long-term renal outcome as the main end-point.

A new bioimplant for the endoscopic treatment of vesicoureteral reflux: experimental and short term clinical results.

Stenberg A and Lackgren G.

We investigated the safety and clinical effects of a new biocompatible, biodegradable treatment, the Deflux system (dextranomer microspheres in sodium hyaluronan solution), for the endoscopic treatment of grades III and IV vesicoureteral reflux.

In a clinical study we investigated the implantation technique and the short (3 months) and long-term (1 year) effects of Deflux implantation in 75 children (101 ureters) with grades III and IV vesicoureteral reflux. We report data from up to 3 months of followup. Implant volumes of 0.4 to 1.0 ml. were sufficient to create distinct boluses and crescent-like ureteral orifices. Although viscous, due to its viscoelastic properties the substance was easy to inject in a well controlled manner.

In preclinical safety studies in pigs histopathological examination demonstrated excellent tolerance. Two weeks after submucous implantation in the pig bladder early ingrowth of fibroblasts and recently generated collagen were noted at the implantation sites. At 14 weeks of followup this ingrowth had slightly increased. Long-term followup in rats showed that the volume of subcutaneous implants was slightly reduced (23%) 1 year after implantation. At cystography 3 months later reflux had resolved in 68% of implants, was reduced to grades I and II in 13% of implants and was unchanged in 19% of treated ureters (grades III and IV reflux). No signs of ureteral obstruction or adverse reactions were noted. Results from 1 year of followup will be reported later.

Our results indicate that the dextranomer microspheres act as micro-carriers that promote ingrowth of fibroblasts and generate new collagen. We conclude that the Deflux system may represent a new, safe, simple alternative to endoscopic treatment of vesicoureteral reflux in children.

VUR - Comparison of Therapies

Does the modified STING method increase the success rate in the management of moderate or high-grade reflux?


PURPOSE: To evaluate the efficacy of subureteral injection types in patients with middle- to high-grade vesicoureteral reflux (VUR).

MATERIALS AND METHODS: Between June 1999 and September 2010, subureteral dextranomer was applied at our clinic to 149 patients (214 refluxing ureters) with grades II, III, and IV VUR. Group 1 consisted of 54 patients (80 ureters), and group 2 consisted of 95 patients (134 ureters). The standard subureteric transurethral injection (STING) procedure was applied to group 1, and the modified STING procedure was applied to group 2. A second and if needed a third injection was applied to unsuccessfully treated patients. The mean follow-up period was 2 years. Patients were evaluated by cystography and ultrasonography in the third month of follow-up.

RESULTS: VUR was resolved completely after a single injection in 54/80 ureters (67.5%) in group 1 and in 94/134 ureters (70.1%) in group 2. Overall successes after a second or a third injection were 61/80 (76.2%) and 111/134 (82.8%), respectively. There was a statistically significant difference between the groups only for grade IV reflux following multiple injections (p<0.05).

CONCLUSIONS: Endoscopic treatment of VUR is a recommended treatment because it is minimally invasive, efficient, and repeatable. Our study confirmed that a modified STING procedure can be an alternative treatment to the standard technique.

Randomized clinical trial comparing endoscopic treatment with dextranomer hyaluronic acid copolymer and Cohen’s ureteral reimplantation for vesicoureteral reflux: long-term results.


PURPOSE: To compare efficacy of Cohen’s ureteral reimplantation and endoscopic treatment with Dx/HA in patients with primary VUR grades II, III and IV.

METHODS: From April 2002 to June 2004, patients over 1 year old with VUR grade I, II, III or IV were included. Patients were randomized into two groups: endoscopic treatment (ET) or ureteral reimplantation (UR). In the ET group, an ultrasonography study was performed 24 h and 1 month after surgery, and two voiding cystourethrographies at 3 and 6 months post treatment. In the UR group, an ultrasonography study was done 7 days and 1 month after surgery and a micturial cystography 6 months post surgery. A postoperative nuclear direct cystogram was performed 5 years later in both groups.

RESULTS: A total of 41 patients were included in this study: in ET 22 patients with 35 refluxing ureters and in UR 19 patients with 32 refluxing ureters. The VUR grades in ET were: 16 grade II, 16 grade III and 3 grade IV; and in UR: 15 grade II, 12 grade III and 5 grade IV. VUR was resolved in 91% (32/35) of ET (28% of ureters needed a second injection), and in 100% of UR group. Five years after the procedure, VUR was still resolved in 30/32 of ET and 32/32 of UR.

CONCLUSION: Short- and long-term follow up shows that multiple endoscopic treatment of VUR grades II, III and IV with Dx/HA is as effective as ureteral reimplantation.
A comparison of calcium hydroxyapatite and dextranomer/hyaluronic Acid for the endoscopic treatment of vesicoureteral reflux.


Purpose. Minimal data exists comparing dextranomer/hyaluronic acid (Dx/HA) and calcium hydroxyapatite (CaHA) for the endoscopic treatment of VUR in the hands of a single user.

Materials and Methods. We reviewed our consecutive single-user case series of 27 children (42 ureters) receiving endoscopic treatment with CaHA and 21 children (33 ureters) who received Dx/HA injection. Children receiving CaHA injections were divided into two groups of 13 and 14 patients (Coaptite I and II) to assess the learning curve effects. Postoperatively, RBUS and VCUG were performed. Multiple regression analysis was performed to assess statistical significance of success rates.

Results. The total CaHA group had a per-ureter success rate (Grade 0) of 52% after one injection. When separated into two cohorts, the single injection per-ureter success rates were 43% for Coaptite I and 62% for Coaptite II. In contrast, the Dx/HA series had a single injection per-ureter success rate (Grade 0) of 78%.

Conclusions. Our consecutive case experience shows improved results for Dx/HA compared to CaHA, though the learning curve effects and evolution of injection technique likely played a role in the improved outcomes in the Dx/HA cohort. A randomized controlled multicenter trial would provide the most accurate data comparing these two agents.

Stredele RJ1, Dietz HG, Stehr M.

OBJECTIVE: To determine the long-term effect in children of endoscopic treatment of vesicoureteral reflux (VUR) using different bulking agents. VUR status, recurrence of urinary tract infection (UTI), and recurrence of febrile UTI were evaluated as endpoints.

METHODS: From 1993 to 2005, we injected 229 refluxive ureters (VUR grade II-IV) in 135 children. Mean age of the children was 55.7 months. We used collagen in 98 (years 1993-2000), polydimethylsiloxane in 32 (years 1999-2000), and dextranomer/hyaluronic acid copolymer (Dx/HA) in 99 ureters (years 2000-2005). Of the 135 children, 127 underwent a voiding cystourethrogram (VCUG) (radiologic or nuclid) 3 months after the first injection, and 88 children a second VCUG (nuclid) after 37 months (mean) postoperatively. Clinically, patients were monitored for non-febrile or febrile UTI. Data were collected and analyzed retrospectively by chart review.

RESULTS: After first injection with collagen, polydimethylsiloxane and Dx/HA, 52%, 55% and 81.5% of the children were without VUR, respectively. Repeated injections were successful in only 21% (collagen) to 42% (Dx/HA). Of the 88 with a second VCUG, 48.5% of the initially reflux-free children developed relapse VUR after collagen, 45.5% after polydimethylsiloxane and 21.5% after Dx/HA injection. Clinically, there was a significant difference in postoperative UTI occurrence in favor of the Dx/HA group.

CONCLUSIONS: Clinically and radiologically, Dx/HA exhibited the best results, giving better protection against UTIs and a better VUR cure rate. There was still a risk of VUR recurrence in successfully treated children after 3 years of follow up.

Does the diameter of dextranomer microspheres affect the success in endoscopic treatment of vesicoureteral reflux?


OBJECTIVE: To evaluate whether the polymer microsphere diameter affects the success rate in the endoscopic treatment of vesicoureteral reflux.

METHODS: In our consecutive series, 56 patients underwent subureteral injection with Dexell and 60 patients were treated with Deflux. Patients were evaluated with pediatric lower urinary tract scoring system, uroflowmetry, and a residual urine volume and voiding diary at the time of injection and control. Patients with grade V reflux, duplex systems, paraureteral diverticula, or refractory lower urinary tract symptoms were excluded. The numbers of renal units with grade II-III vesicoureteral reflux were 78 and 73 in the first (Deflux) and second (Dexell) groups, respectively. The numbers of renal units with grade IV reflux were 24 and 17 in the first and second groups, respectively. The resolution rate was determined by voiding cystourethrogram at the third postoperative month. Postoperative febrile urinary tract infections and de novo scars in dimercaptosuccinic acid were noted. Groups were compared by the $\chi^2$ test.

RESULTS: Mean follow-up time and mean age of the children were not significantly different. The number of nondilating and dilating renal units was not significantly different. Resolution rates were similar between the groups (79.5 and 78%, respectively). There was no significant difference in terms of resolution rates when dilating and nondilating urinary systems were separately analyzed. The average volumes used per renal unit were 0.9 and 1.6 mL in the first and second groups, respectively ($P < .005$). Postoperative febrile urinary tract infection and de novo scar formation rates were similar.

CONCLUSION: The diameter of dextranomer microsphere does not affect the short-term success rate in endoscopic treatment of vesicoureteral reflux. Multicentric, randomized and prospective studies are required for long-term clinical results.

Does the diameter of dextranomer microspheres affect the success in endoscopic treatment of vesicoureteral reflux?

Aydogdu O, Ozcan C, Burgu B, Mermerkeya M, Soygur T.

OBJECTIVE: To evaluate whether the polymer microsphere diameter affects the success rate in the endoscopic treatment of vesicoureteral reflux.

METHODS: In our consecutive series, 56 patients underwent subureteral injection with Dexell and 60 patients were treated with Deflux. Patients were evaluated with pediatric lower urinary tract scoring system, uroflowmetry, and a residual urine volume and voiding diary at the time of injection and control. Patients with grade V reflux, duplex systems, paraureteral diverticula, or refractory lower urinary tract symptoms were excluded. The numbers of renal units with grade II-III vesicoureteral reflux were 78 and 73 in the first (Deflux) and second (Dexell) groups, respectively. The numbers of renal units with grade IV reflux were 24 and 17 in the first and second groups, respectively. The resolution rate was determined by voiding cystourethrogram at the third postoperative month. Postoperative febrile urinary tract infections and de novo scars in dimercaptosuccinic acid were noted. Groups were compared by the χ2 test.

RESULTS: Mean follow-up time and mean age of the children were not significantly different. The number of nondilating and dilating renal units was not significantly different. Resolution rates were similar between the groups (79.5 and 78%, respectively). There was no significant difference in terms of resolution rates when dilating and nondilating urinary systems were separately analyzed. The average volumes used per renal unit were 0.9 and 1.6 mL in the first and second groups, respectively (P < .005). Postoperative febrile urinary tract infection and de novo scar formation rates were similar.

CONCLUSION: The diameter of dextranomer microsphere does not affect the short-term success rate in endoscopic treatment of vesicoureteral reflux. Multicentric, randomized and prospective studies are required for long-term clinical results.

Parental experiences and preferences regarding the treatment of vesicoureteral reflux.


OBJECTIVE: Dilating vesicoureteral reflux (VUR) has been linked to febrile urinary tract infection (UTI) and renal scarring. It is unclear, however, whether children with reflux should be treated surgically or medically, or just kept under close surveillance with prompt treatment of UTIs. This lack of evidence makes parental preferences a crucial factor in the choice of therapy. The Swedish Reflux Trial was set up to compare the three treatment alternatives prospectively. This paper focuses on parental experience and satisfaction after completing the trial.

MATERIAL AND METHODS: A group of 203 children aged 12-24 months with reflux grade III or IV were randomly assigned to antibiotic prophylaxis (n = 69), surveillance (n = 68) or endoscopic injection treatment (n = 66) and followed closely for 2 years. Afterwards, the families were interviewed by an investigator not involved in the care of the children about their experience of the study.

RESULTS: Parental satisfaction with the treatment given was high, with 53% scoring 5 and 35% 4 on a five-grade scale, with no difference between the three groups (p = 0.5). Recurrence of febrile UTI or new kidney scarring did not influence parental satisfaction. Even though the satisfaction was high regardless of therapy, parents of children in the prophylaxis group more often than others would have chosen another treatment if given a choice.

CONCLUSIONS: As far as parental satisfaction and preferences are concerned, antibiotic prophylaxis, surveillance and injection treatment are equivalent treatment strategies in children with VUR.

Surgical treatment of vesicourethral reflux in paediatric population

Aguiar A, Cardoso A, Prisco R, Cruz ME.
Acta Med Port. 2011 Dec;24 Suppl 2:59-64

BACKGROUND: Early diagnosis and adequate follow-up are fundamental principals for the treatment of vesicourethral reflux in children. The treatment options in these cases remain an individual choice based on multiple factors.

OBJECTIVE: To determine and compare the effectiveness of two different surgical techniques (endoscopic and conventional) used on vesicourethral reflux treatment.

METHODOLOGY: Cohort study, based on the clinical files of children and adolescents submitted to surgical treatment of vesicourethral reflux, between the 1st January of 2000 and 30th April 2006. The study included one year period of follow-up. Multiple variables with a presumable influence on the therapeutic option were analysed. In cases of surgical treatment, effectiveness and safety of the surgical technique where determined.

RESULTS: Included 46 children and adolescents, in a total of 68 refluxive units. Thirty seven of all renal units, where submitted to endoscopic treatment: the success rate with one injection of Deflux® was 62% (IC 95% [0.46; 0.78]), increasing for 78% (IC 95% [0.65; 0.91]) when the second injection was performed. Thirty seven renal units were submitted to open surgery: Cohen procedure in 21 patients and nefrourethrectomy in two cases. Excluding the nefrourethrectomy, the classical surgery had a success rate of 97% (IC 95% [0.91; 1]). The reason between probabilities of success, considering endoscopic surgery vs. conventional surgery was 0.8 (IC 95% [0.68; 0.97]). Registered thirteen complications, most of them (85%) after conventional surgery.

Discussion: The high complication rates determined for conventional surgery could justify the frequent option for endoscopic surgery in small centres, despite its lower success rates.

CONCLUSION: This study confirms that this therapeutic option establishes a good commitment between prophylaxis safety and classical surgery effectiveness.
The Swedish reflux trial: review of a randomized, controlled trial in children with dilating vesicoureteral reflux


OBJECTIVES: To evaluate prophylaxis and endoscopic injection for children with dilating vesicoureteral reflux (VUR) compared to surveillance, regarding urinary tract infection (UTI) recurrence, new renal damage, VUR outcome, and impact of lower urinary tract (LUT) dysfunction on these outcomes.

PATIENTS AND METHODS: 203 children (128 girls and 75 boys), aged 1 to <2 years, with VUR grade III or IV were randomized to antibiotic prophylaxis (n = 69), endoscopic injection (n = 66) or surveillance (n = 68). Voiding cystourethrography, dimercaptosuccinic acid scintigraphy and optional LUT function assessment were performed before randomization and after 2 years.

RESULTS: There were 67 febrile UTIs in 42 girls and 8 in 7 boys (p = 0.0001). In girls, recurrence rate was 19% on prophylaxis, 23% with endoscopic treatment and 57% on surveillance (p = 0.0002). In boys, there was no difference between treatment groups. New damage was seen in 13 girls: 8 on surveillance, 5 in the endoscopic group and none on prophylaxis (p = 0.0155), and in 2 boys. In 13 children with no or non-dilating VUR after 1 injection, dilating VUR reappeared at the 2-year follow up. LUT dysfunction at follow up was associated with persistence of VUR.

CONCLUSION: In girls, prophylaxis reduced the rate of UTI recurrence and new renal damage, and endoscopic injection the rate of UTI recurrence. Boys did not benefit from active treatment.

Endoscopic bulking materials for the treatment of vesicoureteral reflux: a review of our 20 years of experience and review of the literature.


Purpose. We reviewed our 20 years of experience and the current literature regarding the long-term outcome of endoscopic treatment of vesicoureteric reflux (VUR) using the different tissue bulking substances with a special emphasis on the long-term efficacy.

Material and Methods. Our own experience and the current literature on the long-term results after endoscopic treatment using various bulking agents were reviewed.

Results. Short-term data following endoscopic treatment of VUR is similar to the various substances and comparable in the majority of the series to the success rate following open surgery. Recently, a relatively high recurrence rate was noticed especially with the use of dextranomer hyaluronic acid (Dx/HA) as a tissue augmenting material which raises the need for further search for alternative substances.

Conclusions. Many materials has been used for the endoscopic correction of VUR; although PTFE gave long-term high success rate 6 Advances in Urology its use was abandoned due to the fear of particle migration. All other substances did not show high success rate and are no longer in use. The currently worldwide used material for endoscopic treatment is Dx/HA. Despite short-term reported high success rate, there is a significant shortage of evidence-based literature on the long-term followup after endoscopic correction of reflux utilizing Dx/HA, the FDA approved tissue augmenting substance for endoscopic correction of VUR. However, the scanty data available clearly demonstrated that there are a high recurrence rate during the long-term followup after Dx/HA injection, which requires close observation beyond the routine protocols and correct parental counseling upon the endoscopic correction.

Clinical efficacy and safety in children with vesicoureteral reflux of a single injection of two different bulking agents-polydimethylsiloxane (Macroplastique) or dextranomer / hyaluronic acid copolymer (Deflux): a short-term prospective comparative study.


PURPOSE: To compare the clinical efficacy and safety in children with vesicoureteral reflux (VUR) of a single injection of two different bulking agents: polydimethylsiloxane (Macroplastique) or dextranomer/hyaluronic acid copolymer (Deflux).

METHODS: A total of 73 patients (106 renal units, 41 boys and 32 girls) aged 2-15 years (mean age, 34.5 months) were included. A single subureteral injection of either Macroplastique or Deflux was performed in 37 children (55 ureters) and 36 children (51 ureters), respectively. VUR was grade II in 34 ureterorenal units, grade III in 23, grade IV in 31, and grade V in 18 ureterorenal units.

RESULTS: Overall, the reflux was corrected in 84 of the renal units (86%) with one injection. The correction rates, according to the reflux grade, were 91, 91, 83, and 72% for grades II-V, respectively. At the 3-month follow-up visit, reflux was corrected in 48 (87%) of 55 refluxing ureters in the Macroplastique group and in 43 (84%) of 51 refluxing ureters in the Deflux group.

CONCLUSIONS: A single subureteral injection of either Macroplastique or Deflux is an effective treatment modality for children with VUR. The procedure was well tolerated, safe, and associated with low morbidity.

Long-term results of endoscopic treatment of vesicoureteral reflux in children: Comparison of different bulking agents

Stredele RJ, Dietz HG, Stehr M.

OBJECTIVE: To determine the long-term effect in children of endoscopic treatment of vesicoureteral reflux (VUR) using different bulking agents. VUR status, recurrence of urinary tract infection (UTI), and recurrence of febrile UTI were evaluated as endpoints.

METHODS: From 1993 to 2005, we injected 229 refluxive ureters (VUR grade II-IV) in 135 children. Mean age of the children was 55.7 months. We used collagen in 98 (years 1993-2000), polydimethylsiloxane in 32 (years 1999-2000), and dextranomer/hyaluronic acid copolymer (Dx/HA) in 99 ureters (years 2000-2005). Of the 135 children, 127 underwent a voiding cystourethrogram (VCUG) (radiologic or nuclid) 3 months after the first injection, and 88 children a second VCUG (nuclid) after 37 months (mean) postoperatively. Clinically, patients were monitored for non-febrile or febrile UTI. Data were collected and analyzed retrospectively by chart review.

RESULTS: After first injection with collagen, polydimethylsiloxane and Dx/HA, 52%, 55% and 81.5% of the children were without VUR, respectively. Repeated injections were successful in only 21% (collagen) to 42% (Dx/HA). Of the 88 with a second VCUG, 48.5% of the initially reflux-free children developed relapse VUR after collagen, 45.5% after polydimethylsiloxane and 21.5% after Dx/HA injection. Clinically, there was a significant difference in postoperative UTI occurrence in favor of the Dx/HA group.

CONCLUSIONS: Clinically and radiologically, Dx/HA exhibited the best results, giving better protection against UTIs and a better VUR cure rate. There was still a risk of VUR recurrence in successfully treated children after 3 years of follow up.
Endoscopic Subureteral Injection for the Treatment of Vescoureteral Reflux in Children: Polydimethylsiloxane (Macroplastique(R)) versus Dextranomer/ Hyaluronic Acid Copolymer (Deflux(R)).

Bae YD, Park MG, Oh MM, Moon du G. Korean J Urol. 2010 Feb;51(2):128-31

PURPOSE: The aim of this study was to compare cure rates and complications of polydimethylsiloxane (Macroplastique(R)) and dextranomer/hyaluronic acid copolymer (Deflux(R)) in the treatment of vesicoureteral reflux (VUR).

MATERIALS AND METHODS: From April 2001 to March 2008, 29 boys and 42 girls (total of 115 ureters) with a mean age of 6 years who had undergone endoscopic subureteral transurethral injection for VUR were enrolled. A single subureteral injection of Macroplastique was performed in 31 ureters in 23 children (group I; grade II: 4; grade III: 12; grade IV: 9; grade V: 6), and a single subureteral injection of Deflux was performed in 84 ureters in 48 children (group II; grade II: 24; grade III: 14; grade IV: 25; grade V: 21). Renal ultrasound was done 1 day after injection, and voiding cystourethrography (VCUG) was done at 3 months. Successful reflux correction was defined as absent or grade I reflux on follow-up VCUG.

RESULTS: No significant difference in success rates was observed between group I and group II [80.6% (25/31) vs. 78.6% (66/84), respectively, p>0.05]. The following postoperative complications developed: ureteral obstruction in 2 ureters of group I and 3 ureters of group II, asymptomatic urinary tract infection in 3 patients of group I and 2 patients of group II, and bladder calcification by erosion or mucosal necrosis in 2 patients of group I.

CONCLUSIONS: Despite differences in material properties, both Macroplastique and Deflux were safe for the treatment of children with VUR. Because of the risk of bladder mucosal necrosis and substantial decreases in volume after implantation, long-term follow-up is required.

The Swedish Reflux Trial in Children: III. Urinary Tract Infection Pattern

Brandström P, Esbjörner E, Herthelius M, Swerkersson S, Jodal U, Hansson S.
J Urol. 2010 Jul;184(1):286-91

Purpose: We evaluated the difference in the febrile urinary tract infection rate in small children with dilating vesicoureteral reflux randomly allocated to 3 management alternatives, including antibiotic prophylaxis, endoscopic treatment or surveillance only as the control.

Materials and Methods: At 23 centers a total of 203 children were included in the study, including 128 girls and 75 boys 1 to younger than 2 years. Vesicoureteral reflux grade III in 126 cases and IV in 77 was detected after a febrile urinary tract infection (194) after prenatal screening (9). Voiding cystourethrography and dimercapto-succinic acid scintigraphy were done before randomization and after 2 years. The febrile urinary tract infection rate was analyzed by the intent to treat principle.

Results: We noted a total of 67 febrile recurrences in 42 girls and a total of 8 in 7 boys (p 0.0001). There was a difference in the recurrence rate among treatment groups in girls with febrile infection in 8 of 43 (19%) on prophylaxis, 10 of 43 (23%) with endoscopic therapy and 24 of 42 (57%) on surveillance (p 0.0002). In girls the recurrence rate was associated with persistent reflux after 2 years (p 0.0095). However, reflux severity (grade III or IV) at study entry did not predict recurrence.

Conclusions: In this randomized, controlled trial there was a high rate of recurrent febrile urinary tract infection in girls older than 1 year with dilating vesicoureteral reflux at study entry but not in boys. Antibiotic prophylaxis and endoscopic treatment decreased the infection rate.

The Swedish Reflux Trial in Children: II. Vesicoureteral Reflux Outcome

Purpose: We compared reflux status in children with dilating vesicoureteral reflux treated in 3 groups, including low dose antibiotic prophylaxis, endoscopic therapy and a surveillance group on antibiotic treatment only for febrile urinary tract infection.

Materials and Methods: A total of 203 children 1 to younger than 2 years with grade III-IV reflux were recruited into this open, randomized, controlled trial. Endoscopic treatment was done with dextranomer/hyaluronic acid copolymer. The main end point was reflux status after 2 years. Data were analyzed by the intent to treat principle.

Results: Reflux status improved in all 3 treatment arms. Of patients in the prophylaxis, endoscopic and surveillance groups 39%, 71% and 47%, respectively, had reflux resolution or downgrading to grade I-II after 2 years. This was significantly more common in the endoscopic than in the prophylaxis and surveillance groups (p = 0.0002 and 0.0030, respectively). After 1 or 2 injections 86% of patients in the endoscopic group had no or grade I-II reflux but recurrent dilating reflux was seen in 20% after 2 years.

Conclusions: Endoscopic treatment resulted in dilating reflux resolution or downgrading in most treated children. After 2 years endoscopic treatment results were significantly better than the spontaneous resolution rate or downgrading in the prophylaxis and surveillance groups. However, of concern is the common reappearance of dilating reflux after 2 years

Our experience using various injectable materials for the endoscopic treatment of vesicoureteral reflux


OBJECTIVES: Vesicoureteral reflux (VUR) is the most common urologic anomaly in childhood, affecting 1% of the pediatric population. Endoscopic treatment of VUR is accepted as the first therapeutic option and various injectable materials have been used since its implantation. We present our experience in the endoscopic treatment of VUR with various substances which we have been employing since we started performing the procedure.

METHODS: We have performed a retrospective descriptive study including 445 patients that underwent endoscopic treatment for vesicoureteral reflux in our centre between 1988 and 2004. We treated a total of 568 ureters, and we analyze results depending on the material employed, grade of reflux and associated pathology.

RESULTS: Among 569 ureters with vesicoureteral reflux undergoing treatment 457 were single VUR (79%), 76 (15%) were part of a double renal system, 24 (4%) were associated with neurogenic bladder, and 12 (2%) were secondary VUR after antireflux open surgery. We use three types of materials, with predominance of polytetrafluorethylene in 257 ureters, followed by hyaluronic acid dextranomer in 159, and finally polydimethylsiloxane in 153. In the cases of single VUR global cure rate was 88% (381 ureters), with significant improvement of the grade of reflux in 7% (51 ureters), and 5.5% of the cases (25 patients) requiring a Cohen type reimplantation. We observed a lower success rate and greater need of repeated injections in grade IV and V refluxes. In VUR associated with duplication results are worse, with less successes and greater need of procedures for its resolution. We cured 59 ureters (77%) out of 76 treated, 13 (19%) improved, and 4% required Cohen type reimplantation. In cases of VUR associated with neurogenic bladder 20 ureters were cured (83%). There was significant improvement in two ureters (8%); there were two failures (8%), requiring Cohen type reimplantation to avoid progressive deterioration of the kidney. In the cases of VUR after open surgical reimplantation all 12 ureters treated were cured (100%). Among 8 single ureters, reflux was solved with 1 procedure in 6 and 1 required 2 procedures. The total number of cured ureters has been 496 (87%), and 51 (9%) have improved. 22 ureters underwent surgery (4%). 68% of the cases were cured after 1 injection, 16.5% after 2, and 1 & after 3. There have been 5 complications (0.8%): 1 case of hemorrhagic cystitis which resolved spontaneously in two days, and 4 pyelonephritis which received the appropriate antibiotic therapy following antibiogram. We did not have any case of recurrent lower urinary tract infections. Follow-up has range it from 1.5 to 15 years.

CONCLUSIONS: It seems that both polydimethylsiloxane and hyaluronic acid dextranomer are good and safe materials, and do not have the risk of distant migration of polytetrafluorethylene.
Incidence of Urinary Tract Infections in Children After Successful Ureteral Reimplantation Versus Endoscopic Dextranomer/Hyaluronic Acid Implantation


Purpose: Endoscopic implantation of dextranomer/hyaluronic acid has proved to be an effective minimally invasive technique for correcting vesicoureteral reflux in children. There is some evidence suggesting that in addition to being less invasive, successful dextranomer/hyaluronic acid implantation compared to successful antireflux surgery is associated with fewer febrile and nonfebrile urinary tract infections. We review the clinical outcomes of 2 groups of children cured of reflux with open surgery and dextranomer/hyaluronic acid implantation to determine if a difference in clinical outcomes exists.

Materials and Methods: We reviewed the charts of 43 patients who underwent dextranomer/hyaluronic acid implantation and 33 who underwent open surgery for vesicoureteral reflux. Data collected included age, gender, preoperative and postoperative grades of reflux, and urinalysis and urine culture results. Urinary tract infection was defined as any culture that grew more than 105 colonies of a single organism, with symptoms typical of cystitis (urgency, frequency, dysuria). A febrile urinary tract infection was defined as an infection accompanied by a temperature greater than 101.5F. Any hospitalizations for febrile episodes were also recorded.

Results: The incidence of urinary tract infection after successful open surgery (38%) was significantly higher than that observed following successful dextranomer/hyaluronic acid treatment (15%, p = 0.03). Febrile urinary tract infections occurred in 24% of the children who underwent open surgery and in 5% of those who underwent dextranomer/hyaluronic acid implantation (p = 0.02). Hospital readmissions occurred only in the group undergoing open surgery.

Conclusions: Children successfully cured of vesicoureteral reflux with dextranomer/hyaluronic acid implantation have a lower incidence of febrile and nonfebrile urinary tract infections compared to those cured with open surgery. These findings suggest that dextranomer/hyaluronic acid implantation, when successful, may result in more favorable clinical outcomes.

Endoscopic treatment of vesicoureteral reflux (VUR). Comparison of various substances. Long-term results

Escala Aguirre JM, Cadena González Y, Retamal Pinto G, López Egaña PJ, Letelier Cancino N, Zubiesta Acuña R.

OBJECTIVES: The VUR is one of the most frequent pathologies in pediatric urology. Classically it has been managed with medical or surgical treatment depending on age, grade, and other variables. Over the last years, urologists have started to perform endoscopic treatment with various substances, surgery but minimally invasive. The objective of this work is to evaluate our results with this method.

METHODS: Between 1996 and 2004 we performed endoscopic treatment on 41 patients (70 ureters) using different substances. We analyze VUR grade and side, improvement with one or more injections, post-operative follow-up with clinical evaluation, bladder ultrasound and voiding cystourethrogram (VCUG), and compare the long-term results of the different substances used, mainly with the evaluation of recurrences and/or urinary tract infections.

RESULTS: 41 patients entered the study; collagen was injected in 13 cases, Macroplastique in 14, and Deflux in 14. Twenty-nine patients underwent bilateral injection, adding up to a total of 70 injected ureters. Collagen injection had a success rate of 53% with the first injection and 77% with the second, Macroplastique success rate was 83% with the first injection and 91% with the second, and Deflux 84% on first injection and 88% with the second. Mean post-operative follow-up was 44 months, with a range of 18-86 months. 18% of the patients presented post operative UTI, they were treatment failures. There are no UTI episodes in patients after successful treatment.

CONCLUSIONS: Endoscopic treatment is a useful tool in the long-term management of VUR, both as definitive treatment or as an alternative to conventional medical management, with better results when using Macroplastique and Deflux.

Endoscopic treatment of vesicoureteral reflux using dextranomer hyaluronic acid copolymer.

Molitierno JA, Scherz HC, Kirsch AJ.

Vesicoureteral reflux (VUR) is a common urinary tract anomaly. Treatment is performed to minimize the risk of febrile urinary UTIs that may result in renal scarring. The endoscopic use of dextranomer hyaluronic acid copolymer has been gaining popularity as an alternative to the traditional methods of open surgery and chronic antibiotic prophylaxis. The aim of this educational review was to present the trends, latest perspectives and surgical techniques regarding this newer method of treatment of VUR.

Evolving techniques are described that have resulted in VUR cure rates that rival that of open ureteral reimplantation with minimal associated morbidity. These have proven to be effective in complex cases that were previously considered as contraindications for endoscopic treatment, including voiding dysfunction, duplex ureters, high-grade VUR and paraureteral diverticuli.

It is recommended that open reimplantation be reserved for those children with ectopic ureters, megaureters that require tapering or secondary grade V VUR, and those who have failed two endoscopic injections. Future advances promise to standardize the injection technique, ensuring optimum needle placement for consistently successful injections.

Endoscopic treatment of vesicoureteral reflux in children

Dahl E, Polacek M, Hagen TS, Refsum S.
Tidsskr Nor Laegeforen. 2007 Apr 19;127(8):1032-5.

BACKGROUND: At Rikshospitalet, Norway, vesicoureteral reflux (VUR) in children has been treated with subureteric teflon (polytetrafluoroethylene) injection (STING) since 1994. After a biological injection substance became commercially available, we changed to Deflux (dextranomer/hyaluronic acid) in 2000. The aim of this study was to assess whether the VUR results following use of the new injection substance are comparable to those for the previously used substance.

MATERIAL AND METHODS: 202 ureters with VUR grade II-V in 132 patients (91 girls) were treated for the first time with subureteric injections of teflon (n = 77) or Deflux (n = 125) during the 5-year period November 1998-2003. The charts were retrospectively reviewed.

RESULTS: 201 ureters (131 patients) were followed up with urinary tract ultrasound and voiding cystogram 1-34 months after the last injection. After the first teflon injection 43% of the ureters had no reflux and an additional 9% were improved. After the first Deflux injection 48% of the ureters had no reflux and 10% were improved. After 1-3 injections 78% (teflon 71%, Deflux 81%) were without or had reduced VUR. Three ureters showed terminal stenosis after the first Deflux injection. Statistically, the results were independent of VUR grade, injection substance and surgeon experience, and similar for duplex and single ureters.

INTERPRETATION: Endoscopic treatment of VUR in children is safe and simple. The results after Deflux and teflon were similar. Urinary tract ultrasound and voiding cystogram should be used for follow-up of all patients some months after injection.

Part 3: Endoscopic injection versus antibiotic prophylaxis in the reduction of urinary tract infections in patients with vesicoureteral reflux

Elder JS, Shah MB, Batiste LR, Eaddy M.

OBJECTIVE: Vesicoureteral reflux (VUR) occurs in approximately 1% of infants and children and is associated with recurrent urinary tract infections (UTIs). The objective of this paper is to examine the use of endoscopic injection with dextranomer/hyaluronic acid copolymer (Dx/HA) as a curative option and as an alternative to antibiotic prophylaxis, as Dx/HA is gaining in popularity in the treatment of VUR.

METHODS: The nationally representative PharMetrics Integrated Medical and Pharmaceutical database was used to conduct this retrospective analysis. Patients < 11 years of age who were continuously eligible and had an International Classification of Diseases (ICD-9-CM) code for VUR were identified. Resource utilization and outcome measures were evaluated over a 6-month pre- and 12-month post-index period. Patients diagnosed with neuropathic bladder, posterior urethral valves, bladder extrophy, ureterocele, or duplication anomaly were excluded. Patients were matched 3:1, antibiotic prophylaxis to Dx/HA, by age, gender, urinary tract infections (UTIs) prior to index date, and diagnosing physician specialty. The primary outcome assessed was UTIs.

RESULTS: Of the matched patients, 114 received a prescription for antibiotic prophylaxis and 38 underwent endoscopic injection with Dx/HA between January 2000 and December 2004. The average number of UTIs per year was 0.28 in the antibiotic cohort and 0.08 in the Dx/HA cohort, respectively. The incidence rate ratio (IRR) of 4.826 (p = 0.029) revealed that the average number of UTIs was 383% higher for patients receiving antibiotic prophylaxis compared with patients who underwent endoscopic injection. The retrospective nature of the analysis did not allow for treatment randomization. Due to the stringent classification of UTIs, rates of UTIs may be underestimated in both cohorts.

CONCLUSIONS: Treatment with endoscopic injection with Dx/HA resulted in significantly fewer UTIs compared with children receiving antibiotic prophylaxis, supporting a role for Dx/HA as a first-line treatment option for patients with VUR.

Assessing the effectiveness of endoscopic injection in treating patients with Vesicoureteral reflux for the reduction of urinary tract infections

Terry W. Hensle MD, Grace Hyun, MD, Amy L. Grogg, PharmD, Manan B. Shah, PhD, PharmD
Presented at the 2006 Annual Meeting of the American Academy of Pediatrics, Atlanta, GA. October 7-10, 2006

Introduction: Vesicoureteral reflux (VUR) occurs in approximately 1% of infants and children and is associated with recurrent urinary tract infections (UTIs) which, in some children, may lead to renal damage and hypertension. The current standard of care for the initial management of VUR is prophylactic antibiotics; however, endoscopic injection with dextranomer/hyaluronic acid (Dx/HA) is gaining in popularity as a curative option, and as an alternative to antibiotic prophylaxis. The purpose of this study was to compare rates of UTIs for patients prescribed prophylactic antibiotics versus those who initially received endoscopic Dx/HA injection.

Materials and Methods: This retrospective analysis was conducted using the nationally representative PharMetrics Integrated Medical and Pharmaceutical database encompassing 45 million lives. Patients <11 years of age who were continuously eligible with an ICD-9-CM for VUR were identified. Resource utilization and outcome measures were evaluated over a 6-month pre and 12-month post index period for patients matched 3:1, prophylactic antibiotics to Dx/HA, by pre-period antibiotic charges, age, gender, and use of specialty care. The primary variable of interest was UTI’s.

Results: There were 140 patients prescribed antibiotics and 48 Dx/HA patients matched in the analysis with a VUR diagnosis between January 2000 to December 2004. The average number of UTIs per year was 0.69 in the antibiotics cohort and 0.42 in the Dx/HA cohort, respectively. The incidence rate ratio (IRR) of 1.79 (P=0.028) revealed that the average number of UTIs were 79% greater for prophylactic antibiotic patients than those treated with endoscopic injection UTIs were observed in 25% of the Dx/HA patients vs 45% of the patients treated with antibiotics (P=0.025).

Conclusions: The use of antibiotic prophylaxis in the treatment of VUR resulted in 79% more UTIs when compared to endoscopic injection with Dx/HA.

Based on the number of UTIs observed, treatment with endoscopic injection of DX/HA offers better outcomes than treatment with prophylactic antibiotics.
Critical appraisal: antibiotic prophylaxis and endoscopic injection for VUR

Koyle MA, Clement M, Cooper CS, Grady R and Kirsch AJ
Issues in Urology May/June 2006; 18 (3)

Vesicoureteral reflux (VUR) is generally diagnosed after a presentation with urinary tract infection (UTI). In some children, complications secondary to VUR and ascending UTI may occur. Traditionally, antibiotic prophylaxis has been the preferred initial treatment approach to prevent UTIs, with the understanding that the reflux will diminish or resolve in many of these patients. Limited data are available to support this approach, though. Antibiotic prophylaxis is not curative; reflux may persist. Problems of compliance and drug-related adverse events occur with all pharmacotherapy, and the potential for bacterial resistance is a concern during long-term therapy. Furthermore, surgical intervention may eventually be pursued in children in whom the condition does not resolve spontaneously. Interventional treatment alternatives to antibiotic prophylaxis for VUR are all potentially curative and minimize the morbidity associated with upper UTI. Recent advances in the endoscopic management of VUR have increased interest in its potential as initial therapy.

Emerging clinical data support endoscopic treatment as an alternative to long-term antibiotic prophylaxis in patients with known VUR. Continued research will help define the role of this minimally invasive technique in the management of VUR, including its possible use as initial therapy for the condition. Successful endoscopic therapy offers the benefits of decreased need for imaging studies for VUR, avoidance of long-term antibiotic prophylaxis, and minimal morbidity. Prospective clinical trials (such as those proposed by the NIH) will likely investigate the optimal indications for treatment of and management options for VUR in children, including the role of endoscopic therapy, intermittent and prophylactic antibiotic therapy, and ureteral reimplantation.

Complex vesicoureteral reflux. Our experience

Argüelles Salido E, García Merino F, Millán López A, Fernández Hurtado M, Borrero Fernández J.

OBJECTIVE: To analize the proportion of complex reflux in the whole amount of patients treated endoscopically of vesicoureteral reflux in our hospital. To determine the endoscopic treatment success in complex reflux, and the influence of reflux grade in it.

MATERIAL AND METHODS: We present our experience between 1992 and 2003 with three kinds of substances (polytetrafluoroethylene, polydimethylsiloxane and dextranomer-hyaluronic acid copolymer). We treated complex reflux in 74 patients with endoscopic injection. All patients were scheduled to have voiding cystourethrogram 3 and 9 moths after injection. A positive response was defined as grade 0 or I reflux.

RESULTS: Reflux was solved using the endoscopic procedure in 86.25% after first injection, 93.75% after second and 96.25% after third. The corresponding results for reflux grade II, III and IV were 88.9%, 83.3% and 100%.

CONCLUSIONS: We conclude that subureteral injection of different sustances (Teflon, Macroplastique or Deflux) is a useful treatment for most cases of vesicoureteral reflux. We propose it as first step of treatment.

Preliminary results of endoscopic treatment of vesicoureteric reflux in children. Prospective comparative study of Deflux vs. Coaptite


INTRODUCTION: The objective of this study is to compare the short-term and medium-term efficacy of Coaptite versus Deflux in the endoscopic treatment of vesicoureteric reflux in children.

MATERIALS AND METHODS: Over a period of 24 months, a cohort of 31 children with 44 refluxing vesicoureteric units were treated alternately by either Deflux implants (Group I, 24 refluxing units) or Coaptite implants (Group II, 20 refluxing units). This series comprised 40 solitary ureteric systems and 2 complete duplications. The two groups were comparable in terms of age at the time of the operation and distribution of severity of reflux. The quantity of product injected was identical in the 2 groups: 0.5 cc per ureter. All patients in group II received only one injection, while 2 Deflux injections were necessary in 2 patients and 3 injections were necessary in 1 patient in group I. All children were reviewed by ultrasound and retrograde cystography 3 months after the operation.

RESULTS: Reflux, regardless of grade, resolved in 70% of cases in the 2 groups (no significant difference). The cure rate was 75% for grade II and III in group I and 62.5% (grade II) and 70% (grade III) in group II, with no significant difference between the 2 groups. Two cases of grade IV reflux were cured after a single implantation of Coaptite in 1 case and Deflux in the other case. Complications, such as ureteric stasis or haemorrhage at the injection site, were not observed.

CONCLUSION: Although the efficacy of endoscopic treatment has now been clearly established, the choice of material to be injected is still controversial. This preliminary study did not reveal any significant difference in terms of cure rate, regardless of grade, between patients treated with Coaptite or Deflux. The medium-term and especially the long-term morbidity of these products still needs to be evaluated.

The effect of location of the ureteric orifice on the efficacy of endoscopic injection to correct vesico-ureteric reflux.


OBJECTIVE: To review our 11-year experience and identify the mechanisms responsible for the failure of endoscopic injection for vesico-ureteric reflux (VUR) with three different injectable agents, based on the location of the ureteric orifice on endoscopy.

PATIENTS AND METHODS: We retrospectively reviewed the charts and endoscopic video-photographs of 46 patients (26 girls, 20 boys, median age 6 years, range 2-16) with VUR treated once or twice by subureteric injection with PTFE, or polydimethylsiloxane or dextranomer/hyaluronic acid copolymer, from 1992 to 2003. Five patients were lost to follow-up and six ectopic and/or duplicated ureters were excluded from the analysis; in all, 52 ureters were analysed. According to the international classification, the VUR was grades I to V in four (8%), 12 (23%), 16 (31%), 13 (25%) and seven (13%) ureters, respectively.

RESULTS: After 3 months, voiding cysto-urethrography showed that VUR continued in six of 19, seven of 12 and eight of 21 ureters (38%), respectively, after subureteric PTFE, polydimethylsiloxane and dextranomer/hyaluronic acid copolymer injection; after the second injection, reflux continued in two of six, four of seven and three of eight ureters, respectively. Mound displacement and/or volume loss was the most common failure with all three bulking agents after both the first (62%) and second injections (44%) (P < 0.05). The first injection failed in 32% (11 of 35) normally located ureters and 10 of 17 lateral ureters (P < 0.05). The second injection failed in 11% (four of 35) normal and five of 17 lateral ureters (P < 0.05).

CONCLUSIONS: A lateral ureteric orifice may decrease the efficacy of endoscopic injection, as the likelihood of a faulty injection is greater. However, a more careful second injection decreases the failure rate, particularly in those with low- to medium-grade refluxing ureters.

The role of endoscopic treatment of vesicoureteral reflux: a 17-year experience.

Capozza N, Lais A, Nappo S, Caione P.

PURPOSE: During the last 20 years endoscopic treatment of vesicoureteral reflux (VUR) has gained popularity in European countries. We performed a retrospective analysis of our 17-year experience with more than 1,000 patients treated to assess whether technique, indications or results of endoscopic treatment of VUR have changed over time.

MATERIALS AND METHODS: From January 1986 to June 2002, 1,244 patients underwent endoscopic treatment for grades II to IV VUR. Polytetrafluoroethylene was injected as the bulking material in the first 14 cases, after 1989 bovine cross-linked collagen was used in 442 and since 1995 dextranomer/hyaluronic acid copolymer was used in 788. Urinary tract ultrasound was performed 1 and 6 months, and micturition cystourethrogram was done 3 and 12 months after endoscopic treatment. All patients included in the study completed a minimum 12-month followup.

RESULTS: Endoscopic treatment was always performed in 1 day. Complications were observed in 0.5% of cases. After 1 or 2 injections the micturition cystourethrogram showed no significant VUR (absent or grade I) in 77% of cases. The success rate was 88%, 75% and 52% for grades II, III and IV VUR, respectively. With increasing experience not only primary VUR, but also secondary reflux was considered eligible for endoscopic treatment, and the number of grade IV VUR cases treated by endoscopy also increased. The presence of voiding dysfunction was identified as a limiting factor in the success of endoscopic treatment.

CONCLUSIONS: The short hospital stay, acceptable success rate and absence of significant complications prompt us to consider endoscopic treatment as first choice treatment of VUR rather than long-term prophylaxis and open surgery. Even grade IV VUR and VUR in complex anatomical situations can be successfully treated by endoscopy. Patients with voiding dysfunction should be identified and adequately treated before any endoscopic attempt.

Endoscopic treatment of vesicoureteral reflux


OBJECTIVES: Endoscopic subureteral injection of tissue-augmenting substances, a 15-minute outpatient procedure has become an alternative to long-term antibiotic prophylaxis and surgical intervention in the treatment of vesicoureteral reflux (VUR) in children.

MATERIALS AND METHODS: We searched MEDLINE using the words: vesicoureteral reflux, treatment, the long-term results of endoscopic treatment of reflux. We summarized the worldwide data regarding endoscopic treatment of VUR using various tissue-augmenting substances presently available.

RESULTS: In terms of effectiveness and long-term successful results, polytetrafluoroethylene is still the most reliable injectable material for the endoscopic treatment of VUR. However, Dextranomer/hyaluronic acid copolymer (Deflux) is a new promising tissue augmenting substance which might be able to replace Teflon in the endoscopic treatment of reflux in terms of a similar to Teflon reflux cessation rate and exhibiting no evidence of migration.

CONCLUSION: Endoscopic subureteral polytetrafluoroethylene injection is a simple and effective outpatient procedure for in the treatment of vesicoureteral reflux. No long-term morbidity was observed in our patients with small amounts of injectable polytetrafluoroethylene.

Long-term outcome of the endoscopic correction of vesico-ureteric reflux: a comparison of injected substances.
Sugiyama T, Hanai T, Hashimoto K, Umekawa T, Kurita T.
BJU Int 2004 Aug;94(3):381-3

OBJECTIVE: To summarize the long-term outcome of endoscopic surgery to correct vesico-ureteric reflux (VUR) using different injected substances, i.e. autologous blood, hyaluronan/dextranomer copolymer (HDC), PTFE and glutaraldehyde cross-linked bovine dermal (GAX) collagen.

PATIENTS AND METHODS: Treatment results on 270 ureters of 185 patients followed for >5 years (mean 8.5) were summarized according to the injected substances. The substances were injected into the 6 o’clock position of the ureteric orifice endoscopically. “Success” was defined as the absence of VUR for >5 years after a single injection.

RESULTS: The treatment was successful in two of 24 patients (8%) with autologous blood, 17 of 32 (53%) with HDC, 108 of 171 (63%) with PTFE and 24 of 43 (56%) with GAX collagen. The success rate was lower in patients with higher grades of VUR.

CONCLUSIONS: Autologous blood is unsuitable for clinical application because of its poor durability. We will no longer use PTFE because its safety is not well established. The overall success rates of endoscopic surgery with GAX collagen and HDC were insufficient compared with surgical reimplantation, but it is advantageous that this procedure is less invasive and can be repeated. The cure rate could be improved by excluding high-grade VUR from the indications for endoscopic surgery.

Role of the endoscopic treatment of vesicoureteal reflux. A 16-years’ experience

Capozza N, Caione P.

AIM: Vesico-ureteral reflux (VUR) is the most common urological malformation in pediatric age; nevertheless its optimal management remains controversial. Until early 80s, treatment guidelines for VUR recommended the use of antibiotic prophylaxis as initial therapy, with surgical repair for patients with persistent VUR. Endoscopic treatment of VUR has gained popularity and has proved successful in a high percentage of cases, but its role in the clinical practice remains to be established.

METHODS: In this paper, our series of 1029 patients and 1478 refluxing ureters, treated from January 1986 to June 2001, is presented. Reflux ranged from grade II to grade IV. In the first 14 cases Teflon was injected. After 1989 bovine collagen was used in 442 children and, since 1996, Deflux, a nonallergenic, biodegradable dextranomer, in 573 cases. All patients were clinically evaluated for possible voiding dysfunctions. All patients completed a 12 month follow-up period.

RESULTS: After 1 or 2 injections, a voiding cystogram showed no VUR (or grade I) in 1123 ureters (76%). In grade II, III and IV success rates were, respectively, 87%, 73% and 48%. Complications were minimal (0.5%).

CONCLUSION: These results confirm that endoscopic treatment of VUR is a valid alternative to “open surgery” and to antibiotic prophylaxis. Failure of treatment is usually due to dislocation of the implanted material, secondary to voiding dysfunction. In conclusion, we recommend the endoscopic treatment in the majority of VUR, for the short hospital stay, the absence of significant complications and the high success rate. In grade IV VUR, the use of endoscopic treatment is still questionable. Patients with voiding dysfunction should be identified and treated with appropriate therapy prior to attempt an endoscopic treatment of VUR.

Prospective comparison and 1-year follow-up of a single endoscopic subureteral polydimethylsiloxane versus dextranomer/hyaluronic acid copolymer injection for treatment of vesicoureteral reflux in children

Oswald J, Riccabona M, Lusuardi L, Bartsch G, Radmayr C.
Urology. 2002 Nov;60(5):894-7;

OBJECTIVES: To compare, in a prospective study, the efficacy of a single injection of polydimethylsiloxane (Macroplastique) or dextranomer/hyaluronic acid copolymer (Deflux), a new biodegradable substance, and to assess the short-term and 1-year clinical effects concerning reflux resolution and the safety of these two bulking agents. Subureteral injection of bulking agents has recently demonstrated good success rates for endoscopic treatment of vesicoureteral reflux. Macroplastique has been one of the most popular bulking agents during the past years. Nevertheless, considering the synthetic property, new biodegradable substances have become more relevant.

METHODS: From January 2000 to June 2001, 16 boys and 56 girls (total of 114 ureters) with a mean age of 34.5 months were treated endoscopically for vesicoureteral reflux. A single subureteral Macroplastique or Deflux injection was performed in 34 children (58 ureters) and 38 children (56 ureters), respectively. Both groups were comparable in terms of baseline parameters. Vesicoureteral reflux was grade II in 52, grade III in 57, and grade IV in 5 ureterorenal units. The procedure was performed on an outpatient basis, with the children under general anesthesia. In addition to the routine parameters, the follow-up evaluation consisted of renal ultrasonography and voiding cystourethrography at 3 and 12 months postoperatively.

RESULTS: Endoscopic treatment was performed without any complications in all cases. At the 3-month follow-up visit, reflux was corrected in 50 (86.2%) of 58 refluxing ureters in the Macroplastique group and in 40 (71.4%) of 56 refluxing ureters in the Deflux group. At 1 year of follow-up, reflux correction was maintained in 80.9% of ureters in the Macroplastique group and in 67.6% of ureters in the Deflux group. No postoperative complications were observed in either group.

CONCLUSIONS: A single subureteral injection of either polydimethylsiloxane (Macroplastique) or dextranomer/hyaluronic acid copolymer (Deflux) is an effective treatment modality for children with vesicoureteral reflux. The procedure was well tolerated, safe, and associated with low morbidity. Deflux, a new biocompatible, biodegradable substance, seems to be an alternative modality to other bulking agents for treating vesicoureteral reflux in children, with acceptable short-term and 1-year results.

VUR - Complicated Cases

Endoscopic management of urinary incontinence in neurogenic bladder due to spinal cord lesions in children

[Article in French]
Dariane C, Peycelon M, Lallemant P, Forin V, Audry G.

INTRODUCTION: The urological management of urinary incontinence in neurogenic bladder due to spinal cord lesions in children is intended to achieve social continence while preserving the upper urinary tract, combining clean intermittent catheterization with anticholinergic agents. The objective of this study was to report the results on continence of endoscopic management of bladder and/or sphincter of children with failure or intolerance to first intention therapy.

PATIENTS AND METHODS: Of the 364 children followed for neurologic bladder in our institution, 22 required endoscopic management between 2000 and 2012. Urinary incontinence was related to detrusor overactivity in 16 children and sphincter deficiency in 13 children, requiring one or several intradetrusor injections of botulinium toxin-A (BTA) and/or dextranomer/hyaluronic acid (Dx/Ha) injection in the bladder neck. Continence was reassessed between six and eight weeks after the last injection using the Schulte-Baukloh score.

At the end of the mean follow-up of four years, 16 children received 54 injections of BTA and 13 children had 24 injections of Dx/Ha. Social continence, defined as a score between 0 and 1, was acquired quickly after injection of BTA and required to repeat the injections every 8.7 months (6-12) with a very low morbidity. After the first injection of Dx/Ha, 69% of the children improved significantly their incontinence score (from 1 to 0 or from 2 or 3 to 1) with better results for girls.

CONCLUSION: An appropriate endoscopic management has enabled an improvement of the continence of two-thirds of children who fail first intention treatment for their neurogenic bladder. This is an alternative to delay or avoid major surgery.

A novel use of dextranomer/hyaluronic acid copolymer.
Lambropoulos V, Mouravas V, Papageorgiou I, Spyridakis I, Marakis G. Urologia. 2014 May 14;0(0):0.

The aim of this study is to present a novel use of Dextranomer/hyaluronic acid copolymer (Deflux) for the treatment of a complicated iatrogenic chronic urethral injury.

A 12-year-old boy with a neuropathic bladder presented a groove in the urethral mucosa due to chronic clean intermittent catheterizations (CICs) and suffered a posterior urethral injury during a failed catheterization for a routine examination. The defect on the urethral wall was repaired using Deflux, a technique that is not described in the literature.

After the intervention the patient is continuing CICs without further complications.

Outcomes of vesicoureteral reflux in children with non-neurogenic lower urinary tract dysfunction treated with dextranomer/hyaluronic acid copolymer (Deflux).


OBJECTIVE: There has been hesitancy to use dextranomer/hyaluronic acid copolymer (DHXA, Deflux for vesicoureteral reflux (VUR) in the setting of lower urinary tract (LUT) dysfunction because of the limited number of published studies, the possibility of less success, and the manufacturer’s recommendations contraindicating its use in patients with active LUT dysfunction. We report on our experience using DXHA in this subset of patients whose VUR persisted despite targeted therapy for their LUT condition.

MATERIALS AND METHODS: We reviewed patients diagnosed with both a LUT condition and VUR who underwent subureteric DXHA while still undergoing treatment for their LUT dysfunction. Persistence of VUR was confirmed by videourodynamic studies (VUDS)/VCUG (voiding cystourethrogram) and all patients were on targeted treatment (TT) and antibiotic prophylaxis prior to and during DXHA injection. VUR was reassessed post-injection.

RESULTS: Fifteen patients (22 ureters; 21F,1M) met inclusion criteria (mean age 6.1 years, range 4-12). Following one to three DXHA injections, VUR resolved in 17 ureters (77%) including eight of nine ureters in dysfunctional voiding (DV) patients, five of nine in idiopathic detrusor overactivity disorder (IDOD), and four of four in detrusor underutilization disorder (DUD) patients.

CONCLUSIONS: DXHA is safe and effective in resolving VUR in children with associated LUT dysfunction, even before their LUT condition has fully resolved. Highest resolution rates were noted in patients with either DV or DUD or who were least symptomatic prior to injection.

The current role of endourologic management of renal transplantation complications.


Introduction. Complications following renal transplantation include ureteral obstruction, urinary leak and fistula, urinary retention, urolithiasis, and vesicoureteral reflux. These complications have traditionally been managed with open surgical correction, but minimally invasive techniques are being utilized frequently.

Materials and Methods. A literature review was performed on the use of endourologic techniques for the management of urologic transplant complications.

Results. Ureterovesical anastomotic stricture is the most common long-term urologic complication following renal transplantation. Direct vision endoureterotomy is successful in up to 79% of cases. Urinary leak is the most frequent renal transplant complication early in the postoperative period. Up to 62% of patients have been successfully treated with maximal decompression (nephrostomy tube, ureteral stent, and Foley catheter). Excellent outcomes have been reported following transurethral resection of the prostate shortly after transplantation for patients with urinary retention. Vesicoureteral reflux after renal transplant is common. Deflux injection has been shown to resolve reflux in up to 90% of patients with low-grade disease in the absence of high pressure voiding. Donor-gifted and de novo transplant calculi may be managed with shock wave, ureteroscopic, or percutaneous lithotripsy.

Conclusions. Recent advances in equipment and technique have allowed many transplant patients with complications to be effectively managed endoscopically.

The outcome of initial endoscopic treatment in the management of concomitant vesicoureteral reflux and ureteropelvic junction obstruction.

Kajbafzadeh AM, Tourchi A, Ebadi M.


OBJECTIVE: To report the results of a single-center experience with the endoscopic injection of Deflux as the initial minimally invasive approach in patients with vesicoureteral reflux (VUR) and coexisting obstruction at the ureteropelvic junction (UPJO) level who presented with VUR.

METHODS: Between May 2004 and July 2011, 2810 children with a diagnosis of VUR were referred to our center; 143 (5%) had concomitant UPJO. On the basis of the study inclusion criteria, 76 were included. All patients received antibiotic therapy. VUR and UPJO resolved in 50 children without the need for further intervention, and 26 underwent endoscopic Deflux injection by applying the hydrodistention autologous blood injection technique (HABIT). All patients received antibiotic prophylaxis until resolution of VUR was confirmed on voiding cystourethrogram (VCUG). Patients underwent follow-up visits at 1, 6, and 12 months postoperatively.

RESULTS: At a mean follow up of 20.0 ± 1.6 months, 20 of those with concomitancy showed resolution of VUR and the coexisting UPJO after the first injection (success rate, 76.9%), and 2 resolved after the second injection, leading to an overall success rate of 84.6%. Finally, 3 patients required further ureteral reimplantation, and 3 underwent pyeloplasty for correction of UPJO by applying miniature pyeloplasty technique. Differential renal function was preserved in all patients.

Performing an initial endoscopic injection of Deflux in the management of concomitant VUR and UPJO provides promising results in terms of spontaneous resolution of obstruction at the UPJ level and complete resolution or decrease in hydronephrosis.

Concomitant endoureterotomy and dextranomer/hyaluronic acid subureteral injection for management of obstructive refluxing megaureter.

Kajbafzadeh AM, Tourchi A.

PURPOSE: To present the results of our experience with combined endoureterotomy and endoscopic injection of dextranomer/hyaluronic acid (Deflux) for the treatment of primary obstructive refluxing megaureter (PORM).

PATIENTS AND METHODS: Eighteen children (12 female, 6 male; mean age-14 months) with 20 PORM units underwent concomitant endoureterotomy and endoscopic subureteral Deflux injection. All patients underwent endoureterotomy at the 6-o’clock position with insertion of a 3F Double-J ureteral stent into the obstructed segment of ureter and subureteral injection of Deflux at the 5-o’clock and 7-o’clock positions. The Double-J stent was left in place with its distal tip fixed with a single knot to the external genitalia for easy removal after 1 week. Patients with refluxing nonobstructive ureter on the contralateral side of the PORM unit (seven children) underwent simultaneous endoscopic subureteral injection of Deflux. Voiding cystourethrogramphy (VCUG) was performed at 6 months, and ultrasonography was performed at 1 week 3, 6, and 12 months postoperatively.

RESULTS: With a mean follow-up of 30 months, the procedure was uneventful in all patients. Follow-up VCUG showed no evidence of reflux in 15 ureterorenal (75%), significant decrease in reflux grade in 2 (10%), and no change in 3 (15%) in the endoscopic treated PORM units. No evidence of reflux was observed in the treated contralateral refluxing nonobstructive ureters. Ultrasonography revealed no ureterovesical junction obstruction. In 19 ureterorenal (95%) units, there was a complete resolution or decrease in hydroureteronephrosis.

CONCLUSIONS: The results of this study demonstrate that combined endoureterotomy and subureteral injection of Deflux is safe and effective in the treatment of PORM in selected patients.

Endoscopic treatment of vesicoureteral reflux in children with posterior urethral valves.

Oktar T, Acar O, Sancaktutar A, Sanlı O, Tefik T, Zylan O.

PURPOSE: We reviewed the clinical outcome of endoscopic injection therapy in children with vesicoureteral reflux persisting after posterior urethral valve ablation.

METHODS: We retrospectively reviewed the charts of 16 patients with posterior urethral valves who have undergone endoscopic injection to correct persistent reflux after successful relief of urethral obstruction. Breakthrough urinary tract infections, persistent high-grade reflux and failed ureteroneocystostomy were the indications of endoscopic antireflux surgery.

RESULTS: Reflux was grade I in 1, grade II in 3, grade III in 11 and grade IV in 4 ureters. Mean age at injection was 6.9 ± 3.8 years and the mean interval from initial intervention to injection was 4.3 ± 2.4 years. Injected material was dextranomer/hyaluronic acid in the majority (87.5 %) of cases. Reflux was resolved or downgraded in 12 ureters (63.1 %) after a single injection. All failed cases had urodynamically documented bladder dysfunction.

CONCLUSION: More than half of the patients with vesicoureteral reflux, persisting after initial valve ablation, showed complete resolution or significant downgrading in their reflux grade after endoscopic injection. Given the technical difficulties and potential complications of open surgical reimplantation in valve patients, endoscopic subureteral injection can be considered as an effective alternative to cure persistent vesicoureteral reflux.

Long-term followup after endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid copolymer in patients with neurogenic bladder.

Polackwich AS, Skoog SJ, Austin JC.

PURPOSE: Subureteral injection of dextranomer/hyaluronic acid copolymer is a minimally invasive method to treat vesicoureteral reflux. We report short and long-term success in treating secondary vesicoureteral reflux in patients with neurogenic bladder dysfunction or severe voiding dysfunction.

MATERIALS AND METHODS: We performed a retrospective chart review of all subureteral injection procedures done to identify patients with neurogenic bladder or severe voiding dysfunction. Short (less than 12 months) and long-term vesicoureteral reflux results for patients and ureters were recorded. Preoperative urodynamics and radiographic findings were reviewed. Preoperative factors were evaluated to identify patients with greater chances of success.

RESULTS: A total of 12 patients (17 ureters) were identified (10 with neurogenic bladder and 2 with Hinman syndrome). Short-term success (no vesicoureteral reflux) was achieved in 50% of patients and 58% of ureters. At a median followup of 4.5 years (range 1 to 9) success decreased to 35% of ureters. Overall, long-term success was found in 25% of patients who were free of vesicoureteral reflux and required no additional surgery. Of the patients 41% required additional urological surgery for vesicoureteral reflux or related conditions.

CONCLUSIONS: With long-term followup many patients who had initial improvement in vesicoureteral reflux ultimately experienced treatment failure and recurrence of reflux. At a median of 4.5 years 25% of patients with neurogenic bladder and vesicoureteral reflux were successfully treated with endoscopic injection of dextranomer/hyaluronic acid copolymer.

Salvage dextranomer-hyaluronic acid copolymer for persistent reflux after ureteral reimplantation: early success rates.


PURPOSE: Endoscopic injection of dextranomer-hyaluronic acid copolymer is an accepted initial procedure to correct vesicoureteral reflux. Less data are available on its role in treating failed ureteral reimplantation.

MATERIALS AND METHODS: We retrospectively reviewed the charts from 2002 to 2008 and identified 21 patients (26 ureteral units) with persistent reflux after reimplantation.

RESULTS: Mean age was 7 years (range 2 to 13). Mean followup was 2 years (range 10 to 46 months). Of the 17 patients with a single system ureteral reimplantation was extravesical in 9 and intravesical in 8 with tapering performed in 5. Three patients underwent reimplantation of duplex systems and 1 underwent reimplantation due to ureterocele. Residual reflux grade was 1 to 4 in 3 (11%), 17 (65%), 3 (11%) and 3 ureteral units (11%), respectively. Dextranomer-hyaluronic acid copolymer was injected transurethrally. The mean volume injected was 1.2 ml (range 0.7 to 3). After 1 injection reflux resolved in 15 patients (71%) or a total of 20 ureteral units (77%), including 12 of 14 (86%) extravesically and 8 of 12 (66%) intravesically reimplanted units. The resolution rate improved to 84% after multiple injections. Two of the 6 patients with reflux after 1 injection had a single system, 2 had an obstructive megaureter with tapered reimplantation, 1 had a duplicated system and 1 had a ureterocele. Three of the 5 patients with persistent reflux underwent revision surgery. Ureteral abnormalities other than reflux and tapered reimplantation were associated with a statistically significant inferior success rate.

CONCLUSIONS: Dextranomer-hyaluronic acid copolymer injection is an efficacious salvage procedure for persistent reflux after ureteral reimplantation. The success rate is inferior for ureteral abnormalities other than primary vesicoureteral reflux and after tapering.

An all-endo Approach to Complete Ureteral Duplications Complicated by Ureterocele and/or Vesicoureteral Reflux: Feasibility, Limitations, and Results
Calisti A, Perrotta ML, Coletta R, Olivieri C, Briganti V, Oriolo L, Fabbri R.

Purpose. Totally endoscopic management (all-endo) of patients with a duplicated renal system (DS) associated with severe vesicoureteral reflux (VUR) or obstructive ureterocele (UC) is an attractive alternative to traditional open procedures. The authors discuss feasibility and results of an all-endo approach on a consecutive series of patients.

Methods. From 1999 to 2009, all patients with a complete DS associated with UC and/or VUR were proposed for primary all-endo approach. UC puncture was performed using a 3Fr Bugbee electrode. Deflux (dextranomer/hyaluronic acid copolymer) injection was administered for VUR. The need for secondary surgery was evaluated on followup.

Results. Of the 62 patients recruited, 46 were treated using a primary all-endo approach and 16 patients received no treatment. Of the 46 treated patients with 56 affected renal units, 32 (97%) UCs collapsed following puncture and 29 (63%) VURs were resolved or downgraded. Secondary VUR occurred in 13 (39%) renal units. Secondary surgery was performed on 23 (41%) renal units.

Conclusion. The all-endo approach for VUR in DS is an effective therapeutic option. UC collapse was achieved by puncture in most of the patients; secondary VUR was the main complication in a small group of extravesical UC.

Single injection results of endoscopic treatment of vesicoureteric reflux with different tissue-bulking substances in patients with end stage renal failure.

Dirim A, Hasirci E, Turunc T, Aygun C, Ozkardes H.

PURPOSE: To evaluate the outcome of subureteral injections by using calcium hydroxyapatite (CaHa), dextranomer/hyaluronic acid copolymer (Dx/HA), and polydimethylsiloxane (PDS) in patients with end-stage renal failure (ESRF) who have vesicoureteral reflux (VUR).

PATIENTS AND METHODS: One hundred-one patients (166 renal units) with ESRF secondary to VUR were included in this retrospective study. The reflux was bilateral in 65 of the cases. CaHa, Dx/HA and PDS were used in 57, 26, and 18 patients, respectively. All patients were reviewed with regard to age, sex, reflux grade, type of injected materials, injectable agent volume, and outcome.

RESULTS: The reflux resolved completely in 30 patients (50/96 renal units, 52.1%), in 17 patients (27/44 renal units, 61.4%), and in 4 patients (5/26 renal units, 19.2%) with CaHa, Dx/HA, and PDS, respectively. Regression rates of reflux to grade I with these agents in the same order were 3.1% (2 patients, 3/96 renal units), 4.5% (1 patient, 2/44 renal units), and 11.5% (2 patients, 3/26 renal units). Thus, the overall success rate were noted as 55.2%, 65.9%, and 30.7%, respectively. There was no difference among these three injectables with regard to overall success rates (P = 0.062). No significant correlation with age, reflux grade, agent volume, and significant difference with sex were observed (P > 0.05).

CONCLUSIONS: In this group of patients, the success rate of the subureteral injection treatment does not appear to be affected by the type of the injectable agent. In addition, the cure rates were independent from the individual factors, reflux grades, and injected volumes.

Is endoscopic injection therapy a reasonable treatment option for low-grade vesicoureteral reflux in association with overactive bladder?

Kraft KH, Molitierno JA Jr, Dewhurst L, Geers C, Gunderson K, Scherz HC, Kirsch AJ.
Urology. 2011 Sep;78(3):675-8

OBJECTIVE: To assess the clinical outcome of endoscopic injection in children with vesicoureteral reflux (VUR) and concomittant overactive bladder (OAB).

METHODS: A total of 41 patients with VUR and OAB underwent endoscopic injection of dextranomer/hyaluronic acid. At surgery, 13 patients had been successfully treated for their OAB (urgency with or without wetting) with behavior modification with or without anticholinergic therapy, and 28 had persistent OAB despite treatment. Voiding cystourethrogram was obtained 6-12 weeks postoperatively, and patients were followed up clinically for 1-5 years.

RESULTS: Negative voiding cystourethrogram findings after a single treatment were seen in 34 (82.9%) of 41 patients. The radiographic success rate in patients with well-controlled OAB was 76.9% (10 of 13) compared with 85.7% (24 of 28) of those with poorly controlled OAB. The overall clinical success rate, defined as no evidence of urinary tract infection in the setting of negative voiding cystourethrogram findings, reached 78.0% (32 of 41). After successful endoscopic treatment, an unanticipated return to normal voiding patterns without the need for postoperative anticholinergic therapy was seen in 4 of the children with well-controlled OAB (40.0%) and in 4 with poorly controlled OAB (16.7%).

CONCLUSION: Our data suggest that endoscopic injection is a viable treatment option for VUR in those with OAB, with postoperative rates of resolution comparable to those found in patients without OAB. Furthermore, 40.0% of children with well-controlled OAB no longer required therapy for OAB after resolution of their VUR.

Endoscopic application of dextranomer/hyaluronic acid copolymer in the treatment of vesico-ureteric reflux after renal transplantation.

Pichler R, Buttazzoni A, Rehder P, Bartsch G, Steiner H, Oswald J.

OBJECTIVE: To evaluate the success of endoscopic dextranomer/hyaluronic acid copolymer (DHAC) application in the treatment of patients with recurrent urinary tract infections (UTIs) and vesico-ureteric reflux (VUR) into the transplanted graft after renal transplantation.

PATIENTS AND METHODS: Between January 2008 and April 2009, 19 patients with recurrent UTIs presented VUR proven by voiding cystourethrography. To correct VUR of the transplanted ureter, DHAC was injected endoscopically using hydrodistention technique. Pre- and postoperative serum creatinine levels, the number of pre- and postoperative UTIs, postoperative complications and reflux resolution rate were recorded. The mean follow-up was 6.5 months.

RESULTS: The average number of UTIs was reduced significantly from 4.89 (range 2-14) to 1.31 (range 0-4) on pre- and postoperative follow-up, respectively, of 6 months (P < 0.001). The success rate increased from 57.9% after the first injection to 78.9% after the second injection. The remaining four patients with residual VUR received long-term low dose antibiotic prophylaxis. In total, two (10.5%) patients developed increasing creatinine levels postoperatively as a result of distal ureteral obstruction, and temporary urinary drainage was necessary in both patients.

CONCLUSIONS: DHAC appears to be an efficient and minimal invasive method for treating VUR after renal transplantation with respect to short-term success. Further investigation with a larger group of patients and longer follow-up is needed to evaluate the prolonged effect, as well as any potential side effects.

Deflux injections for vesicoureteral reflux in transplanted kidneys.


INTRODUCTION: Vesicoureteral reflux (VUR), a complication after kidney transplantation, may be caused by recurrent urinary tract infections evaluating in life-threatening pyelonephritis and urosepsis. Open surgical correction is the standard treatment despite its morbidity. However, minimally invasive approaches are available.

MATERIALS AND METHODS: Our study group describes seven patients with functioning kidney grafts and a diagnosis of VUR associated with recurrent urinary tract infections. The procedure was performed under antibiotic prophylaxis and spinal anesthesia. An endoscopic injection of 1 mL of biomaterial (copolymer of dextranomer and hyaluronic acid) was administered into the ureteral neo-orifice following the Sting technique. The catheter was removed within 24 hours in all cases.

RESULTS: Between June 2009 and January 2010, nine procedures were performed in seven patients. Two patients experienced self-limiting post-surgical episodes of hematuria that did not need urologic manipulation. There were no episodes of retention, ureteral obstruction, or urinary infections. One patient required a reinjection 5 months later as a result of clinical failure. Apart from this one case, the other patients showed improvements with no infectious complications.

CONCLUSIONS: Endoscopic correction with VUR seems to be a reliable and safe option as a first treatment for the transplant patient. More cases are required in order to improve the learning curve and, therefore, the success rate. Closer monitoring is needed to evaluate the efficiency of the copolymer, the evolution of the reflux, and the possible long-term complications in this sort of patients.

Endoscopic treatment of symptomatic refluxing renal transplant ureteroneocystostomies in children


To present a multi-center experience with the use of Dx/HA copolymer for treatment of symptomatic refluxing renal transplant UNC in children. A multi-center, retrospective chart review was performed.

Eleven patients with a mean age of eight yr underwent renal transplantation with an anti-refluxing UNC. Data were collected to determine the safety and effectiveness of the procedure and to identify possible predictors of success.

Endoscopic treatment was successful in one of five males and five of six females, for an overall success rate of 54.5%. The etiology of renal failure was associated with success of treatment, with 4/6 (67%) patients with upper tract pathology demonstrating resolution of the VUR, as compared with one of three (33%) patients with lower tract pathology. Male patients had a higher incidence of lower tract pathology. No complications were associated with the endoscopic procedure.

Endoscopic injection of Dx/HA remains a safe option for the treatment of symptomatic refluxing transplant UNC in children. Although the success rate is lower than that seen in the treatment of primary VUR, the minimally invasive nature and safety of this technique may offer advantages over open reconstruction of the refluxing transplant ureter.

Endoscopic vesicoureteral reflux correction in transplanted kidneys: does injection technique matter?
Yucel S, Akin Y, Celik O, Erdogru T, Baykara M.
J Endourol. 2010 Oct;24(10):1661-4

AIM AND BACKGROUND: Posttransplant vesicoureteral reflux (VUR) is a common urologic complication after renal transplantation, although its management is controversial. The treatment of choice is open surgical revision ureteral reimplantation with significant morbidity. Recently, endoscopic correction by using nonanimal dextranomer/hyaluronic acid copolymer (NA Dx/HA) injection has been reported to be effective in the treatment of VUR of transplanted kidneys. Herein, we present our 3-year endoscopic correction results in transplanted kidneys where we used two different injection techniques, subureteral and intraureteral.

MATERIALS AND METHODS: We retrospectively reviewed all patients who underwent endoscopic VUR correction of posttransplant VUR by NA Dx/HA injection between July 2005 and March 2009. We excluded patients with underlying urologic abnormalities.

RESULTS: A total of 26 patients (14 women and 12 men) with a mean age of 32.2 years (range: 15–55) were studied. The VUR was also graded as nondilating reflux in 10 (grade I–II) and dilating reflux in 16 (grade III–IV). Seventeen ureters (5 nondilating and 12 dilating VUR) were injected NA Dx/HA intraureterally, and 9 ureters (5 nondilating and 4 dilating VUR) were injected NA Dx/HA subureterally. Overall success rate was 53.8% (14 out of 26). Intraureteral injection technique was successful in nine cases (52.9%), and subureteral injection technique was successful in five cases (55.5%). In nondilating VUR, injection corrected 90% (9 out of 10) of posttransplant patients, whereas in dilating VUR group injection corrected only 31.25% (5 out of 16). We found no statistical significance of injection technique on the success rate.

CONCLUSIONS: Endoscopic correction by using NA Dx/HA with any injection technique seems to be a plausible alternative to correction of refluxing posttransplant ureters, particularly in nondilating VUR.

Endoscopic treatment with Deflux for refluxing duplex systems


PURPOSE: The aim of this study was to review the experience of a single institution with the endoscopic Deflux (Q-Med Scandinavia, Uppsala, Sweden) procedure and assess its effectiveness in the treatment of refluxing duplex systems.

MATERIALS AND METHODS: A retrospective review of all patients that underwent endoscopic Deflux treatment for vesicoureteral reflux (VUR) in duplex systems between June 2003 and July 2007 was performed. Data collection included: age, gender, side of refluxing ureter, preoperative radiologic grade of VUR on a voiding cystourethrogram (VCUG), presence of VUR on a radionuclide VCUG 3 months postprocedure, volume of Deflux injected, number of Deflux injections performed per patient, and number of patients that underwent reimplantation surgery.

RESULTS: Sixteen patients with duplex systems, two being bilateral, for a total of 18 duplex ureteral systems, underwent the Deflux procedure. Grades of reflux were as follows: grade II: 4 ureters; grade III: 8 ureters; grade IV: 4 ureters; and grade V: 2 ureters. Deflux injection volume ranged from 0.28 to 1.5 cc (mean, 0.84). Fourteen ureteral systems required one injection, three required two injections, and one required three injections. The overall success rate of the procedure after a maximum of three injections was 94%. One patient with preoperative unilateral grade V reflux had persistent high-grade reflux after two injections and opted to proceed with surgical reimplantation. The mean follow-up was 24 months (mean, 6-48).

CONCLUSIONS: We conclude that the Deflux procedure is a safe, effective minimally invasive treatment alternative for patients with refluxing duplex systems.

Endoscopic treatment of vesicoureteral reflux in the previously reimplanted ureter: technical aspects and results

Capozza N, Nappo S, Caione P.

OBJECTIVES: To assess the feasibility and results of the endoscopic treatment of vesicoureteral reflux (VUR) after a failed ureteral reimplantation.

METHODS: From January 1996 to October 2006, 28 patients underwent endoscopic treatment for VUR grade II to V persisting after open ureteral reimplantation. VUR was bilateral in 11 patients, for a total of 39 ureteral units (UU) treated. The endoscopic treatment was performed 1 to 7 years after surgery (average 2.5 years). Dextranomer/Hyaluronic acid Copolymer (Dx/HA) was used as injectable material. The amount of injected material ranged from 0.5 to 2.8 ml (average: 1.2 ml). Some technical refinements were required to increase the success of the procedures. Patients were followed up from 2.5 to 17 years. Voiding cystourethrogram (VCUG) was performed at 6 months and MAG3 renal scan with voiding phase at 24 months. Results were compared with the outcome of the endoscopic treatment in patients treated by the same surgeons for primary VUR, matched for grade (control group).

RESULTS: All treatments were performed as one-day procedure. No complications were observed. Success was achieved in 22/28 patients (78.5%) and in 30/39 UU (76.9%) after failed ureteral reimplantation. No significant difference in success rate was found from the control group (p = ns).

CONCLUSIONS: Endoscopic treatment of VUR after a failed reimplantation is a feasible, minimally invasive procedure. The short hospital stay, the absence of complications, the safety of the currently available injectable materials, and the high rate of success lead us to strongly recommend the subeteric injection of a bulking material as a first line treatment, even in these particular patients. We believe endoscopic treatment should always be attempted in these complex cases of VUR, before committing patients to more difficult open procedures, which are not devoid of complications.

Unilateral vesicoureteral reflux and history of contralateral vesicoureteral reflux warranting routine bilateral endoscopic correction.

Chertin B, Natsheh A, Fadeev D, Shenfeld OZ, Farkas A.
J Urol. 2008 Oct;180(4 Suppl):1601-3;

PURPOSE: It has been shown that the incidence of de novo vesicoureteral reflux following unilateral endoscopic correction is low and does not justify prophylactic injection into the nonrefluxing ureter. We analyzed whether we should routinely treat each ureter in patients with a history of bilateral vesicoureteral reflux in whom reflux previously disappeared spontaneously on 1 side.

MATERIALS AND METHODS: Between 1991 and 2005, 458 children underwent endoscopic correction of unilateral vesicoureteral reflux. Of the children 15 with bilateral vesicoureteral reflux at the beginning of followup showed spontaneous reflux resolution on 1 side. Resolved reflux was grade II to IV in 5, 8 and 2 children, respectively. Mean time to reflux resolution was 3.3 years (range 2 to 5). Reflux corrected endoscopically was grade II to IV in 1, 6 and 8 children, respectively. All children were female and age at endoscopic correction was 2 to 16 years. None of the children had voiding dysfunction at the time of injection. Injection was performed routinely only into the refluxing ureter. Configuration of the orifice of the ureter with resolved vesicoureteral reflux was recorded at injection.

RESULTS: Vesicoureteral reflux was corrected in all except 1 ureter, in which reflux was downgraded to grade I. The configuration of the orifice of the ureter with resolved reflux was normal in all children. Of the 15 children 14 (93%) showed recurrent vesicoureteral reflux in previously resolved ureters. Recurrent reflux grade was I to III in 1 (7.1%), 6 (42.8%) and 7 children (50%), respectively. All children required endoscopic correction on the side of recurrence due to high grade reflux in 7 and breakthrough urinary tract infection in the remaining 7. In 2 cases (14.2%) renal scan revealed new renal scarring.

CONCLUSIONS: There is a high incidence of recurrent vesicoureteral reflux in previously resolved ureters following endoscopic correction on the contralateral side. Therefore, we recommend routine injection of the 2 ureters in patients with a history of bilateral vesicoureteral reflux.

Endoscopic treatment of vesicoureteral reflux in pediatric patients with the diagnosis of neurogenic bladder. Results and long-term outcome

Estornell Moragues F, Serrano Durbá A, Domínguez Hinarejos C, Ayuso González L, Martínez Verduch M, García Ibarra F.

OBJECTIVES: To know the results, complications and outcomes of eight patients with the diagnosis of neurogenic bladder (NB) who underwent vesicoureteral reflux surgery by subureteral injection of inert substances, trying to precise its indication in the therapeutic scheme for neurogenic bladder dysfunction.

METHODS: Retrospective review of the results and complications recorded during follow-up in eight pediatric patients with NB secondary to various pathologies and the diagnosis of VUR treated by subureteral injection of Teflon paste (1 case), polydimethylsiloxane (6) and dextranomer/hyaluronic acid copolymer (1).

RESULTS: In 8 (72.7%) of the 11 ureters treated VUR was cured after first injection. VUR stopped after second endoscopic treatment in 2 of the 3 ureters with persistent VUR. The efficacy of endoscopic treatment after second injection achieved 90.9%. In 2 unilateral cases we observed contralateral VUR, which cured in one case after endoscopic treatment and the other one followed a conservative scheme. Over the follow-up period (Mean FU time 51.8 +/- 28.5 months) 4 cases presented complications. VUR recurred in two: in one contralateral VUR was detected 19 months after first treatment, the other one presented bilateral ureterohydronephrosis with recurrent urinary tract infections and required augmentation cystoplasty.

CONCLUSIONS: Endoscopic treatment is an effective option when choosing surgical treatment for VUR in a patient with neurogenic bladder. It is necessary to follow the long-term outcome of patients after surgery, mainly those with abnormal bladder capacity and compliance and active or dyssynergic urethra due to the possibility of recurrence of the VUR.

The efficacy of endoscopic treatment for secondary vesicoureteral reflux. Analysis of a series of 142 cases

Fernández Hurtado MA, Barrero Candau R, Argüelles Salido E, Fernández Pineda I, García Merino F.

OBJECTIVES: To evaluate the rate of secondary or complicated vesicoureteral reflux (VUR) among the total number of VUR cases treated in our institution. To determine the efficacy of the endoscopic treatment in secondary or complicated VUR depending on etiology and grade.

METHOD: We review our experience with endoscopic treatment for VUR from 1992 to 2006. We have used three different materials: polytetrafluoroethylene (Teflon), polydimethylsiloxane (Macroplastique) and dextranomer/hyaluronic acid copolymer (Deflux). 479 ureters with VUR were treated in 402 patients; 124 patients and 142 ureters of them were secondary or complicated VUR cases. All patients were followed up with urinary tract ultrasound and radiological or isotopic voiding cystogram. Success is defined as VUR disappearance or improvement to grade I VUR without urinary infection after removing antibiotic prophylaxis.

RESULTS: The success rate has been 71.13% after the first injection, 85.92% after the second injection and 90.14% after the third injection. Mean subureteral dose has been 0.65 ml. The complications rate has been 0%.

CONCLUSIONS: The endoscopic treatment in secondary or complicated VUR is a minimally invasive procedure. It seems to be more difficult than in primary VUR cases, but its low morbidity and efficacy indicate this may be a proper first option in selected patients. In cases of VUR secondary to neurogenic bladder dysfunction it seems to be less successful, probably because of a worse control of the high bladder pressure.

Endoscopic injection of dextranomer hyaluronic acid copolymer for the treatment of vesicoureteral reflux in duplex ureters.


PURPOSE: Endoscopic injection of dextranomer hyaluronic acid copolymer (DxHA) has been increasingly utilized for the treatment of complex cases of vesicoureteral reflux (VUR). We present our 6-year experience with the use of DxHA for the treatment of VUR in duplex ureters.

MATERIALS AND METHODS: Between July 2001 and April 2007, 52 children were identified retrospectively who had been treated by endoscopic injection of DxHA for VUR into duplex ureters. Mean age was 3 years (range 9 months-10 years) with a mean maximum grade of reflux of III (range 2-5). The refluxing lower pole ureter was injected using a subureteric injection technique (STING) or intraureteric injection technique (utilizing the hydrodistention implantation technique). The endpoint in all cases was the loss of hydrodistention of the ureteral orifice. Voiding cystourethrograms was obtained at 6 weeks-3 months to evaluate for the presence of VUR. Cure was defined as complete resolution of reflux in the treated moiety.

RESULTS: After initial treatment, 38/52 (73%) patients were cured. Of the 14 failures, nine children underwent repeat endoscopic treatment with a 67% (6/9) resolution rate for repeat injection. Seven of the initial failures failed to grade I VUR. Overall, 85% (44/52) were cured after one or two treatments, 98% (51/52) were improved and only one (1.9%) with grade V VUR required open surgery. The treatment was well tolerated and there were no associated complications.

CONCLUSION: Endoscopic injection of DxHA copolymer corrected VUR in 85% of children with VUR into duplex ureters. This minimally invasive approach should be considered as a viable alternative to open surgery or antibiotic prophylaxis for the treatment of VUR associated with duplex ureters.

Utility of dextranomer/hyaluronic acid injection in setting of bladder and ureteral anomalies.

Routh JC, Kramer SA, Inman BA, Ashley RA, Wolpert JJ, Vandersteen DR, Husmann DA, Reinberg Y.


OBJECTIVES: Previous studies have shown that the cure rates after dextranomer/hyaluronic acid (Dx/HA) injection can be decreased in patients with neurogenic bladder, previous ureteroneocystostomy, duplicated ureters, or periureteral diverticula. We attempted to determine whether these factors reduce the efficacy of Dx/HA injection compared with that in otherwise normal patients.

METHODS: All children with vesicoureteral reflux (VUR) undergoing Dx/HA injection from April 2002 to March 2006 at two institutions were eligible for this study. Multivariate logistic regression models were built to assess the effect of bladder/ureteral anomalies on the success of Dx/HA injection. We adjusted for previously described predictors of injection success, including VUR grade, sex, age, surgeon experience, and injection technique.

RESULTS: A total of 543 refluxing ureters (373 patients) were included, of which 145 (27%) had persistent VUR on postoperative voiding cystourethrography; 86 ureters (16%) had anatomic anomalies. On univariate analysis, the most important predictors of injection failure were increasing VUR grade, male sex, younger age, subureteral injection, ureteral duplication anomaly, increasing Dx/HA volume, and surgeon experience. On multivariate analysis, however, the only significant predictors of injection failure were increasing VUR grade, subureteral injection technique, and surgeon experience. No anatomic or functional abnormalities, considered individually or grouped, significantly affected the probability of injection failure.

CONCLUSIONS: In our experience, children with functional and anatomic bladder/ureteral anomalies were no more likely to have Dx/HA injection fail than were children with uncomplicated VUR. The most important predictors of Dx/HA success remained VUR grade, injection technique, and surgeon experience. Dx/HA injection in patients with complex bladders could be a reasonable therapeutic option.

Endoscopic Deflux injection for pediatric transplant reflux: a feasible alternative to open ureteral reimplant.


OBJECTIVE: Pediatric renal transplantation is frequently performed using a freely refluxing vesicoureteral anastomosis. The resulting vesicoureteral reflux (VUR) may increase the morbidity of urinary tract infections (UTIs) that commonly occur in this setting, yet open surgical correction of the refluxing anastomosis can prove difficult. We report our experience using endoscopic injection of dextranomer/hyaluronic acid (Deflux) to correct transplant VUR.

MATERIALS AND METHODS: We retrospectively reviewed the charts of patients treated with endoscopic injection of Deflux (Q-Med, Uppsala, Sweden) for VUR into their renal allograft. Indications for inclusion in the study were renal allograft transplantation for primary end-stage renal disease, radiographically proven VUR into the allograft, normal voiding history, and at least one documented febrile UTI. Preoperative and postoperative images, including voiding cystourethrogram and allograft ultrasound, were compared. Location of the transplant orifice and volume of Deflux were recorded. Clinical outcomes, including documented UTI and changes in serum creatinine following treatment, were also assessed.

RESULTS: Eight patients were identified who were treated for transplant VUR, with a total of nine transplant ureters injected. Mean patient age at time of injection was 11.6 years (range: 7-19 years). Post-injection voiding cystourethograms and allograft ultrasound were available for all patients. Following treatment, four ureters demonstrated resolution of VUR and one ureter demonstrated improvement to grade 1 VUR. The remaining four ureters demonstrated no change in VUR grade. No patients showed any change in their serum creatinine, and no episodes of transplant pyelonephritis have occurred during the follow-up period. Mean post-injection follow-up has been 17.3 months (range 9-26 months).

CONCLUSION: Initial results demonstrate that endoscopic treatment with Deflux is feasible and may provide a less invasive alternative for treatment of transplant VUR. Further investigation with a larger group of patients and longer follow-up is needed.

Endoscopic treatment of vesicoureteral reflux associated with paraureteral diverticula in children.

Cerwinka WH, Scherz HC, Kirsch AJ.

PURPOSE: Paraureteral or Hutch diverticula are congenital bladder diverticula that occur at or adjacent to the ureteral hiatus and are associated with vesicoureteral reflux in the majority of cases. Surgical treatment has traditionally been ureteral reimplantation with or without diverticulectomy. We present our experience with endoscopic treatment of vesicoureteral reflux associated with paraureteral diverticula.

MATERIALS AND METHODS: Of 745 patients undergoing endoscopic treatment for vesicoureteral reflux between 2002 and 2006, 17 (2.3%) had paraureteral diverticula located at the refluxing ureter. The hydrodistention implantation technique was used and dextranomer/hyaluronic acid copolymer was used as bulking material. Success was defined as vesicoureteral reflux grade 0 on postoperative voiding cystourethrogram at 1 to 3 months after a single treatment.

RESULTS: A total of 20 refluxing ureters with associated paraureteral diverticula were treated in 17 patients. Of the cases 14 were unilateral and 3 were bilateral. Reflux was grade I in 6 patients, grade II in 4, grade III in 8, grade IV in 1 and grade V in 1. A mean of 1.2 ml bulking agent was injected per ureter. Overall success was 81% (13 of 16 patients) after a single injection. Success per vesicoureteral reflux grade was 100% (6 of 6 patients) for grade I, 100% (3 of 3) for grade II, 63% (5 of 8) for grade III, 100% (1 of 1) for grade IV and 100% (1 of 1) for grade V. Endoscopic treatment failed in 3 patients. Multivariate analysis identified large diverticular size and high bulking agent volume as predictors of treatment failure. Age, reflux grade and the presence of unilateral vs bilateral paraureteral diverticula did not impact outcome.

CONCLUSIONS: Endoscopic injection of dextranomer/hyaluronic acid copolymer is an excellent choice for the treatment of vesicoureteral reflux associated with paraureteral diverticula because it has a high success rate and avoids open surgery.

Subureteral injection of dextranomer/hyaluronic acid copolymer for persistent vesicoureteral reflux following ureteroneocystostomy.


PURPOSE: We sought to evaluate the use of subureteral dextranomer/hyaluronic acid copolymer injection for persistent vesicoureteral reflux following ureteroneocystostomy.

MATERIALS AND METHODS: We performed a retrospective review of patients who had undergone dextranomer/hyaluronic acid injection between 2002 and 2005 for persistent vesicoureteral reflux following ureteroneocystostomy. Analysis included evaluation of patient demographics, reflux grades, voiding dysfunction, reflux resolution rates and operative complications. Success was defined as no reflux on voiding cystourethrogram at 1 to 6 months postoperatively.

RESULTS: A total of 12 cases with 14 refluxing ureters were reviewed. Of the 12 patients treated 9 (10 ureters) had adequate followup. Mean followup was 10 months. Seven of 10 ureters (70%) demonstrated resolution of reflux after the initial injection. A second dextranomer/hyaluronic acid injection resulted in complete resolution in 2 of the 3 failed ureters (67%). Resolution in the remaining failed ureter could not be assessed due to insufficient patient followup. In children with adequate followup success was ultimately achieved in 9 of 9 ureters (100%) using up to 2 injections. A comparison of clinical factors between patients with success after the initial injection and those requiring 2 injections showed that the presence of persistent voiding dysfunction was the only parameter that was statistically significant. All patients tolerated the procedure without complications.

CONCLUSIONS: Considering the difficulties inherent in repeat surgery and the high success rate of dextranomer/hyaluronic acid injection in this series, this treatment is an appealing and reasonable option for patients with persistent vesicoureteral reflux following open ureteroneocystostomy.

Endoscopic Treatment With Stabilized Nonanimal Hyaluronic Acid/Dextranomer Gel is Effective in Vesicoureteral Reflux Associated With Bladder Dysfunction

Läckgren G, Sköldenberg E, Stenberg A. J Urol. 2007 Mar;177(3):1124-8

PURPOSE: Endoscopic injection of stabilized nonanimal hyaluronic acid/dextranomer gel is an established treatment for vesicoureteral reflux in children. We performed a subgroup analysis to assess this treatment in reflux associated with bladder dysfunction.

MATERIALS AND METHODS: Of 308 consecutive children treated endoscopically with stabilized nonanimal hyaluronic acid/dextranomer gel for dilating vesicoureteral reflux 54 were observed retrospectively to have bladder dysfunction. Initial followup consisted of voiding cystourethrogram at 3 and 12 months after injection, with positive response defined as reflux grade 0 or I. At 7 to 12 years following treatment patient charts were checked for urinary tract infections and bladder dysfunction, and a followup survey (postal questionnaire) was administered.

RESULTS: A positive response to therapy (cure) was observed in 45 children (83%) after 1 to 3 endoscopic treatments. Concurrently, bladder dysfunction had resolved in 32 patients (59%). After the last stabilized nonanimal hyaluronic acid/dextranomer gel implantation 45 patients (83%) were free of urinary tract infections. Questionnaire results were similar to chart based findings. Stabilized nonanimal hyaluronic acid/dextranomer gel implantation was well tolerated, with no associated complications.

CONCLUSIONS: Endoscopic treatment with stabilized nonanimal hyaluronic acid/dextranomer gel appears to be similarly effective in patients with vesicoureteral reflux with and without bladder dysfunction. These data indicate that bladder dysfunction should not be considered a contraindication to endoscopic treatment for reflux.
Transurethral injection therapy with dextranomer/hyaluronic acid copolymer (Deflux) for treatment of secondary vesicoureteral reflux after renal transplantation.


BACKGROUND AND PURPOSE: Secondary vesicoureteral reflux (SVUR) after renal transplantation may cause recurrent urinary-tract infections (UTI) and loss of renal function. There are only a few reports on the endoscopic treatment of SVUR by transurethral injection therapy. This is the first report of transurethral injection of dextranomer/hyaluronic acid copolymer (Deflux; Q-Med Scandinavia, Uppsala, Sweden) to relieve SVUR after renal transplantation.

PATIENTS AND METHODS: Between November 2003 and October 2005, four women were treated for SVUR with transurethral injections of dextranomer/hyaluronic acid copolymer. All patients had deterioration of renal function attributable to SVUR, recurrent UTI, or both. The mean follow-up was 29 months (range 16-38 months).

RESULTS: Initially, SVUR was corrected in all patients. Recurrent SVUR made a second treatment necessary in two patients. Three patients had no signs of SVUR 15, 27, and 36 months after the treatment. Renal function remained stable in these patients, and two were free of UTI. One of the patients who received two Deflux injections developed a filiform stenosis of the distal ureter, which was corrected by ureteropyeloplasty with the native ureter.

CONCLUSION: Transurethral injection therapy with Deflux is a minimally invasive treatment option for patients with SVUR after renal transplantation. A second treatment seems to be necessary in some cases. Complications such as ureteral obstruction may occur.

Endoscopic injection of dextranomer/hyaluronic acid copolymer to correct vesicoureteral reflux following failed ureteroneocystostomy


PURPOSE: The efficacy of endoscopic injection of dextranomer/hyaluronic acid to correct primary vesicoureteral reflux is well documented. We present experience at 2 institutions with endoscopic treatment for vesicoureteral reflux after failed ureteroneocystostomy.

MATERIALS AND METHODS: A retrospective review was performed of the records of all patients who underwent endoscopic dextranomer/hyaluronic acid injection to correct vesicoureteral reflux following ureteral reimplantation between April 2002 and July 2005. De novo ipsilateral vesicoureteral reflux was noted after repair of primary nonrefluxing megaureters or renal transplantation and persistent vesicoureteral reflux was noted following attempted vesicoureteral reflux repair. Injection was performed using the standard technique if the ureteral orifice was easily accessible, and percutaneously if access was difficult.

RESULTS: Nine male and 9 female patients were identified. Median age was 1.9 years at reimplantation and 6.5 years at injection, and median followup was 19 months. Ten patients underwent extravesical detrusorrhaphy and 8 underwent cross-trigonal reimplantation. Six patients underwent reimplantation for primary megaureter repair and all had resolution of vesicoureteral reflux with injection. Of the 20 renal units 16 (80%) and 15 of 18 patients (83%) had complete resolution of vesicoureteral reflux after 1 injection. One patient had improvement in vesicoureteral reflux and 2 had no improvement. There were no complications resulting from injections.

CONCLUSIONS: Endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid following extravesical or cross-trigonal reimplantation is safe and efficacious, at least at short-term followup. Endoscopic injection should be considered first line treatment for this situation.

Subureteral dextranomer/hyaluronic acid copolymer injection for vesicoureteral reflux in transplant candidates.


BACKGROUND AND PURPOSE: Endoscopic subureteral injection of tissue-augmenting substances has become an alternative to antibiotic prophylaxis and open surgery for the management of vesicoureteral reflux (VUR). Several injectable materials have been tried for this purpose. In this study, we tried to determine the efficacy of dextranomer/hyaluronic acid copolymer (Dx/HA) injection for the treatment of VUR in renal-transplant candidates.

PATIENTS AND METHODS: A total of 21 transplant candidates (29 ureteral units; 13 females, 8 males) with a mean age of 20.2 years (range 14-26 years) underwent endoscopic correction of VUR with Dx/HA. Diagnosis of VUR was made by voiding cystourethrography. The efficacy of the treatment was assessed with voiding cystourethrography at 3 months and 1 year postoperatively. Renal transplantation with living related donor organs was performed in 11 of the 21 patients.

RESULTS: Endoscopic treatment was performed without complication in all cases. Higher success rates were obtained in patients with low-grade reflux, the overall success rate in the series being 82.7%. The mean follow-up after renal transplantation was 21.8 months (range 5-45 months). In one patient, reflux recurred after renal transplantation and was treated successfully by a repeat Dx/HA injection. The urine cultures of all patients remained sterile.

CONCLUSION: Transplant candidates with VUR can be treated with Dx/HA, which cured the majority of our patients after one or two treatments with few low side effects. Endoscopic subureteral injection of Dx/HA has become an alternative treatment for VUR in transplant candidates. Long-term results are needed before making a final statement about its value.

Endoscopic treatment with dextranomer/hyaluronic acid for complex cases of vesicoureteral reflux


Purpose: The surgical correction of primary vesicoureteral reflux (VUR) is highly successful. This success decreases in more complex cases and often involves reoperation and increased morbidity. We present our experience with the use of subureteral injection of dextranomer/hyaluronic acid (Dx/HA) in complex cases of vesicoureteral reflux in which open surgery would have been indicated.

Materials and Methods: Between October 2001 and July 2003, 72 patients 9 months to 31 years old (mean age 5.6 years) underwent subureteral injection of Dx/HA for complex VUR at our institutions. Dx/HA was injected submucosally within the intramural ureter (modified STING) in most cases. A guidewire was used to manipulate the ureteral orifice and a retrograde ureterogram was used to delineate the anatomy in selected cases. The average volume of injected material was measured for each ureter. Renal sonography was performed to determine if hydronephrosis was present. At 3 months fluoroscopic voiding cystourethrograms were used to evaluate for the presence of VUR.

Results: A total of 93 ureters were treated in 55 girls and 17 boys. All cases were considered to be complex as 17 had persistent reflux after open surgery (7 megaureters repairs, 2 extravesical repairs, 7 intravesical reimplants and 1 blind ureter), 11 had persistent reflux and neurogenic bladder, 7 had ectopic ureters to bladder neck, 6 had bilateral Hutch diverticulum, 6 had persistent stump reflux, 5 had ureteroceles after puncture or incision, 15 had duplications, 1 had the prune belly syndrome, 2 had posterior urethral valve following resection, 1 had epispadias and 1 had urogenital sinus. The average maximum reflux grade was IV. An average of 1.1 cc (range 0.4 to 2) was injected per ureter. Of the patients 69 had 3-month followup results. The overall success rate was 68% after 1 implantation (47 of 69).

Conclusions: Submucosal intravesical implantation with Dx/HA corrected complex vesicoureteral reflux in 68% of patients. In all of these patients open surgery would have potentially been difficult. The use of fluoroscopy and/or guidewires is a useful adjunct in these cases. We believe that this minimally invasive approach is warranted as an initial step in the management of complex cases of VUR before resorting to more difficult open surgical procedures.
Endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid copolymer is effective in either double ureters or a small kidney.

Läckgren G, Wåhlin N, Sköldenberg E, Nevéus T, Stenberg A.

PURPOSE: Endoscopic injection of dextranomer/hyaluronic acid (Dx/HA) copolymer is an increasingly established treatment for primary vesicoureteral reflux (VUR) in children. We performed a retrospective analysis to assess this treatment for VUR associated with either double ureters or a small kidney.

MATERIALS AND METHODS: The study included 68 children with duplex ureters and 40 with a small kidney (1 kidney contributing 10% to 35% of total renal function) who underwent endoscopic treatment with Dx/HA copolymer for VUR. Followup consisted of voiding cystourethrography 3 and 12 months after injection. Positive response was defined as reflux grade 0 or I. As many as 2 repeat injections were offered to nonresponders, and those with persistent reflux were referred for open surgery. Long-term clinical followup with renal function testing was continued for 4 to 9 years.

RESULTS: A positive response was observed in 63% of children with duplex ureters, with only 17 (25%) patients requiring open surgery. Among children with a small kidney the response rate was 70%, and open surgery was performed in 9 (23%). In both treatment groups a positive response to treatment was sustained throughout the followup period in all cases. The treatment was well tolerated, with no complications associated with the procedure.

CONCLUSIONS: Endoscopic treatment with Dx/HA copolymer appears to be an effective and well tolerated alternative to open surgery for first line treatment of VUR associated with double ureters or a small kidney.

Endoscopic treatment of children with bladder dysfunction and vesicoureteral reflux with dextranomer/hyaluronic acid copolymer - long-term results

G. Läckgren, N. Wählin, E. Sköldenberg, A. Stenberg
Presented at ICCS 2002

Background: For children with coexistent high-grade vesicoureteral reflux (VUR) and bladder dysfunction, it is generally believed that active treatment for VUR should be delayed until after the bladder has been treated. We performed a retrospective study to assess the outcome of endoscopic injection with dextranomer/hyaluronic acid (Dx/HA) copolymer among children with VUR and bladder dysfunction.

Material and methods: In total, 309 consecutive children with persistent VUR (grade III-V) were treated endoscopically with Dx/HA copolymer between May 1993 and May 1998. Fifty children (45 girls and 5 boys; mean age 5 years) had bladder dysfunction at the time of treatment i.e. at least one of the following symptoms: high urinary urgency/frequency; daytime wetting or “lazy bladder”; poor emptying). A retrospective control of these children’s medical records was performed in 2002, and cure was defined as reflux grade 0-1 at the last investigation.

Results: One patient was lost to follow-up; the remaining 49 were followed for a period of 4-9 years (mean 5.5 years) after the last endoscopic treatment. Fifteen patients received more than one endoscopic treatment, resulting in a mean of 1.3 treatments/patient. The post-treatment cure rate was 82% (40 patients) and two further patients were improved. Seven patients (14%) did not respond to treatment, but no children were referred for open surgery.

Conclusion: The present study indicates that minor bladder dysfunction does not reduce the cure rate of endoscopic treatment with Dx/HA copolymer for VUR. This suggests that VUR may contribute to the cause of bladder dysfunction.
VUR - Cost Analysis

Injection volumes of dextranomer/hyaluronic acid are increasing in the endoscopic management of vesicoureteral reflux.


PURPOSE: Dextranomer/hyaluronic acid (Deflux) has been increasingly used for the treatment of vesicoureteral reflux (VUR). Experience has shown that injecting more volume of material is necessary to achieve greater success. We evaluate trends in the number of vials being used to treat VUR using a multi-institutional database and data from patients treated at our own institution.

METHODS: Children of age 0-19 years in the Pediatric Health Information System (PHIS) database from 2003 to 2008 were extracted with a VUR diagnosis (ICD-9 593.7x) and subureteric injection procedure code (CPT 52327). We identified children with reflux treated with endoscopic injection at Seattle Children’s Hospital from 2005 to 2008. Hospital trends of the number of vials used were evaluated using multivariate linear regression.

RESULTS: From 2003 to 2008, we identified 4,078 endoscopic injection procedures in PHIS. There was a 33% increase in the average number of vials used per patient (p < 0.0001) with more than a threefold increase in the number of patients receiving three or more vials per procedure. All institutions increased the average vials used per patient with the most pronounced increase at the highest-volume centers. These trends were also present in the 186 children treated at our own institution.

CONCLUSION: Over the study period there was an increase in the number of vials of dextranomer/hyaluronic acid being used per patient to treat children with VUR. This practice may improve success rates but will increase the cost of treatment due to the inherent expense of the material.

The cost-effectiveness of endoscopic injection of dextranomer/hyaluronic acid copolymer for vesicoureteral reflux.


PURPOSE: Vesicoureteral reflux is a risk factor for progressive renal damage associated with urinary tract infection. Mild to moderate reflux is routinely treated with long-term antibiotic prophylaxis to prevent recurrent infections and open surgical reimplantation for breakthrough infections despite antibiotic therapy. Endoscopic subureteral injection of implant material is a therapeutic alternative to long-term prophylaxis and open surgery but its widespread use in the United States has been prevented by the lack of a stable implant material. Dextranomer/hyaluronic acid copolymer has been shown to be a safe, effective and durable implant material and was recently approved in the United States. We estimate the effect on costs and cure rates of introducing endoscopic injection with dextranomer/hyaluronic acid copolymer as a treatment alternative in the United States.

MATERIALS AND METHODS: We constructed a model that mimics current clinical practice of vesicoureteral reflux treatment for 6 years, and incorporates spontaneous resolution and surgical intervention rates obtained from 2 long-term followup studies. The treatment algorithm was established using medical data from the literature, and clinical management practices from a Delphi survey of 27 pediatric urologists and nephrologists across the United States. Endoscopic injection was introduced into the model as replacement to surgery or alternative to long-term antibiotic prophylaxis. The effectiveness of dextranomer/hyaluronic acid copolymer was calculated from 140 patients (208 ureters) with grade III reflux treated in a clinical study of 221 children in Sweden.

RESULTS: With current practice, the average cost per patient in 6 years was 6,640 US dollars and 23.5% of patients continued to have reflux. Replacing open surgery with endoscopic injection led to similar cure rates (22.2% failures) but costs were reduced to 5,522 US dollars. When injection was performed after 1 year of antibiotic therapy failure rates were reduced to 8.5% but costs increased to 7,644 US dollars.

CONCLUSIONS: Our results show that a persistent approach to endoscopic surgery can be expected to result in overall success that equals or exceeds open surgery at a lower cost. This finding is particularly true if open reimplant is reserved for patients with high grade or persistent vesicoureteral reflux.

**VUR - Diagnostic**

The appearance of dextranomer-hyaluronic acid copolymer implants on ultrasound may predict resolution of vesicoureteral reflux after injection therapy.

Park KJ, Jeon TY, Yoo SY, Kim JH, Eo H, Song KD
Clin Radiol. 2014 Sep;69(9):939-44.

**AIM:** To investigate the correlation between implant appearance on ultrasound (US) and voiding cystourethrogramy (VCUG) results after dextranomer-hyaluronic acid copolymer (DxHA) injection in children with vesicoureteral reflux (VUR).

**MATERIALS AND METHODS:** Consecutive cases of primary VUR treated by endoscopic subureteral injection of DxHA were retrospectively reviewed. All children had postoperative bladder US and VCUG with a mean interval of 34 days and 47 days after injection, respectively. VUR resolution at postoperative VCUG was considered as treatment success. Implant appearance on US was graded according to the retained volume and its location by visual inspection; it was then correlated with VCUG results using the Spearman correlation coefficient.

**RESULTS:** A total of 36 children (56 ureters) were identified in which 38 ureters (68%) had a clearly visualized implant on postoperative US and 40 ureters (71%) showed VUR resolution. The sensitivity of implant visualization on US for predicting reflux resolution was 73% (29/40), specificity 44% (7/16), positive predictive value 76% (29/38), and negative predictive value 39% (7/18). The grade 1, grade 2, and grade 3 implant appearances showed VUR resolution in 88% (22/25), 54% (7/13), and 61% (11/18), and showed persistent VUR in 8% (2/25), 15% (2/13), and 28% (5/18), respectively (p = 0.032).

**CONCLUSION:** The implant appearance on postoperative US showed good correlation with VCUG results in the early post-injection period. Large retained implants were associated with treatment success, while small or non-visualized implants were related to the persistent reflux.

Intraoperative contrast-enhanced urosonography during endoscopic treatment of vesicoureteral reflux in children.

Woźniak MM, Osemłak P, Pawelec A, Brodzisz A, Nachulewicz P, Wieczorek AP, Zajączkowska MM.

BACKGROUND: There are many controversies surrounding the effectiveness of endoscopic treatment of vesicourethral reflux (VUR) in children, thus it is of highest priority to analyze factors influencing the outcome of therapy and to search for new methods that would increase the success rate and reduce the number of reinjections.

OBJECTIVE: The aim of the study was to analyze whether intraoperative contrast-enhanced urosonography (ce-US) may increase the effectiveness of endoscopic anti-reflux therapy.

MATERIALS AND METHODS: Intraoperative contrast-enhanced urosonography (ce-US) with SonoVue® was performed in 17 patients (25 ureteral units) undergoing endoscopic treatment of VUR. Ce-US was performed in the operating room before the procedure and after injection of the bulking material. When VUR persisted, the operator repeated the injection, which was followed by ce-US. The results were compared with those obtained from a control group (15 patients; 22 ureteral units).

RESULTS: A repeat injection during a single endoscopic treatment was required in 24% of cases. The overall success rate confirmed at 6-12 months’ follow-ups was 84%. The success rate was significantly higher in comparison to the control group (success: 64%).

CONCLUSION: Intraoperative ce-US performed during endoscopic treatment of VUR enables immediate monitoring of outcome and provides the opportunity for repeat injection during the same procedure, thus increasing the efficacy of the procedure and reducing the number of reinjections.

Is the appearance of the Deflux Mound predictive of Reflux Resolution?

Hidas G, Soltani T, Lusch A, Khoury AE.

PURPOSE: To correlate the appearance of the Deflux mound after endoscopic correction of vesicoureteral reflux with the outcome

MATERIAL AND METHODS: We created an online survey based on 11 primary vesicoureteral reflux (VUR) cases (15 renal units, 6 failed and 9 successful procedures). Cases were selected randomly from our video library. All cases were performed by a single surgeon using the double hydrodistention-implantation technique (HIT) until a satisfactory mound was achieved and hydro-distention (HD) corrected. Online survey questionnaire was emailed to 234 members of the society of pediatric urology. Each survey question contained preoperative voiding cystourethrogram (VCUG) image as well as figures of the ureteral orifice before and after injection. Responders were asked to predict whether they thought that appearance of the Deflux mound appearance will be associated with a successful resolution of reflux at a 3 month postoperative VCUG. Percentage of correctly answered questions as well as sensitivity and specificity and predictive values of expert ability to predict outcome were analyzed.

RESULTS: 104 Pediatric urologists responded to the survey. Overall 66.4% of the responders were able to predict the resolution of reflux based on the appearance of the Deflux mound, (66% were able to correctly predict success and 67% correctly predicted failure). Mean outcome predictability per responders was 66% (range 26% to 86%).

CONCLUSION: The appearance of the Deflux mound and the lack of HD at the completion of the procedure are not a reliable predictor of outcome. Based on the above experience, postoperative VCUG is still required to truly determine reflux resolution.

Factors that impact the outcome of endoscopic correction of vesicoureteral reflux: a multivariate analysis.

Kajbafzadeh AM, Tourchi A, Aryan Z.
Int Urol Nephrol. 2012 Nov 17. [Epub ahead of print]

PURPOSE: To identify independent factors that may predict vesicoureteral reflux (VUR) resolution after endoscopic treatment using dextranomer/hyaluronic acid copolymer (Deflux®) in children free of anatomical anomalies.

MATERIALS AND METHODS: A retrospective study was conducted in our pediatric referral center from 1998 to 2011 on children with primary VUR who underwent endoscopic injection of Deflux® with or without concomitant autologous blood injection (called HABIT or HIT, respectively). Children with secondary VUR or incomplete records were excluded from the study. Potential factors were divided into three categories including preoperative, intraoperative and postoperative. Success was defined as no sign of VUR on postoperative voiding cystourethrogram. Univariate and multivariate logistic regression models were constructed to identify independent factors that may predict success. Odds ratio (OR) and 95 % confidence interval (95 % CI) for prediction of success were estimated for each factor.

RESULTS: From 485 children received Deflux® injection, a total of 372 with a mean age of 3.10 years (ranged from 6 months to 12 years) were included in the study and endoscopic management was successful in 322 (86.6 %) of them. Of the patients, 185 (49.7 %) underwent HIT and 187 (50.3 %) underwent HABIT technique. On univariate analysis, VUR grade from preoperative category (OR = 4.79, 95 % CI = 2.22-10.30, p = 0.000), operation technique (OR = 0.33, 95 % CI = 0.17-0.64, p = 0.001) and presence of mound on postoperative sonography (OR = 0.06, 95 % CI = 0.02-0.16, p = 0.000) were associated with success. On multivariate analysis, preoperative VUR grade (OR = 4.85, 95 % CI = 2.49-8.96, p = 0.000) and identification of mound on postoperative sonography (OR = 0.07, 95 % CI = 0.01-0.18, p = 0.000) remained as independent success predictors.

CONCLUSION: Based on this study, successful VUR correction after the endoscopic injection of Deflux® can be predicted with respect to preoperative VUR grade and presence of mound after operation.

The Value of PIC Cystography in Detecting De Novo and Residual Vesicoureteral Reflux after Dextranomer/Hyaluronic Acid Copolymer Injection

Palmer BW, Hemphill M, Wettengel K, Kropp BP, Frimberger D.
Int J Nephrol. 2011;2011:276308

The endoscopic injection of Dx/HA in the management of vesicoureteral reflux (VUR) has become an accepted alternative to open surgery. In the current study we evaluated the value of cystography to detect de novo contralateral VUR in unilateral cases of VUR at the time of Dx/HA injection and correlated the findings of immediate post-Dx/HA injection cystography during the same anesthesia to 2-month postoperative VCUG to evaluate its ability to predict successful surgical outcomes. The current study aimed to evaluate whether an intraoperatively performed cystogram could replace postoperative studies.

But a negative intraoperative cystogram correlates with the postoperative study in only 80%. Considering the 75-80% success rate of Dx/HA implantation, the addition of intraoperative cystograms cannot replace postoperative studies. In patients treated with unilateral VUR, PIC cystography can detect occult VUR and prevent postoperative contralateral new onset of VUR.

Presence of dextranomer-hyaluronic acid (DxHA) mound on postoperative ultrasound does not predict resolution of vesicoureteral reflux.


OBJECTIVE: Dextranomer-hyaluronic acid (DxHA) injection is an accepted treatment for vesicoureteral reflux (VUR), with success rates as high as 85-90% in selected patients. The DxHA mound can often be seen on postoperative ultrasound. We sought to determine whether the presence or absence of this mound on ultrasound can predict resolution of VUR on voiding cystourethrogram (VCUG).

MATERIALS AND METHODS: A retrospective study evaluating patients who underwent cystoscopy and injection of DxHA from 2003 to the present was performed. Demographic variables, laterality and grade of VUR, postoperative ultrasound findings, and presence of VUR on postoperative VCUG were recorded.

RESULTS: Fifty-one patients (95 ureters) underwent DxHA injection and had a postoperative ultrasound and VCUG for review. Five patients with persistent voiding dysfunction were excluded, leaving 46 patients and 86 ureters for review. The mean age at time of injection was 5.2 years (range 0.75-11 years) and mean grade of VUR was 2.5 (range 1-5). After DxHA injection, 75% of the ureters showed resolution of VUR, while 25% demonstrated persistent VUR. No correlation was made between the presence of DxHA mound and resolution of VUR on VCUG.

CONCLUSION: In this series, the presence of a DxHA mound on initial postoperative ultrasound does not predict resolution of VUR. A larger prospective study is needed to evaluate additional parameters.


OBJECTIVES: We evaluated whether real-time 3D ultrasound (4D-US) together with clinical evaluation is an alternative to voiding cystourethrography (VCUG) after endoscopic treatment of vesicoureteral reflux (VUR) in children at postoperative follow-up.

MATERIAL AND METHODS: We reviewed 178 children who underwent endoscopic therapy with dextranomer/hyaluronic acid copolymer in grade II or III VUR between 2002 and 2005. 4D-US was performed in all patients 1 day and 3, 9 and 18 months after endoscopic therapy. Only children with postoperative urinary tract infections (UTIs) and/or nonorthotopic position of the bulking agent were referred for VCUG.

RESULTS: In 93% of the ureteral units, the depot could be detected in the orthotopic position after 3, 9 and 18 months. None of these children developed UTIs in the postoperative follow-up. Twelve children demonstrated a shifting of the depot, indicating a possible therapy failure. Eight of these 12 patients (66.7%) presented a positive VCUG, and 50% of them sustained UTIs.

CONCLUSIONS: 4D-US seems to be a sufficient protocol in the follow-up of children after endoscopic treatment of low-grade VUR. VCUG should be performed in cases of a shifted position of the depot; invasive investigations are unnecessary in asymptomatic children with orthotopic bulk.

Can we rely on the presence of dextranomer-hyaluronic acid copolymer mounds on ultrasound to predict vesicoureteral reflux resolution after injection therapy


PURPOSE: We determined whether the presence or absence of dextranomer-hyaluronic acid copolymer mounds on bladder ultrasound coincides with voiding cystourethrogram results after injection therapy in children with primary vesicoureteral reflux.

MATERIALS AND METHODS: We retrospectively reviewed consecutive cases of dextranomer-hyaluronic acid copolymer injection for primary vesicoureteral reflux. The primary outcome investigated was the appearance of dextranomer-hyaluronic acid copolymer mounds on ultrasound and their association with voiding cystourethrogram results postoperatively. An intramural dextranomer-hyaluronic acid copolymer mound on ultrasound was considered a negative test result for vesicoureteral reflux.

RESULTS: A total of 187 cases were identified, of which 132 had imaging available for evaluation. Intramural mounds were seen on ultrasound in 86 cases postoperatively, of which 34 (40%) had a positive voiding cystourethrogram. Of 46 cases in which no mound was identified 21 (46%) had a positive voiding cystourethrogram. The sensitivity of ultrasound to determine the presence or absence of vesicoureteral reflux was 38%, specificity was 67%, accuracy was 55%, the positive predictive value was 46% and the negative predictive value was 60%.

CONCLUSIONS: Our results indicate poor correlation of dextranomer-hyaluronic acid copolymer mound appearance on ultrasound with voiding cystourethrogram results after injection. To adequately evaluate for the resolution of vesicoureteral reflux a voiding cystogram or nuclear medicine cystogram needs to be performed after injection therapy.

Appearance of Deflux implants with magnetic resonance imaging after endoscopic treatment of vesicoureteral reflux in children.


OBJECTIVE: With the increasing popularity of endoscopic treatment for vesicoureteral reflux (VUR) in children, dextranomer/hyaluronic acid copolymer (Deflux) implants are more frequently detected by magnetic resonance imaging (MRI). Such findings on MRI may be misinterpreted and lead to unnecessary intervention. The objective of this study was to characterize the appearance of Deflux implants on MRI.

MATERIALS AND METHODS: Between July 2001 and November 2007, hospital charts of patients with a history of Deflux injection for VUR were evaluated to identify those who had subsequent MRI studies. The indications were determined, and the appearance of Deflux implants analyzed and compared to findings on ultrasound, voiding cystourethrography and kidney ureter bladder radiography.

RESULTS: Of 893 patients who underwent endoscopic treatment for VUR, subsequently 16 patients (1.8%) had MRI scans. Twenty-seven Deflux implants were identified on MRI as bright structures on T2-weighted sequences only. Neither T1-weighted images nor excretory MR urography visualized the Deflux implants, which did not enhance with gadolinium. Deflux was not detected by kidney ureter bladder radiography; however, voiding cystourethrography and more reliably ultrasound could identify implants.

CONCLUSIONS: Deflux implants appear on MRI as bright structures on T2-weighted sequences. History of VUR/VUR treatment and the presence of a single urinary system should provide reassurance and prevent inappropriate intervention for misdiagnosed ureteroceles.

Clinical experience with positional installation of contrast cystography and simultaneous Deflux injection in children with occult vesicoureteral reflux.

Noe HN, Williams MA.

Forty-seven otherwise healthy children with a diagnosis of urinary tract infection and pyelonephritis were referred for evaluation following standard imaging studies which showed no renal abnormalities and a normal voiding cystourethrogram.

All were evaluated with positional instillation of contrast at the time of cystoscopy using spot fluoroscopy to detect vesicoureteral reflux. Simultaneous Deflux injection was performed if reflux was demonstrated at cystoscopy. These findings may provide new insights on the entity of non-refluxing pyelonephritis.

Seventy-five per cent had reflux demonstrated and were treated. The study group was followed for an average of 16 months and the incidence of pre- and post-treatment febrile infections were compared. A significant reduction in febrile infections was noted following treatment. Three children continued to have febrile urinary infections and were successfully reimplanted and experienced no further febrile urinary infections.

No complications from this study occurred and some factors were discovered which may help in deciding which patients may benefit from this approach.

Bladder ultrasound in the evaluation of the efficacy of dextranomer/hyaluronic acid injection for treatment of vesicoureteral reflux


PURPOSE: To determine whether sonographic examination of subureteral implants after endoscopic dextranomer/hyaluronic acid (DHA) injection would help to evaluate the efficacy of this method in the treatment of vesicoureteral reflux.

MATERIALS AND METHODS: Thirty-six patients (49 ureters) who underwent endoscopic subureteral DHA injection were evaluated using voiding cystourethrography (VCUG) and bladder sonography for a mean duration of 2.1 years (range, 3 months to 6.5 years) after treatment. Patient records-including the results of VCUG, renal sonography, Dimercapto succinic acid (DMSA) scintigraphy, and periodic urinary analysis-were also reviewed to determine the outcome of treatment.

RESULTS: Reflux was corrected in 43/49 (88%) ureters (complete cure in 38, downgrading of reflux in 5). No change was noted in 6 (12%) ureters on VCUG. The reflux was found to be corrected in 19/22 (86%) ureters, with the implants clearly identifiable on sonography. However, reflux was documented in only 3/27 (11%) ureters, around which no implant was seen on sonography.

CONCLUSION: The identification of the implant in the subureteral region by bladder sonography correlated with resolution of reflux in the early postinjection period. On the other hand, the majority of the implants disappeared on sonography in the long term despite correction of reflux. Therefore, we believe that the use of bladder sonography is not useful in the evaluation of patients in long-term follow-up.

Lack of usefulness of positioned instillation of contrast cystogram after injection of dextranomer/hyaluronic acid.

Pinto KJ, Pugach J, Saalfield J.

PURPOSE: Positioned instillation of contrast cystograms have been touted as possibly being more sensitive than standard cystograms for evaluation of vesicoureteral reflux. We performed positioned instillation of contrast cystograms intraoperatively, immediately after the injection of dextranomer/hyaluronic acid to treat vesicoureteral reflux, to determine whether they might be predictive of operative success and obviate the need for the standard postoperative voiding cystourethrogram, which is usually performed at 3 months.

MATERIALS AND METHODS: Patients with vesicoureteral reflux and no confounding conditions were treated with dextranomer/hyaluronic acid and subsequent positioned instillation of contrast cystogram while under the same anesthesia between November 2003 and March 2005. The results of this intraoperative cystogram were compared to the results of the postoperative voiding cystourethrogram performed 3 to 4 months later.

RESULTS: A total of 61 patients met the inclusion criteria and underwent positioned instillation of contrast cystogram after dextranomer/hyaluronic acid injection. Only 53 patients (86 ureters) completed the necessary postoperative evaluation. Positioned instillation of contrast cystogram added 4 minutes to the procedure and required about 4 seconds of fluoroscopy per ureter evaluated. The overall success rate for correcting reflux was 84% (72 of 86 ureters cured). None of the 14 ureters with persistent postoperative reflux was identified by intraoperative cystogram, and 3 patients were misidentified as having reflux despite cure confirmed postoperatively. Intraoperative positioned instillation of contrast cystogram was predictive of treatment failure 0% of the time (sensitivity 0%). There were no complications.

CONCLUSIONS: Positioned instillation of contrast cystogram performed immediately after injection of dextranomer/hyaluronic acid was not useful in predicting which patients would have persistent reflux postoperatively. Patients are best served with the extant protocol of conventional cystography 3 to 4 months postoperatively.

Renal ultrasound studies after endoscopic injection of dextranomer/hyaluronic acid copolymer for vesicoureteral reflux.

Yu RN, Jones EA, Roth DR. Urology. 2006 Oct;68(4):866-8

OBJECTIVES: To examine the outcomes of renal ultrasound studies after subureteral injection of dextranomer/hyaluronic acid copolymer and provide recommendations for postoperative management of vesicoureteral reflux (VUR).

METHODS: Pediatric patients aged 15 years or younger with uncomplicated primary VUR were recruited for endoscopic treatment with dextranomer/hyaluronic acid gel. After undergoing the procedure, patients were instructed to continue prophylactic antibiotic treatment until a follow-up voiding cystourethrogram was obtained 2 weeks or more after treatment. VUR resolution was defined as grade 0. Repeat endoscopic injection was offered to patients with persistent VUR. Postoperative renal ultrasound scans were obtained on the same day as the voiding cystourethrogram.

RESULTS: Of 120 patients treated, 6 were lost to follow-up and 14 had not yet undergone the posttreatment evaluation. The 100 remaining patients (efficacy population) had a mean age of 4.2 years (range 0.5 to 15), and the median reflux grade was 2 (range 1 to 5). The overall VUR resolution rate for the patients was 87% after endoscopic injection. Of 100 patients, 88 achieved complete resolution after a single injection and 19 required a repeat injection. Of the 100 patients who underwent postoperative ultrasound examination, none demonstrated renal ultrasound changes consistent with significant ureteral obstruction or renal parenchymal changes.

CONCLUSIONS: Renal ultrasound studies after endoscopic treatment with dextranomer/hyaluronic acid gel are unnecessary after determination of reflux resolution by voiding cystourethrography.

VUR - Quality of Life

Vesicoureteral reflux: Endoscopic therapy and impact on health related quality of life.


AIM: To evaluate the health related quality of life (HRQOL) after endoscopic injection treatment for vesico ureteral reflux (VUR) in children.

MATERIALS AND METHODS: Fifty four children received treatment and were prospectively evaluated for their quality of life scores, according to resolution of reflux on cystograms and status of renal scars.

RESULTS: Of the 81 refluxing units, 72 (89%) had resolution of reflux whereas 9 (11%) did not resolve. The total average QOL was higher for the patients in the resolved group as compared to the non resolved group. Comparison of pre and post procedure renal DMSA scans in 44 patients showed status quo in 26, regression of scars in six, progression in two and formation of new scars in 6. The total increase in HRQOL was highest in regression group (67.91), and lowest in progression group (36.45).

Successful endoscopic treatment of VUR is associated with improved quality of life, as indicated by higher HRQOL scores in the resolved group.

Health-related quality of life in children with vesicoureteral reflux - impact of successful endoscopic therapy.


OBJECTIVES: Endoscopic therapy for vesicoureteral reflux (VUR) using dextranomer/hyaluronic acid (Dx/HA) has become increasingly popular, but the subjective impact of this therapy and subsequent reflux resolution on health-related quality of life (HRQoL) remains unclear. The aim of this study was to address this issue.

MATERIALS AND METHODS: One hundred children (65 girls, 35 boys; mean age 4.46 years) cured of primary VUR by endoscopic treatment were retrospectively reviewed. The Glasgow children's benefit inventory (GCBI) - a validated, reproducible, post-interventional questionnaire consisting of four subscales - supplemented by sociodemographic and disease-specific questions was employed. The HRQoL benefit was calculated on a scale ranging from -100 (complete failure) to +100 (complete success) and correlated with supplementary data.

RESULTS: Total response rate was 88%. Mean total GCBI score was 28.4 +/- 20.3 representing a significant HRQoL amelioration. All GCBI subscores improved with the physical health subscale being most relevant. A gender-specific, significant difference in relative GCBI scores was discovered. Correlation with critical life events and time since operation proved the positive effect on HRQoL to be durable.

CONCLUSIONS: Resolution of primary VUR secondary to Dx/HA treatment significantly improves HRQoL. HRQoL is positively affected in many areas and not only in those directly associated with VUR. These improvements are not temporary, suggesting that successful Dx/HA therapy may be superior to medical management in terms of children’s quality of life.

VUR - Technique

Evaluation of new Deflux administration techniques: intraureteric HIT and Double HIT for the endoscopic correction of vesicoureteral reflux.


Vesicoureteral reflux (VUR) is one of the most common urologic diagnoses affecting children, and optimal treatment requires an individualized approach that considers potential risks. Management options include observation with or without continuous antibiotic prophylaxis and surgical correction via endoscopic, open or laparoscopic/robotic approaches.

Endoscopic correction of VUR is an outpatient procedure associated with decreased morbidity compared with ureteral reimplantation. The concept of ureteral hydrodistention and intraluminal submucosal injection (Hydrodistention Implantation Technique [HIT]) has led to improved success rates in eliminating VUR compared with the subureteral transurethral injection technique.

Further modifications now include use of proximal and distal intraluminal injections (Double HIT) that result in coaptation of both the ureteral tunnel and orifice.

Endoscopic injection of dextranomer/hyaluronic acid copolymer, via the HIT and Double HIT, has emerged as a highly successful, minimally invasive alternative to open surgical correction, with minimal associated morbidity.

Current trends in dextranomer hyaluronic acid copolymer (Deflux) injection technique for endoscopic treatment of vesicoureteral reflux.

Kirsch AJ, Arlen AM, Lackgren G.

OBJECTIVE: To determine the current preferred injection technique(s) for endoscopic management of pediatric vesicoureteral reflux (VUR). Since the approval of dextranomer hyaluronic acid copolymer (Dx/HA) in 2001, injection methods have evolved and now include the hydrodistention implantation technique (HIT) and double HIT as well as subureteral transurethral injection (STING) method.

In July 2012, 278 pediatric urologists in the United States were contacted to complete a 15-question survey regarding Dx/HA injection technique(s) currently used in their practice.

RESULTS: Fifty board-certified pediatric urologists completed the survey for a response rate of 18%. Most respondents (60%) were in a single-specialty group practice, and 12% were affiliated with an academic- or university-based practice. Respondents reported seeing a mean of 159 pediatric patients (range, 40-400 patients) with VUR annually, and 94% used Dx/HA ≥4 times in the past year. Forty-seven respondents (94%) reported using double HIT over the course of their career compared with 36 (72%) for STING and 30 (60%) for HIT (P <.05). Double HIT gained widespread acceptance between 2007 and 2008, paralleled by a decline in use of other injection techniques. A significantly higher percentage currently perform double HIT (92%) compared with either STING (24%) or HIT (34%; P <.001). Respondents reported the use of double HIT 15 times more often than STING technique and 5 times more often than HIT during the past 12 months (P <.001).

CONCLUSION: The double HIT method is currently the most commonly performed technique for endoscopic correction of VUR by pediatric urologists in the United States.

Long-term ultrasound appearance of concomitant autologous blood and dextranomer/hyaluronic acid copolymer implants: is it associated with successful correction of vesicoureteral reflux?


OBJECTIVE: To find the association between mound appearance on ultrasound imaging and successful correction of vesicoureteral reflux (VUR).

METHODS: We retrospectively reviewed the ultrasound and voiding cystourethrogram (VCUG) results of patients who underwent dextranomer/hyaluronic acid injection via the hydrodistention injection technique (HIT) or HIT with concomitant autologous blood injection (HABIT) for 5 years postoperatively. VUR resolution at postoperative VCUG was considered as a success. Retained volumes of implants were measured and compared between HABIT and HIT and successful and failed treatments. Presence of mound on ultrasound imaging was also evaluated as a predictor of VUR resolution on VCUG.

RESULTS: Measured mound volume was significantly higher in treatments that were successful than in those that were failures (P < .05). During 5-year follow-up, measured mound volumes in the HABIT group were significantly higher than in the HIT group (P < .05). Sensitivity, specificity, positive predictive value, and negative predictive value of mound visualization on the first-month sonography to predict success were 97.7%, 21.5%, 89.6%, and 60%, respectively. These results were dramatically changed for the 50 patients with further VCUG after 1 year of follow-up, with 95.7% sensitivity, 37.0% specificity, 54.0% positive predictive value, and 90.9% negative predictive value.

CONCLUSION: Reduction or absence of the mound after implantation is more frequent among failed treatments in which visualization of the mound on postoperative sonography can predict VUR resolution. Autologous blood injection concomitant with dextranomer/hyaluronic acid implantation results in better immediate and long-term mound preservation, which could possibly be the reason for the higher success rate in HABIT group.

Endoscopic treatment for vesicoureteral reflux: how important is technique?
Watters ST, Sung J, Skoog SJ.

PURPOSE: Endoscopic dextranomer/hyaluronic acid (Dx/HA) injection by subureteric transurethral injection (STING) or hydrodistention implantation technique (HIT) for treatment of vesicoureteral reflux (VUR) has variable results with HIT reporting better outcomes. We determined outcomes with each technique comparing reflux resolution rates and evaluating predictors of treatment success and failure.

METHODS: Univariate and multivariate analysis compared 163 patients (246 ureters) who underwent a single endoscopic Dx/HA injection from December 2001 to April 2010. Data on pre, peri, and post-operative variables were prospectively collected. Resolution was defined as no reflux on voiding cystourethrogram (VCUG) at 3 month follow up. Calculated ellipsoid volume (CEV) of Dx/HA mounds was defined as \( \frac{4}{3}\pi \times (\text{height}/2) \times (\text{length}/2) \times (\text{width}/2) \) based on post-operative ultrasound dimensions.

RESULTS: Ureter resolution was 79.75% and 80.84% for STING and HIT, respectively (p = 0.86). Patient resolution was 70.0% and 74.3% for STING and HIT, respectively (p = 0.57). Multivariate ureter analysis revealed lower pre-operative grade (p = 0.004) and injected Dx/HA volume 0.80-1.00 mL (p = 0.039) as predictors of success. CEV <0.20 mL (p = 0.002) and CEV/injected-volume <25% (p = 0.006) were predictors of failure. Volcano morphology (p = 0.004) and lower pre-op grade (p = 0.015) were predictors of success for STING and HIT, respectively.

CONCLUSIONS: We found no differences in ureter or patient resolution between endoscopic Dx/HA injection techniques STING or HIT. Lower pre-operative grade and moderated Dx/HA volume were predictors of success regardless of technique.

Usefulness of concomitant autologous blood and dextranomer/hyaluronic acid copolymer injection to correct vesicoureteral reflux.

Kajbafzadeh AM, Tourchi A.
J Urol. 2012 Sep;188(3):948-52

PURPOSE: We present the long-term results of a new modification of endoscopic treatment of vesicoureteral reflux involving concomitant injection of autologous blood following the standard hydrodistention injection technique to prevent bulking agent leakage immediately after the procedure.

MATERIALS AND METHODS: A total of 341 children underwent endoscopic implantation of dextranomer/hyaluronic acid for vesicoureteral reflux. A subset of 171 patients underwent hydrodistention autologous blood injection, while 170 underwent classic hydrodistention injection. Frequency of symptomatic urinary tract infection after endoscopic treatment was recorded. Success was defined as absence of vesicoureteral reflux on postoperative voiding cystourethrography.

RESULTS: A total of 523 ureters in 214 girls and 127 boys were treated. In patients undergoing hydrodistention autologous blood injection mean age was 39.48 months, mean maximal reflux grade was 3.02 and success rate was 93.6% after the first injection (98.0% in patients with grade II, 92.1% with grade III, 93.3% with grade IV and 85.7% with grade V reflux). In patients who underwent classic hydrodistention injection mean age was 36.12 months, mean maximal reflux grade 3.05 and success rate was 81.8% after the first injection (91.5% in patients with grade II, 89.4% with grade III, 74.4% with grade IV and 44.4% with grade V reflux). The success rate was significantly higher (p = 0.001) in patients undergoing hydrodistention autologous blood injection vs classic hydrodistention injection. Of the patients 1.7% in the hydrodistention autologous blood injection group and 2.9% in the classic hydrodistention injection group reported symptomatic urinary tract infection during followup.

CONCLUSIONS: Immediate injection of autologous blood following dextranomer/hyaluronic acid injection to create a blood clot and barricade against bulking agent leakage is more effective than pure dextranomer/hyaluronic acid implantation. This novel modification stabilizes the subureteral implant mount and may affect the antireflux outcome.

Intermediate to long-term follow-up indicates low risk of recurrence after Double HIT endoscopic treatment for primary vesico-ureteral reflux.

Kalisvaart JF, Scherz HC, Cuda S, Kaye JD, Kirsch AJ.

PURPOSE: Follow-up of patients undergoing dextranomer/hyaluronic acid injection for vesico-ureteral reflux (VUR) is controversial. The purpose of our study was to test the hypothesis that patients undergoing the double hydrodistention-implantation technique (Double HIT) have a higher clinical and radiographic success rate.

MATERIALS AND METHODS: Patients undergoing Double HIT endoscopic injection for VUR were prospectively identified. Patients underwent an ultrasound at 6 weeks to assess the implants, and, if visible, prophylactic antibiotics were discontinued and patients were scheduled for a 1-year voiding cystourethrogram (VCUG). Radiographic success was defined as a negative VCUG and clinical success as no febrile urinary tract infections at 1 year.

RESULTS: A total of 54 patients underwent endoscopic injection for VUR. Twenty-five (51%) were compliant with the 1 year follow-up; 18 non-compliant patients were contacted and their clinical status assessed. Thirty patients eventually completed the 1-year VCUG at a mean of 12.2 months (range 10-20). Among the 60% of patients with 1-year radiographic follow-up, 2 had persistent VUR for a radiologic success rate of 93%. All radiographic failures were infection-free. Of the 80% (43/54) of patients with available clinical data, 3 (7%) had afebrile UTI for a clinical success rate of 93%.

CONCLUSIONS: The Double HIT leads to a 93% clinical and 93% radiographic intermediate/long-term success rate. With this technique, better outcomes were achieved with fewer recurrences than previously reported. These favorable results challenge the need for postoperative VCUG in asymptomatic patients after the Double HIT.

Efficacy of hydrodistention implantation technique in treating high-grade vesicoureteral reflux.

Shim JS, Kim JW, Oh MM, Moon du G.

PURPOSE: In the endoscopic treatment of vesicoureteral reflux, the relatively high rate of success, the simplicity of the procedure, high patient compliance, and a lack of complications has led to the increased development of injection materials and techniques. We report a method of identifying and maintaining a clear visual field during ureteral and bladder submucosal wall injection of a dextranomer/hyaluronic acid copolymer (Deflux, Oceana, Therapeutics Inc.) by use of the hydrodistention implantation technique (HIT) with the aid of temporary ureteral catheter insertion.

MATERIALS AND METHODS: We prospectively reviewed patients with grade IV or V reflux who received an endoscopic injection of Deflux. Reflux grade was evaluated before and after treatment (3 months) by use of voiding cystourethrograms. Conventional sub-trigonal injection (STING) was performed with injection of Deflux underneath the bladder mucosa at the 6 o’clock position. HIT was performed either with hydrodistention or with guidewire insertion. These techniques increase visualization of the intramural portion of the distal ureteral wall. Patients with treatment failures were offered reinjection up to three times.

RESULTS: Sixty-three patients completed endoscopic injection and follow-up of 3 months. The overall resolution rate for conventional STING was 58%, i.e., 67% for grade IV and 43% for grade V. The overall resolution rate for HIT was 80%, i.e., 93% for grade IV and 66% for grade V. The modified methods showed higher resolution rates for overall cure owing to the success in patients with grade IV reflux (p=0.026). Although the success of grade V treatment was higher with the modified method, the success rate was not statistically significant (p=0.27).

CONCLUSIONS: HIT with the use of either hydrodistention or a guidewire to aid in visualization of the intramural portion of the distal ureter is an effective treatment for high-grade vesico-ureteral reflux.

Is there a learning curve for subureteric injection of dextranomer/hyaluronic acid in the treatment of vesicoureteral reflux?


OBJECTIVE: To answer the question: ‘Is there a learning curve associated with a subureteric injection of Deflux(®)?’

MATERIALS AND METHODS: We retrospectively reviewed charts of patients who received subureteric injection of dextranomer/hyaluronic acid (Deflux(®){AQ2}) (225 procedures) for treatment of vesicoureteral reflux (VUR) by four surgeons. The study included 55 patients, 82 ureters, who had postoperative follow-up with a voiding cystogram or nuclear medicine cystogram. Exclusion criteria were prior anti-refluxing procedures, duplicated collecting systems, and non-achievement of a negative intraoperative cystogram. Patients were divided into two groups based on whether or not they received an intraoperative cystogram after the injection. The two groups were compared for VUR resolution rates on follow-up imaging.

RESULTS: Twenty patients underwent an intraoperative cystogram (Group 1, 33 ureters) and 35 did not (Group 2, 49 ureters). The two groups were similar in age, preoperative reflux grade, amount of Deflux injected into each ureter, and time to postoperative studies. In Group 1, 11 ureters (33.3%) and also, in Group 2, 11 ureters (22.4%) had reflux on follow-up imaging.

CONCLUSIONS: There was no improvement in VUR resolution rate following subureteric injection of Deflux(®) when an intraoperative cystogram demonstrated no reflux to be present immediately after injection. Of ureters that did not reflux on intraoperative cystograms, one-third displayed return of reflux on follow-up imaging, which suggests no learning curve and that failures are not likely to be caused by poor surgical technique.

The “incidental anesthetic” — an opportunity for the endoscopic correction of vesicoureteral reflux in children

INTRODUCTION: The endoscopic management of vesicoureteral reflux (VUR) with subureteric injection (STING) has become more popular. The low morbidity associated with the STING procedure has led to some authors advocating its use as a first-line therapy. Many parents are uncomfortable with this procedure being performed in children because of the potential morbidity associated with general anesthesia. We present an alternative without added anesthetic morbidity: offering the parents a STING when their child is undergoing an anesthetic for another surgical indication.

METHODS: We reviewed the records of 10 children who underwent incidental dextranomer/hyaluronic acid copolymer (DHA) injection over a 2-year period.

RESULTS: We considered the treatment outcome after a single STING procedure to be successful in 8 (80%) patients and a failure in 2 (20%). Distribution of VUR grade, according to the highest grade per patient, was high in 5 (50%) patients, moderate in 3 (30%) and low in 2 (20%). We observed no complications.

CONCLUSION: The idea of performing STING in children under incidental anesthetic introduces yet another possibility in the paradigm of VUR care. Though the long-term efficacy of DHA remains to be determined, this option reduces the potential morbidity of DHA as first-line therapy while favourably altering the cost benefit.

http://europepmc.org/articles/PMC2692163/reload=0;jsessionid=3KleRmSLN12StU3b1bYA.20
Modification of the sting procedure for vesicoureteral reflux: ureteral repositioning and injection.

Capozza N, Caione P.

OBJECTIVE: Over the past 20 years endoscopic treatment (ET) of vesicoureteral reflux (VUR) has changed the algorithm of reflux management. We describe a modification of the standard subureteral injection (STING) that has contributed to the increased success rate of this procedure.

METHODS: Between January 2006 and December 2006 192 children, 5 months to 10 years old (mean age 2.8 years) underwent endoscopic treatment for VUR, with injection of dextranomer/hyaluronic acid copolymer (Dx/HA). Standard STING procedure was used in 165 patients (235 ureters). A modified STING procedure, here described as “ureteral repositioning and injection” (URI) was used in 27 patients (38 ureters). In the URI technique, the needle was inserted as for standard STING; subsequently the distal part of the ureter was raised and levered towards the lumen of the bladder; Dx/HA was then injected. Renal/bladder ultrasound was performed 1 month after treatment and a voiding cystourethrogram (VCUG) at 4-6 months.

RESULTS: After a single injection the VCUG showed no reflux in 203 ureters of STING group (86%) and in 34 ureters of URI group (91%). Mean injected volume of Dx/HA was 0.7 ml (0.3-1.8 ml) for STING and 0.4 ml (0.3-0.8 ml) for URI.

CONCLUSION: The modified STING we have proposed, presents some advantages. It is very easy to perform and needs less material to inject. The ureteral repositioning into the bladder, with the support of the implanted material, may reconstruct a true flap-valve mechanism, without the risk of ureteral obstruction.

Dynamic hydrodistention classification of the ureter and the double hit method to correct vescoureteral reflux.


OBJECTIVES: The objective of this monograph is to familiarize the reader with dynamic hydrodistention classification of the ureter and Hydrodistention Implantation Technique (HIT) methodology for the endoscopic correction of vescoureteral reflux (VUR). The indications, current success rates, complications, and potential future applications of these methods are reviewed.

METHODS: Hydrodistention (HD) of the ureteral orifice and distal ureter permits visualization of the intraureteral submucosal injection site and assessment of the degree of ureteral coaptation. We have designated 4 levels of HD. HO denotes absence of ureteral dilation, H1 indicates dilation of the ureteral orifice only. H2 allows visualization of the intramural ureter, and H3 allows visualization of the extramural ureter. The Double HIT method is a systematic technique that utilizes HD to both classify the ureter and gauge the degree of ureteral coaptation secondary to bulking during endoscopic injection. The needle is inserted at the mid ureteral tunnel at the 6 o’clock position. The first injection coapts the detrusor tunnel (until H1 or H0 is achieved), while a second implant within the most distal intramural tunnel leads to complete coaptation of the ureteral orifice (H0).

RESULTS: HD grade correlated significantly with VUR grade. Normal ureters rarely hydrodistended. While non-refluxing contralateral ureters demonstrated low HD grades, all contralateral ureters that subsequently developed VUR showed H2 or H3. The HIT method has not only been employed for primary VUR (90% cure), but also for repeat endoscopic injections (90%), VUR associated with paraureteral diverticula (81%), complex cases such as post-reimplantation (88%), neurogenic bladders (78%), duplication anomalies (80%), and in adults (88%). Furthermore, injection of contralateral VUR-negative but hydrodistending ureters may be treated to prevent new contralateral VUR. While decreasing success was seen with increasing VUR grade with the STING method, superior success rates have been realized with the HIT method.

CONCLUSIONS: The dynamic hydrodistention classification reflects the competency of the ureterovesical junction. The HIT and Double HIT methods achieve superior cure rates and are likely to become the method of choice for the treatment of primary as well as complex cases of VUR.

Intra-orifice versus hydrodistention implantation technique in dextranomer/hyaluronic acid injection for vesicoureteral reflux.

Gupta A, Snodgrass W.

PURPOSE: Original implantation procedures used dextranomer/hyaluronic acid to create a volcano-like mound at the orifice. Subsequently the hydrodistention implantation technique was described to coapt the intramural ureteral wall with less emphasis on achieving a mound at the orifice and it was reported to be associated with improved outcomes. We compared the results of intra-orifice injection to establish a mound vs the hydrodistention implantation technique.

MATERIALS AND METHODS: Univariate and multivariate logistic regression analysis was used to compare results in 96 ureters undergoing intra-orifice injection vs 52 undergoing the hydrodistention implantation technique. We evaluated patient gender and age, reflux grade, injection technique, injected volume and the number of injection sites.

RESULTS: Successful reflux resolution was achieved in 124 ureters (84%) with a single implantation, including 83 (86.5%) with intra-orifice injection and 41 (79%) with HIT (p = 0.23). Mean injected volume was significantly increased for the hydrodistention implantation technique vs intra-orifice injection (0.68 vs 0.51 cc, p = 0.002). Univariate analysis showed that female gender, older age, reflux grade and number of injection sites were associated with success. On multivariate analysis only reflux grade remained significant.

CONCLUSIONS: Despite using an increased volume of dextranomer/hyaluronic acid to coapt the intramural ureter and orifice, the hydrodistention implantation technique did not improve results over those of intra-orifice injection with a lesser implant volume.

The modified sting procedure to correct vesicoureteral reflux: improved results with submucosal implantation within the intramural ureter.


PURPOSE: With the advent of tissue bulking agents, in particular dextranomer/hyaluronic acid copolymer (Dx/HA), for endoscopic implantation for vesicoureteral reflux (VUR), there has been a major shift in the surgical paradigm throughout Europe, and more recently, in the United States. We describe a modification of the technique used for implantation that has significantly improved our results.

MATERIALS AND METHODS: Between October 2001 and October 2003, 285 children 7 months to 15 years old (mean age 4.6 years) underwent endoscopic implantation of Dx/HA for VUR at our institutions. A modified STING (subureteral transurethral injection) procedure (implantation submucosally within the intramural ureter) was introduced during the last year of the study. The average volume of injected material was measured for each ureter. Renal sonography was performed to determine if hydronephrosis was present. At 3 months fluoroscopic voiding cystourethograms were used to evaluate for the presence of VUR. A subset of 122 patients treated with STING (52) were compared to those treated with modified STING (70).

RESULTS: A total of 459 ureters in 231 girls and 54 boys were treated (174 bilateral cases). Mean maximum grade per patient was 2.5/5. Mean injected volume was 0.9 cc ureter. There were 181 patients with at least 3 months of followup. After 1 treatment 76% (137 of 181) of cases were cured (grade 0 reflux), while 54% (24 of 44) of the failures were improved. The overall cure rate was 94% for grade I, 85% for grade II, 78% for grade III and 71% for grade IV reflux. The patients treated with STING had a mean age of 4.8 years, mean maximum reflux grade was 2.5 and success rate was 71% (37 of 52; 86% grade I, 89% grade II, 70% grade III and 63% grade IV reflux). The patients treated with modified STING had a mean age of 5.5 years, mean maximum grade was 2.8 and a success rate was 89% (62 of 70; 100% grade I, 92% grade II, 91% grade III and 90% grade IV reflux). Ureteral success rates were significantly (p <0.01) greater for the modified STING (92%) vs the standard STING (79%). There were no cases of hydronephrosis at 3 months postoperatively.

CONCLUSIONS: The majority of patients undergoing minimally invasive therapy for VUR with Dx/HA are cured after 1 treatment. The modified STING is our preferred method of implant injection for the correction of VUR and in our hands produces a resolution rate of 89% (92% of ureters). The technique optimizes ureteral coaptation, is easy to perform and is not associated with any significant short-term complications. Persistence of VUR in a minority of patients continues to be the only significant adverse effect of endoscopic implantation.

Injection of Deflux®/ Zuidex using a new injection device - Magnetic Resonance Imaging confirms the periurethral location of deposits

Aino Fiantl-jonasson (aino.fiantljonasson@obgyn.hs.sll.se) and Lena Edvall, Maria Kristo./forsen Wiberg, 2003
HUDDINGE-UNIVERSITETSSJUKHUS

Background: Injection of periurethral bulking agents has been used for the treatment of stress urinary incontinence with varying degrees of success. However, the bulking agents used so far have all been associated with certain shortcomings, i.e. lack of biocomparibility, insufficient longevity in the tissue or a need for endoscopic guidance when performing the injections. Dextranomer in a base of non-animal stabilized hyaluronic acid (NASHA) has been approved as an injectable implant for the endoscopic correction of vesicoureteral reflux in children in Europe and in the U.S. and for women with SUI in Europe (Oeflux®/Zuidex™ Q-Med, Uppsala, Sweden). A newly developed injection device, the Implacer, provides a method of injecting the dextranomer/hyaluronic acid (Dx/HA) copolymer without direct cystoscopic visualization.

Methods: Forty-two patients were included in the main study and received Dx/HA copolymer injections administered transurethrally using the Implacer device for guidance of the needles. Two injection volumes were investigated: 4x1.0 ml and 4x0.7 ml. Sixteen of the patients, eight from each dosage group, were examined by MRI to verify the correct periurethral localization of deposits. Patients were examined within a mean of 35 days after treatment (range 1 to 92 days in the 4x1.0 ml group and 29 to 41 days in the 4x0.7 ml group).

Results: It was possible to visualize the Dx/HA deposits by MRI, and the majority of deposits were identified periurethrally in the submucosa as was the aim (Fig. 2 and 3). Three or more deposits were identified in 11 out of 16 patients, one to two deposits were identified in three patients and in two patients there were no identifiable deposits. In the 4x1.0 ml group, the size of the deposits ranged from 5x5x4 mm to 29x13x17 mm. At three months, all eight patients in this group were improved as measured by a Pad Test and seven patients reported a decrease in the number of incontinence episodes. In the two patients without identifiable deposits on MRI, an improvement was still noted on both efficacy measures. In the 4x0.7 ml group, the size of the deposits ranged from 2x2x3 mm to 20x24x20 mm. Five patients were improved as measured by the Pad Test and six patients had a decrease in the number of incontinence episodes. Three and four deposits, respectively, were identified in the two patients in this dosage group registering no improvement on either efficacy measure.

In 11 out of 14 patients with identifiable deposits, the deposits were located periurethrally in the submucosa, whereas in the remaining three patients, the deposits were identified between the mucosa and the muscle layer or in the muscle layer. This study showed that by using the Implacer the Dx/HA copolymer could be deposited in the periurethral location in the submucosa without endoscopic guidance in the majority of cases. Ongoing trials will further address questions regarding the relationship between treatment success and the localization of deposits raised by this study.
Safety

Calcification

Distal ureteral calcification secondary to deflux injection: a reality or myth?

Palagiri AV, Dangle PP.

Dextranomer/hyaluronic acid (Dx/HA) copolymer (Deflux) subureteral injection has become a widely accepted form of treatment for vesicoureteral reflux. Long-term histologic studies, both experimental and clinical, have supported and proven the occurrence of calcification at the site of previous injection. These calcifications in clinical settings may be perceived as ureteral stones.

We report a case of an adolescent female with unresolved right-sided abdominal pain with a past surgical history of Deflux injection, who presented with a distal ureteral calcification. Upon further investigation the calcification was found to be confined to the submural portion rather than the intraluminal ureter.

Radiologic features of implants after endoscopic treatment of vesicoureteral reflux in children.


OBJECTIVE. Implants after endoscopic treatment of vesicoureteral reflux (VUR) in children will be more frequently detected on imaging studies and may lead to misinterpretation and unnecessary intervention. This article reviews the radiologic appearance of implants.

CONCLUSION. Radiologic findings of implants depend on the imaging technique, bulking agent, and time after injection. A history of VUR or an antireflux procedure and the absence of hydronephrosis in cases of suspected urolithiasis are important clues to suggest implants.

Appearance of dextranomer/hyaluronic Acid copolymer implants on computerized tomography after endoscopic treatment of vesicoureteral reflux in children.


PURPOSE: With the increasing popularity of endoscopic treatment for vesicoureteral reflux in children, dextranomer/hyaluronic acid copolymer implants are more frequently detected on computerized tomography, which may lead to misinterpretation and unnecessary intervention. The objective of this study was to characterize the long-term appearance of dextranomer/hyaluronic acid copolymer implants on computerized tomography.

MATERIALS AND METHODS: We evaluated the hospital charts of 893 patients who had undergone dextranomer/hyaluronic acid copolymer injection for vesicoureteral reflux between July 2001 and November 2007 to identify those who underwent subsequent computerized tomography of the abdomen and pelvis. A total of 30 patients with ureterovesical junction stones served as the control group. Seven patients who proceeded to extravesical reimplantation after failed endoscopic treatment had dextranomer/hyaluronic acid copolymer implants explanted and microscopically evaluated.

RESULTS: Of 893 patients who had undergone endoscopic treatment for vesicoureteral reflux 17 (1.9%) underwent subsequent computerized tomography. A total of 33 dextranomer/hyaluronic acid copolymer implants were detected on computerized tomography, and were classified as low density (21) or high density (12). Median density was 22 HU (range 15 to 27) for low density implants and 193 HU (126 to 367) for high density implants. Radiograph of the kidneys, ureters and bladder, and fluoroscopy did not visualize high density implants. Neither gender, age at endoscopic treatment, vesicoureteral reflux grade, hydrodistention grade, injection volume, success nor second injection was associated with a high density implant. Only elapsed time between surgery and computerized tomography was associated with increased implant density (p = 0.02).

CONCLUSIONS: Dextranomer/hyaluronic acid copolymer implants may be encountered on computerized tomography as low or high density lesions. History of vesicoureteral reflux and absence of hydronephrosis as well as hematuria should provide reassurance and prevent inappropriate intervention for misdiagnosed ureteral stones.

Malpositioning

Open ureteroneocystostomy after failed endoscopic injection with three different bulking agents for the treatment of vesicoureteral reflux.

Sencan A, Yıldırım H, Özkan KU, Uçan B, Hoşgör M.

BACKGROUND/PURPOSE: To evaluate the success rate of open ureteroneocystostomy (UNC) after failed endoscopic treatment of vesicoureteral reflux (VUR) in children and to discuss the reasons for failure under the light of histopathological findings.

METHODS: The clinical data of 371 patients who underwent endoscopic injection for VUR at our institution for the treatment of VUR between January 2008 and January 2014 were reviewed. Patients who were submitted to open ureteral reimplantation following failed endoscopic injection were included in the study.

RESULTS: Among 371 patients, 34 (49 ureters) were submitted to open UNC (9.1%). There were 22 female and 12 male patients. Three different injection materials were used; dextranomer/hyaluronic acid in 29, carbon-coated beans in 7 and polyacrylate polyalchohol copolymer in 13. Histological study revealed that the injected material was identified in 34 ureters as malpositioned. Control VCUG 6 months after UNC showed complete resolution in 46 of 47 ureters (97.87%).

CONCLUSIONS: Previous endoscopic injection, although causing difficulty in dissection to some degree, does not alter the success rate of UNC. According to the histopathological findings, the cause of failure of injection seems to be attributable to incorrect plane of injection or leakage of the agent after injection.

Histology proved malpositioning of dextranomer/hyaluronic acid in submucosal ureter in patients after failed endoscopic treatment of vesicoureteral reflux. 


PURPOSE: We histologically investigated the cause of failed endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid injections in children

MATERIALS AND METHODS: A total of 192 children underwent dextranomer/hyaluronic acid injection at our institution between January 2008 and September 2010. The study population consisted of 13 children (22 ureters) with vesicoureteral reflux who underwent ureteroneocystostomy following failed endoscopic injections (1 to 2) of dextranomer/hyaluronic acid. In all cases the dextranomer/hyaluronic acid was implanted in the mucosa of the mid to distal ureteral tunnel following hydrodistention of the ureter. The medical records were reviewed, and specimens of the archived distal ureters removed during surgery were examined histologically.

RESULTS: Mean patient age was 4.1 years. Mean dose of dextranomer/hyaluronic acid was 0.9 ml (both treatments) and mean lag between treatments was 13.4 months. Indications for open surgery were recurrent urinary tract infections and/or residual or aggravated reflux grade IV or higher. Histological study revealed that the dextranomer/hyaluronic acid was malpositioned in 21 of 22 ureters, residing in the muscle fibers in 2, adventitia in 14 and periureteral space in 5.

CONCLUSIONS: This is the first known study to provide a histologically proved cause of failure of endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid injections in children. Malpositioning of the material outside the submucosal ureter was identified in a high percentage of cases. Larger studies are needed to corroborate these findings.

Migration

Lack of distant migration after injection of a 125iodine labeled dextranomer based implant into the rabbit bladder.


PURPOSE: In recent years endoscopic treatment of stress incontinence and vesicoureteral reflux has been introduced. Reports of possible particle migration of the injected material to distant organs in humans and experimental animals have led to a search for biological nonmigration products. An implant found to have a good clinical effect in these conditions is dextranomer in hyaluronan. We performed this study in rabbits to investigate the possible migration of dextranomer particles.

MATERIALS AND METHODS: 125iodine labeled dextranomer particles were injected into the submucosal space of rabbit bladders, and samples of blood and various tissues were examined for radioactivity at scheduled intervals during a 28-day period. Furthermore, whole body autoradiography was performed 1 day, and 1 and 4 weeks after injection.

RESULTS: Radioactivity was found in blood samples and in all tissues but it remained at the background activity level except in the thyroid, where uptake representing free 125iodine was detected. In the bladder 41 and 45% of the injected dose remained within the bladder wall 1 day and 4 weeks, respectively, after injection. The remainder of the dose probably disappeared from the bladder wall by leakage into the urine shortly after deposition, as indicated by the finding of 10-fold higher urine radioactivity levels at day 1 than at day 28 after injection.

CONCLUSIONS: No distant migration of dextranomer particles occurs after submucosal injection of such an implant in the rabbit bladder wall.

New Contralateral Versicoureteral Reflux - NCVUR

Selective endoscopic treatment of the non-refluxing contralateral ureter prevents new contralateral vesicoureteral reflux.


OBJECTIVE: The objective of this study was to evaluate risk factors for new contralateral vesicoureteral reflux (NCVUR) and to investigate whether assessment of the non-refluxing contralateral ureter (NRCU) by hydrodistention and selective treatment can reduce the incidence of NCVUR.

MATERIALS AND METHODS: From 2001 to 2007, 339 of 841 patients (40%) were treated for unilateral VUR by endoscopic injection. While in the first 267 patients the NRCU was only assessed by hydrodistention but not injected (observation group), NRCUs of the subsequent 72 patients were prophylactically treated if deemed at high risk for NCVUR (H2 or H3) (prophylaxis group).

RESULTS: NCVUR occurred in 30 of 267 patients (11.2%) whose NRCUs were observed. No statistically significant risk factors for NCVUR were found in this group. In the subsequent 72 patients, whose H2 and H3 ureters were selectively injected (N = 56), no cases of NCVUR were seen.

CONCLUSIONS: Prophylactic endoscopic treatment of NRCU H2 and H3 ureters successfully prevented the occurrence of NCVUR.

New contralateral vesicoureteral reflux following dextranomer/hyaluronic Acid implantation: incidence and identification of a high risk group.


PURPOSE: To our knowledge the incidence of NCVUR (New contralateral vesicoureteral reflux) following the endoscopic treatment of VUR with Dx/HA has not been reported previously. We evaluated the outcomes in a group of patients to determine the incidence, and to attempt to identify risk factors.

MATERIALS AND METHODS: A total of 126 children with primary unilateral VUR underwent unilateral Dx/HA implantation at our institutions. The incidence of NCVUR was determined by postoperative VCUG. Indications for surgery, patient age and gender, preoperative grade of VUR and volume of Dx/HA injected were assessed as possible risk factors for NCVUR.

RESULTS: Of the patients 96 (76.2%) were female, and mean age was 4.8 years. The principal indications for Dx/HA implantation were persistent reflux in 56 patients (44.4%) and primary therapy in 51 (40.5%). At followup VCUG 17 patients (13.5%) had NCVUR. No variable independently appeared to influence the incidence of NCVUR. Statistical analysis suggests that females younger than 5 years have an increased incidence of NCVUR (13 of 62, or 21% vs 4 of 64, or 6.3% of the remaining patients, p = 0.016).

CONCLUSIONS: NCVUR occurred in approximately 13% of our patients. Patients with higher preoperative VUR grade or a lower number of preoperative VCUGs and those undergoing treatment as primary therapy did not have an increased incidence. Girls younger than 5 years had the highest incidence of NCVUR, and initial bilateral injection may be a consideration for this group. Further effort directed at identifying the etiology and risk factors for NCVUR is needed.

**Obstruction**

Acute and delayed vesicoureteral obstruction after endoscopic treatment of primary vesicoureteral reflux with dextranomer/hyaluronic acid copolymer: why and how to manage.


OBJECTIVE: To present our cases of ureteral obstruction after endoscopic treatment of vesicoureteral reflux (VUR) with dextranomer/hyaluronic acid (Dx/HA).

PATIENTS AND METHODS: We collected data from patients who had suffered ureteral obstruction after endoscopic treatment of VUR with Dx/HA in our institution.

RESULTS: From April 2002 to April 2011 we treated endoscopically 475 ureters with VUR, and detected 5 ureteral obstructions. Median age at reflux treatment was 39 months. Reflux grade before treatment was III in one patient and IV in four. Three ureterovesical junctions (UVJ) were blocked after a second endoscopic treatment. The median of Dx/HA injected was 1 ml (0.6-1.1). In two patients ureteral obstruction presented acutely and was treated with a ureteral stent. In the other three, the ureteral obstruction appeared gradually and was detected by ultrasound scans and MAG3 diuretic renogram; one underwent nephrectomy because of poor renal function, and the other two were treated with endoscopic dilatation of the UVJ. In all these patients both reflux and obstructions have resolved.

CONCLUSIONS: On preoperative cystography, three of the patients had a narrowed distal ureter, and probably had a refluxing and obstructive megaureter. Other causes are not clear, except for those patients with acute presentation in whom edema of the UVJ was found. Ureteral obstruction after endoscopic treatment of VUR is rare. Endoscopic intervention such as ureteral stent placement or high-pressure balloon dilatation of the UVJ has good results as a treatment of acute and delayed obstruction.

Delayed onset ureteral obstruction following Deflux® injection for vesicoureteral reflux.

Zemple RP, Potretzke AM, Kryger JV

Endoscopic injection treatment of vesicoureteral reflux is an increasingly common and successful option. Obstruction is an infrequent postoperative complication, occurring in 1% of patients; delayed onset of obstruction is even rarer. There is a paucity of literature describing possible treatments.

We present a novel approach by excision of the implanted material.

Postoperative ureteral obstruction after endoscopic antireflux therapy
García Mérida M, Moreno Román J, Miguélez Lago C, Rius Díaz F, Mieles Cerchar M, Galiano Duro E.
Arch Esp Urol. 2008 Mar;61(2):328-34.

OBJECTIVES: To know the incidence of new contralateral VUR and its evolution in children with primary unilateral vesicoureteral reflux (VUR) managed with endoscopic treatment (ET).

METHODS: During 7.5 years a total of 228 children with primary VUR underwent endoscopic implantation of bulking material, 90 of them (39.5%) have been unilateral. The inclusion criterion was: unilateral primary VUR managed with ET, without previously contralateral VUR. Collected data included: patient age, gender, indications for surgery, number of preoperative cystourethograms, preoperative and new contralateral postoperative VUR grades, nephropathy in the ipsilateral or contralateral sides, type and volume of bulking material used, and VUR outcome. An update bibliographic review with methanalysis is also performed to compare results.

RESULTS: Six children (6.7%) developed new contralateral VUR. Mean age was 3.3 years. Four patients were females and 2 males. The bulking material used was polydimethylsiloxane in one and Dextranomer/Non animal stabilised hyaluronic acid in 5. The initial grades of primary VUR were: II in 1 case, III in 3, and IV in 2. Four patients had previous history of bladder dysfunction. The new contralateral VUR was II in 5 and III in one. In 5 patients initial VUR persisted, always of lower grade than previously, and new contralateral VUR appeared. In one patient initial VUR disappeared and appeared in the contralateral side. Five patients were reinjected and VUR was cured, except one who is waiting for a new endoscopic procedure. One patient with grade II contralateral VUR is under observation. In the metanalysis performed nine issues have been found with an incidence of 8.2%.

CONCLUSION: Contralateral VUR is a relatively frequent complication in unilateral primary VUR treated by endoscopic procedures (6.7%), but not enough as to perform bilateral endoscopic treatment in all unilateral VUR. Contralateral VUR etiology is not clear but bladder dysfunction can be an important factor.

Postoperative ureteral obstruction after subureteral injection of dextranomer/hyaluronic acid copolymer.

Vandersteen DR, Routh JC, Kirsch AJ, Scherz HC, Ritchey ML, Shapiro E, Wolpert JJ, Pfefferle H, Reinberg Y.

PURPOSE: Subureteral injection of dextranomer/hyaluronic acid copolymer is widely accepted for the treatment of primary vesicoureteral reflux. Few studies document the incidence of surgically relevant postoperative obstruction or the characteristics of patients at risk.

MATERIALS AND METHODS: Four institutions had reported surgically relevant postoperative obstruction to representatives of Q-Med Scandinavia, the manufacturers of Deflux (dextranomer/hyaluronic acid). All children undergoing dextranomer/hyaluronic acid injection at these institutions were evaluated in this study. Patients requiring postoperative stenting were retrospectively reviewed for pertinent history, volume injected, technique of injection, duration of symptoms before intervention, duration of intervention and final outcome.

RESULTS: A total of 745 patients (1,155 ureters) underwent injection. Five patients (6 renal units, 7 ureters) required stenting for obstructive symptoms and hydronephrosis, of whom 4 immediately became symptomatic. All patients had been injected with up to 1 ml dextranomer/hyaluronic acid. Four patients (80%) had either a neurogenic bladder or dysfunctional voiding. All stents were placed and removed without complications, with complete resolution of symptoms in all patients. Length of stenting ranged from 2 to 6 weeks. No patient required open surgery. One of 2 patients undergoing postoperative voiding studies had development of recurrent vesicoureteral reflux.

CONCLUSIONS: Dextranomer/hyaluronic acid injection is associated with a small risk of postoperative ureteral obstruction requiring endoscopic intervention, with an overall incidence of less than 0.7% of patients injected. Patients with voiding dysfunction or neurogenic bladder may be at increased risk. Intervention with temporary ureteral stenting is effective, technically simple and curative.

Obstruction of a dysmorphic ureter following dextranomer/hyaluronic acid copolymer.
Snodgrass WT.

No abstract published. Report of an obstruction observed in one patient with dysmorphic ureters, following injection of dextranomer/hyaluronic acid. Sixteen weeks later, reflux was resolved but an obstruction was observed in the left ureter (washout half-time of 18 minutes versus 6 minutes for the right side). A distal narrowed segment was revealed on dissection.

Tissue Changes

Dextranomer/hyaluronic Acid copolymer implant for vesicoureteral reflux: role of myofibroblast differentiation

Arena S, Fazzari C, Implatini A, Torre S, Villari D, Arena F, Di Benedetto V.

PURPOSE: Dextranomer/hyaluronic acid implantation is associated with a granulomatous inflammatory reaction, replaced by fibrosis. Appearance of myofibroblasts is considered a crucial event in fibrosis, and CD68 positive cells and other factors are implied in their activation. Mast cells are a source of these factors and tryptase can induce fibroblast to express alpha-smooth muscle actin, which is characteristic of myofibroblasts. We evaluated histological changes in refluxing ureters treated with dextranomer/hyaluronic acid and immunolocalized CD68 positive cells, tryptase mast cells and myofibroblasts.

MATERIALS AND METHODS: We performed histological, histochemical and immunohistochemical analyses in 22 refluxing ureters treated with dextranomer/hyaluronic acid in comparison with 17 refluxing ureters who underwent ureteral reimplantation but did not receive endoscopic bulking agent. We used CD68 antibody for monocytes/macrophages and epithelioid cells, mast cell tryptase mouse antibody for mast cells, and alpha-smooth muscle actin and vimentin antibodies for myofibroblasts. The area of the ureteral lumen in dextranomer/hyaluronic acid treated and untreated ureteral endings was measured.

RESULTS: Sirius red documented a major grade of histological lesions in dextranomer/hyaluronic acid treated refluxing ureters. CD68 and tryptase mast cell staining showed a significant enhancement of positive cells in dextranomer/hyaluronic acid treated refluxing ureters. Immunostaining for alpha-smooth muscle actin and vimentin displayed a myofibroblastic invasion in dextranomer/hyaluronic acid. Measurement of surface in treated refluxing ureters was significantly less than in untreated refluxing ureters.

CONCLUSIONS: Our data documented a recruitment of CD68 and tryptase positive cells, abnormal accumulation of collagenous stroma and successive extracellular matrix remodeling through differentiation of myofibroblasts. Myofibroblasts might provoke tissue contraction, decreasing the ureteral diameter and modifying the ureteral length-to-diameter ratio, preventing urine reflux.

Endoscopic treatment of vesicoureteral reflux: histologic findings
Arch Esp Urol. 2008 Mar;61(2):112-6

OBJECTIVES: Vesicoureteral reflux is a pathologic entity with different forms of therapeutic management, one of which is endoscopic injection of various materials. We show some histological changes produced by these materials in the bladder wall.

METHODS: We study three samples of intravesical ureter from three children suffering vesicoureteral reflux. The ureters were obtained during ureteral reimplantation surgery.

RESULTS: We show the changes found with various materials under study (polytetrafluorethylene, polydimethylsiloxane, hyaluronic acid and dextranomer copolimer) observing less conjunctive tissue with the two latter and with the more encapsulated hyaluronic acid - dextranomer copolimer.

CONCLUSIONS: Migrations and granulomas are described with various materials and we ascertained the presence of foreign body reaction and fibrosis within the bladder wall. More studies in human beings are required to determine the best product for endoscopic injection.

Histopathological changes associated with dextranomer/hyaluronic acid injection for pediatric vesicoureteral reflux.


PURPOSE: Few studies have examined the medium and long-term histological changes associated with periureteral injection of dextranomer/hyaluronic acid copolymer (Deflux(R)). We present the results of a histological review of a series of distal ureteral excisions in patients undergoing ureteroneocystostomy after failed dextranomer/hyaluronic acid injection.

MATERIALS AND METHODS: All patients undergoing ureteroneocystostomy after failed dextranomer/hyaluronic acid injection(s) at 1 institution were eligible for this study. Excised ureteral segments were histologically examined by a single urological pathologist. An immunohistochemical battery was used for each specimen, including hematoxylin and eosin, CD3, CD20, MIB-1 and trichrome stains. Pathological criteria included the presence, location and intensity of fibrosis, giant cell reaction, chronic inflammation, free dextranomer/hyaluronic acid, and CD3, CD20 and MIB-1 staining. Pathological features were correlated with the time from injection to surgical excision.

RESULTS: The ureters of 16 children with a mean age of 4.5 years were examined. Median time from injection to implant excision was 8 months. Giant cell reaction was present in 94% of patients and it was typically located in the serosa. No histological or immunophenotypical feature correlated with the duration of implantation except CD3+ and CD20+ lymphocyte counts, which increased with time from injection (p = 0.06 and 0.02, respectively).

CONCLUSIONS: Dextranomer/hyaluronic acid appears to be stable and safe for use after 3 to 22 months of followup of subureteral injection. The periureteral inflammatory reaction increases with time, although no increases in nuclear turnover or fibrosis were detected.

Endoscopic treatment with dextranomer-hyaluronic acid for vesicoureteral reflux: histological findings.


PURPOSE: Dextranomer-hyaluronic acid co-polymer is the first endoscopic bulking agent approved for vesicoureteral reflux in the United States. We evaluated the histopathological changes associated with this treatment in children with vesicoureteral reflux.

MATERIALS AND METHODS: Children 1 to 11 years old in whom treatment with dextranomer-hyaluronic acid co-polymer for grades III or greater vesicoureteral reflux had failed were eligible for the study. Failure was defined as persistent vesicoureteral reflux on voiding cystourethrography done approximately 3 months after implantation. At ureteral reimplantation the implant and surrounding ureteral tissue were resected and fixed for histopathological analysis. Tissue sections (4 to 5 microm.) were stained for routine histology and examined under a light microscope. Patients with a similar grade of vesicoureteral reflux who had not undergone endoscopic treatment served as the control group.

RESULTS: The study population comprised 23 patients with vesicoureteral reflux, of whom 13 with a mean age of 2 years 8 months at diagnosis underwent 1 to 3 treatments with dextranomer-hyaluronic acid co-polymer. The remaining 10 patients with a mean age of 1 year 10 months at diagnosis did not receive the bulking agent before ureteral reimplantation. The implant remained in situ 13 to 39 months (mean 22). On ureteral reimplantation the implant was located at the site of injection in 12 of the 13 patients. Histologically a granulomatous inflammatory reaction indicated by giant cell infiltration was observed at the implantation site. At ureteral reimplantation 9 implants were pseudo-encapsulated. Calcification was present in 9 ureters, while the eosinophil count was greater than 5 cells per 0.125 mm² in 7 ureters treated with dextranomer-hyaluronic acid co-polymer. Mast cell infiltration was similar in the treatment and control groups.

CONCLUSIONS: Endoscopic treatment with dextranomer-hyaluronic acid co-polymer for vesicoureteral reflux is associated with a granulomatous reaction of the giant cell type, inflammatory cell infiltration and implant pseudo-encapsulation. They are typical histological findings associated with implantation of a foreign material. Dextranomer-hyaluronic acid co-polymer remains safe and effective for vesicoureteral reflux in children.

Injectable dextranomer-based implant: histopathology, volume changes and DNA analysis


OBJECTIVE: To study the tissue reaction in and around the implant, the changes in implant volume and the DNA profile of the invading cells when a new substance, dextranomers in sodium hyaluronan solution (DiHA), was injected into experimental animals.

MATERIALS AND METHODS: Nine pigs were followed up from 2 weeks to 3.5 months and 34 rats were followed up from 3 weeks to 16 months after injection of DiHA into the bladder in pigs and into the subcutaneous tissue in rats. Histopathological analysis was performed in 16 pig and 63 rat implants. In 31 of the rat implants the DNA profile was analysed. Changes in implant volume over time were estimated in 51 rat implants during the period up to 12 months after implantation.

RESULTS: Histologically, in the early phases the area within and around the implant was fairly rich in cells, predominantly fibroblasts, inflammatory cells and giant cells of the foreign body type. Later in the process an increase in extracellular matrix around the microspheres and ingrowth of blood vessels was seen. No tissue necrosis or significant eosinophilia was observed around the implants. DNA measurements by flow cytometry revealed no aneuploid cells. There was a decrease in implant volume by 23% over a period of 12 months.

CONCLUSIONS: DiHA does not induce any major tissue changes in and around the implants. No DNA changes were observed during the study period of 16 months. DiHA seem to be a safe and suitable injectable substance with good tissue-augmenting properties.

Urinary Tract Infection

Long-term incidence of febrile UTI after DxHA treatment of VUR.

Fotso Kamdem A, Galli G, Aubert D.

PURPOSE: To assess the long-term incidence of febrile urinary tract infection (fUTI) in children treated by endoscopic injection of dextranomer/hyaluronic acid (DxHA) for vesicoureteral reflux (VUR).

MATERIALS AND METHODS: Prospective study from January 2002 to December 2009 in children treated at our institution for VUR by endoscopic injection of DxHA. All children underwent clinical and renal/bladder ultrasound follow up at 3 months after procedure, then annually. Post-operative voiding cystourethrogram (VCUG) control was performed only for patients with recurrent fUTI.

RESULTS: 227 children (177 female) were included. Mean patient age at inclusion was 4.7 years. The mean duration of follow-up was 51.6 months. During follow-up, 18.9% had one or several fUTIs, of whom 48.8% had VUR at VCUG. No recurrence of fUTI was observed after 4 years of follow-up. We identified three risk factors for fUTI recurrence: cystitis cystica at the time of injection (p = 0.007), preoperative renal scarring (p = 0.018), and the disappearance of the implant at 3-month follow-up ultrasound (p = 0.037).

CONCLUSIONS: The long-term incidence of recurrent fUTI after endoscopic treatment of VUR is low. Our data show that the clinical results of endoscopic treatment should be interpreted with a follow up of at least 4 years.

Renal scarring and urinary tract infection after successful endoscopic correction of vesicoureteral reflux.

Chertin B, Natsheh A, Fridmans A, Shenfeld OZ, Farkas A.

PURPOSE: We evaluated renal function and the incidence of urinary tract infection after successful endoscopic correction of vesicoureteral reflux.

MATERIALS AND METHODS: From 1988 to 2007, 169 male and 338 female patients (696 refluxing renal units) with a median age of 3.7 years underwent successful endoscopic correction of primary vesicoureteral reflux using polytetrafluoroethylene and dextranomer/hyaluronic acid copolymer. Reflux was grades I to V in 36 (5.2%), 178 (25.6%), 298 (42.7%), 163 (23.4%) and 21 refluxing renal units (3.1%), respectively. Renal ultrasound and (99m)technetium-dimercaptosuccinic acid scan were performed in all patients preoperatively, and in all patients and in 509 of 696 refluxing renal units (73%) postoperatively, respectively. All patients were followed 1 to 20 years (median 13).

RESULTS: Preoperatively (99m)technetium-dimercaptosuccinic acid scan revealed scarring in 543 of 696 refluxing renal units (78%). Reflux resolved after 1 injection in 473 refluxing renal units (68%), in 161 (23%) after 2 and in 25 ureters (3.6%) after 3. In 37 refluxing renal units (5.4%) reflux improved to grade I, which required no further treatment. Renal deterioration was noted in 11 of 26 refluxing renal units with initially severe renal scarring (less than 20% uptake on (99m)technetium-dimercaptosuccinic acid scan). The remaining refluxing renal units in this group showed an insignificant 2.3% change in relative function after successful reflux correction (p >0.005). Patients with vesicoureteral reflux downgrading did not show new renal scars. Of the remaining 446 refluxing renal units 27 (6.1%) showed a greater than 5% decrease in relative function without new scarring. Eight children in the polytetrafluoroethylene group and 3 in the dextranomer/hyaluronic acid copolymer group (overall 2.2%) had febrile urinary tract infection after successful endoscopic correction, leading to reevaluation that resulted in the diagnosis of recurrent reflux in 8 (72.7%). A total of 28 children (5.6%) had afebrile urinary tract infection without recurrent vesicoureteral reflux.

CONCLUSIONS: Our data show that successful endoscopic correction of vesicoureteral reflux is accompanied by a low incidence of new renal scarring and febrile urinary tract infection. Patients who initially have corrected reflux but who have a febrile urinary tract infection at long-term followup require prompt reevaluation to rule out recurrent reflux.

Risk factors for urinary tract infection after dextranomer/hyaluronic acid endoscopic injection.


PURPOSE: Endoscopic injection of dextranomer/hyaluronic acid is an option for primary vesicoureteral reflux. Few groups have assessed the rate of urinary tract infection after dextranomer/hyaluronic acid injection. We reviewed our experience with dextranomer/hyaluronic acid injection, and determined the incidence of and risk factors for postoperative urinary tract infection.

MATERIALS AND METHODS: A retrospective cohort study was performed of all children with primary vesicoureteral reflux treated with dextranomer/hyaluronic acid from 2002 to 2007 at a single institution. Patient demographics and clinical outcomes were abstracted from the medical record. Risk factors for postoperative urinary tract infection, including female gender, preoperative vesicoureteral reflux grade, recurrent urinary tract infection, bladder dysfunction, nephropathy and persistent vesicoureteral reflux after surgery, were analyzed in a multivariate logistic regression model.

RESULTS: We treated 311 children, of whom 87% were female and 13% were male (464 renal units), during the study period. Mode of presentation was urinary tract infection in 85% of cases. Mean followup was 2.6 years. Postoperatively urinary tract infection developed in 40 patients (13%) and febrile urinary tract infection developed in 11 (3.5%). Of patients with urinary tract infection 26 had initially negative postoperative voiding cystourethrogram, of whom 16 underwent repeat voiding cystourethrogram and 9 showed recurrent vesicoureteral reflux. Five of these 9 patients had clinical pyelonephritis. Of assessed risk factors only preoperative recurrent urinary tract infection (OR 2.2, p = 0.03) and bladder dysfunction (OR 3.3, p = 0.001) were independent predictors of post-injection urinary tract infection.

CONCLUSIONS: In our series urinary tract infection after dextranomer/hyaluronic acid injection was rare. Patients with recurrent urinary tract infections and bladder dysfunction preoperatively are at increased risk for urinary tract infection after treatment. Patients with febrile urinary tract infection after dextranomer/hyaluronic acid injection are at high risk for recurrent vesicoureteral reflux.

Urinary Tract Infection Following Successful Dextranomer/Hyaluronic Acid Injection for Vesicoureteral Reflux

Chi A, Gupta A, Snodgrass W

Purpose: The incidence of symptomatic urinary tract infection following reflux resolution by endoscopic injection is unclear. We determined the occurrence of febrile and nonfebrile urinary tract infections, and factors relating to development of infection after reflux correction with dextranomer/hyaluronic acid injection.

Materials and Methods: We identified 175 patients with more than 6 months of followup after successful dextranomer/hyaluronic acid injection by one of us (WS) to resolve vesicoureteral reflux. Of these patients data regarding post-injection symptomatic urinary tract infection could be obtained from parents and/or primary care physicians and urological records in 167, who comprised the study group. All patient reported infections were additionally verified by review of medical records. Univariate and multivariate logistic regression analyses were done, evaluating factors including gender, age, voiding dysfunction, reflux grade, unilateral vs bilateral reflux, number of pretreatment infections, number of infections within 12 months of injection and febrile vs nonfebrile urinary tract infection in predicting the likelihood of post-injection urinary tract infection.

Results: Urinary tract infection occurred in 159 patients (95%) before injection, and was febrile in 82%. With a median followup after reflux correction of 32 months (range 7 to 53) symptomatic infections developed in 40 children (24%), of which half were febrile. Multivariate analysis showed that the number of preoperative urinary tract infections best predicted the likelihood of infection after dextranomer/hyaluronic acid injection. Nearly half of the patients with febrile urinary tract infection undergoing followup cystography had recurrent reflux.

Conclusions: Patients with more than 3 pre-injection infections were 8.5 times more likely than those with 1 pre-injection infection to have post-injection symptomatic urinary tract infection. Overall rates of symptomatic and febrile infections after dextranomer/hyaluronic acid reflux resolution were similar to those reported following ureteral reimplantation.

Urinary Tract Infection

Antibiotic Prophylaxis

Long-term, low-dose prophylaxis against urinary tract infections in young children.


Urinary tract infection (UTI) affects about 2% of boys and 8% of girls during the first 6 years of life with Escherichia coli as the predominant pathogen. Symptomatic UTI causes discomfort and distress, and carries a risk of inducing renal damage. The strong correlation between febrile UTI, dilating vesicoureteral reflux (VUR), and renal scarring led to the introduction of antibiotic prophylaxis for children with VUR to reduce the rate of UTI recurrence. It became common practice to use prophylaxis for children with VUR and other urinary tract abnormalities. This policy has been challenged because of a lack of scientific support.

Now, randomized controlled studies are available that compare prophylaxis to no treatment or placebo.

They show that children with normal urinary tracts or non-dilating VUR do not benefit from prophylaxis. Dilating VUR may still be an indication for prophylaxis in young children. After the first year of life, boys have very few recurrences and do not benefit from prophylaxis. Girls with dilating VUR, on the other hand, are more prone to recurrences and benefit from prophylaxis. There has been a decline in the use of prophylaxis due to questioning of its efficacy, increasing bacterial resistance, and a propensity to low adherence to medication. Alternative measures to reduce UTI recurrences should be emphasized.

However, in selected patients carefully followed, prophylaxis can protect from recurrent UTI and long-term sequelae. 1. There is a strong correlation between UTI, VUR, and renal scarring. 2. Children with normal urinary tracts or non-dilating VUR do not benefit from prophylaxis. 3. Young children, mainly girls, with dilating VUR are at risk of recurrent UTI and acquired renal scarring and seem to gain from antibiotic prophylaxis. 4. Increasing bacterial resistance and low adherence with prescribed medication is a major obstacle to successful antibiotic prophylaxis.

Combination of probiotics and antibiotics in the prevention of recurrent urinary tract infection in children.


OBJECTIVE: We examined the preventive effect of probiotic and antibiotics versus antibiotics alone, in children with recurrent urinary tract infections (RUTI) in a preliminary randomized clinical trial.

METHODS: Between March 2007 and April 2011, children with the history of RUTI and unilateral vesicoureteral reflux (VUR) were randomly assigned to receive concomitant probiotic and antibiotics (Lactobacillus acidophilus and bifidobacterium lactis, 10(7)/ml, as 0.25 ml/kg three times a day regimen in addition to Nitrofurantoin, 1mg/kg daily (group I). In group II, all children received conventional prophylactic antibiotics alone (Nitrofurantoin, 1 mg/kg daily). Randomization was performed via using the random numerals table in a 1:1 manner with stratification by sex, age and grade of reflux. The urine examinations were done monthly and the incidence of UTI was evaluated in these two groups.

FINDINGS: Forty-one children (age: 8.3±3.1 years) in group I and 44 children (age: 8.0±3.0 years) in group II were compared. During the course of three years, 39% in group I and 50% of participants in group II experienced RUTIs (P=0.4). Incidences of UTI - febrile and afebrile - reduced in both groups without any significant differences after two years of prophylaxis. Also, incidence of afebrile UTIs did not significantly differ (0.51±1.30 and 0.81±1.41 respectively, P =0.3); however, the incidence of febrile UTIs in particular were lower in group I (0.00±0.00 versus 0.13±0.40, P =0.03) in the last year.

CONCLUSION: The consumption of probiotic and antibiotics in children with RUTI is safe and more effective in reducing the incidence of febrile UTI in comparison to prophylactic antibiotics alone.


Conway PH, Cnaan A, Zaoutis T, Henry BV, Grundmeier RW, Keren R.

CONTEXT: The evidence regarding risk factors for recurrent urinary tract infection (UTI) and the risks and benefits of antimicrobial prophylaxis in children is scant.

OBJECTIVES: To identify risk factors for recurrent UTI in a pediatric primary care cohort, to determine the association between antimicrobial prophylaxis and recurrent UTI, and to identify the risk factors for resistance among recurrent UTIs.

DESIGN, PATIENTS, AND SETTING: From a network of 27 primary care pediatric practices in urban, suburban, and semirural areas spanning 3 states, a cohort of children aged 6 years or younger who were diagnosed with first UTI between July 1, 2001, and May 31, 2006, was assembled. Time-to-event analysis was used to determine risk factors for recurrent UTI and the association between antimicrobial prophylaxis and recurrent UTI, and a nested case-control study was performed among children with recurrent UTI to identify risk factors for resistant infections.

MAIN OUTCOME MEASURES: Time to recurrent UTI and antimicrobial resistance of recurrent UTI pathogens.

RESULTS: Among 74,974 children in the network, 611 (0.007 per person-year) had a first UTI and 83 (0.12 per person-year after first UTI) had a recurrent UTI. In multivariable Cox time-to-event models, factors associated with increased risk of recurrent UTI included white race (0.17 per person-year; hazard ratio [HR], 1.97; 95% confidence interval [CI], 1.22-3.16), age 3 to 4 years (0.22 per person-year; HR, 2.75; 95% CI, 1.37-5.51), age 4 to 5 years (0.19 per person-year; HR, 2.47; 95% CI, 1.19-5.12), and grade 4 to 5 vesicoureteral reflux (0.60 per person-year; HR, 4.38; 95% CI, 1.26-15.29). Sex and grade 1 to 3 vesicoureteral reflux were not associated with risk of recurrence. Antimicrobial prophylaxis was not associated with decreased risk of recurrent UTI (HR, 1.01; 95% CI, 0.50-2.02), even after adjusting for propensity to receive prophylaxis, but was a risk factor for antimicrobial resistance among children with recurrent UTI (HR, 7.50; 95% CI, 1.60-35.17).

CONCLUSION: Among the children in this study, antimicrobial prophylaxis was not associated with decreased risk of recurrent UTI, but was associated with increased risk of resistant infections.

Diagnostic

Urinary tract infection and vesicoureteral reflux in children with mild antenatal hydronephrosis.


OBJECTIVE: The postnatal management of mild antenatal hydronephrosis (ANH) remains controversial. The purpose of this study was to evaluate the incidence of UTI and VUR in children with mild ANH in order to determine the necessity of antibiotic prophylaxis (ABP) and VCUG.

METHOD: The data of 1511 patients with various grades of ANH who were referred to Department of Urology, Boston Children’s Hospital between January 1998 and January 2010 were reviewed and 760 patients who had mild ANH were identified. The inclusion criteria were: 1) A confirmed report of ANH or actual prenatal ultrasound (US) images. 2) Postnatal evaluation and management conducted at the hospital. 3) Persistent mild hydronephrosis on the first US done between two weeks and three months of age. 4) No other US findings such as ureteral dilatation, duplication anomalies or bladder abnormalities. 5) At least one three-month follow up. Univariate statistical analysis was performed using a Student’s t test.

RESULTS: Of the 760 patients who were identified, 608 (80%) were males, and 225 (30%) had bilateral mild hydronephrosis. Of these, 475 patients (63%) underwent an initial screening VCUG. VUR was identified in 13 patients (1.7%) with grades varying from 1 to 5. At follow up, hydronephrosis resolved in 67% of the renal units and worsened in 3.3%. Among the 692 patients with available follow-up data, 23 (3.3%) had a documented UTI. Twelve of these children had an initial screening VCUG that was negative for VUR. Of these 12 patients, seven underwent a subsequent RNC with none having VUR; five of the 12 patients did not undergo a repeat evaluation for VUR (four had a UTI after the screening VCUG and one had an afebrile UTI). Eleven of the 23 children with mild ANH did not have an initial screening VCUG, and all underwent a subsequent VCUG/RNC. Only two children were then found to have VUR Grade 4-5.

CONCLUSION: The incidence of UTI and VUR in children with mild ANH is low. Consequently, routine VCUG screening for VUR and the use of long-term ABP is not necessary for all patients with asymptomatic mild ANH. Evaluation for VUR in children with mild ANH should be reserved for those who subsequently present with a UTI.


BACKGROUND: To our knowledge, the risk of renal scarring in children with a urinary tract infection (UTI) has not been systematically studied.

OBJECTIVE: To review the prevalence of acute and chronic renal imaging abnormalities in children after an initial UTI.

METHODS: We searched Medline and Embase for English-, French-, and Spanish-language articles using the following terms: “Technetium 99mTc dimercaptosuccinic acid (DMSA),” “DMSA,” “dimercaptosuccinic,” “scintigra*,” “pyelonephritis,” and “urinary tract infection.” We included articles if they reported data on the prevalence of abnormalities on acute-phase (15 days) or follow-up (5 months) DMSA renal scans in children aged 0 to 18 years after an initial UTI. Two evaluators independently reviewed data from each article.

RESULTS: Of 1533 articles found by the search strategy, 325 full-text articles were reviewed; 33 studies met all inclusion criteria. Among children with an initial episode of UTI, 57% (95% confidence interval [CI]: 50–64) had changes consistent with acute pyelonephritis on the acute-phase DMSA renal scan and 15% (95% CI: 11–18) had evidence of renal scarring on the follow-up DMSA scan. Children with vesicoureteral reflux (VUR) were significantly more likely to develop pyelonephritis (relative risk [RR]: 1.5 [95% CI: 1.1–1.9]) and renal scarring (RR: 2.6 [95% CI: 1.7–3.9]) compared with children with no VUR. Children with VUR grades III or higher were more likely to develop scarring than children with lower grades of VUR (RR: 2.1 [95% CI: 1.4-3.2]).

CONCLUSIONS: The pooled prevalence values provided from this study provide a basis for an evidence-based approach to the management of children with this frequently occurring condition.

Management

NICE Guidelines Cannot Be Recommended for Imaging Studies in Children Younger Than 3 Years with Urinary Tract Infection.

Ristola MT, Hurme T.

Introduction: We assessed the possible consequences of applying the National Institute of Health and Clinical Excellence (NICE) guidelines for imaging studies of children younger than 3 years with urinary tract infection (UTI) to clinical practice, in terms of altered diagnoses and treatment.

Material and Methods: In a retrospective cohort of 672 patients with UTI, we evaluated indications for and results of renal and bladder ultrasonography, voiding cystourethrography (VCUG), dimercaptosuccinic acid scintigraphy, UTI recurrence, antimicrobial prophylaxis (AMP), antireflux procedures, and other urological procedures.

Results: There were a total 125 patients with vesicoureteral reflux (VUR), of whom 59 patients (47%) would have been missed, had the NICE guidelines being applied. These included 20 of the 64 patients (31%) with dilating VUR and 13 of the 30 patients (43%) who underwent antireflux procedures. A VCUG would have been avoided in 184 patients (74%) with no VUR in VCUG.

Conclusion: Based on the results in this cohort of 672 patients, we cannot recommend the use of the NICE guidelines for imaging studies in children younger than 3 years with UTI.

Committee on Quality Improvement, Subcommittee on Urinary Tract Infection - Practice Parameter: The Diagnosis, Treatment, and Evaluation of the Initial Urinary Tract Infection in Febrile Infants and Young Children
Kenneth B. Roberts, MD, Chairperson, Stephen M. Downs, MD, MS, Stanley Hellerstein, MD, Michael J. Holmes, MD, PhD, Robert L. Lebowitz, MD, Jacob A. Lohr, MD, Linda D. Shortliffe, MD, Russell W. Steele, MD, Pediatrics 1999;103;843

Objective. To formulate recommendations for health care professionals about the diagnosis, treatment, and evaluation of an initial urinary tract infection (UTI) in febrile infants and young children (ages 2 months to 2 years).

Design. Comprehensive search and analysis of the medical literature, supplemented with consensus opinion of Subcommittee members. Participants. The American Academy of Pediatrics (AAP) Committee on Quality Improvement selected a Subcommittee composed of pediatricians with expertise in the fields of epidemiology and informatics, infectious diseases, nephrology, pediatric practice, radiology, and urology to draft the parameter. The Subcommittee, the AAP Committee on Quality Improvement, a review panel of office-based practitioners, and other groups within and outside the AAP reviewed and revised the parameter.

Methods. The Subcommittee identified the population at highest risk of incurring renal damage from UTI—infants and young children with UTI and fever. A comprehensive bibliography on UTI in infants and young children was compiled. Literature was abstracted in a formal manner, and evidence tables were constructed. Decision analysis and cost-effectiveness analyses were performed to assess various strategies for diagnosis, treatment, and evaluation.

CONCLUSIONS: Eleven recommendations are proposed for the diagnosis, management, and evaluation of infants and young children with UTI and unexplained fever. Infants and children younger than 2 years of age with unexplained fever are identified for particular concern because UTI has a high prevalence in this group (;5%), may cause few recognizable signs or symptoms other than fever, and has a greater potential for renal damage than in older children. Strategies of diagnosis and treatment depend on how ill the clinician assesses the infant or young child to be, ie, whether antimicrobial therapy is warranted immediately or can be delayed safely until the results of urine culture are available. Diagnosis is based on the culture of an appropriately collected specimen of urine; urinalysis can only suggest the diagnosis. Imaging studies should be performed on all infants and young children with a documented initial UTI.

**VUR**

**Antibiotic Prophylaxis**

*The RIVUR study: a review of its findings.*

Cara-Fuentes G, Gupta N, Garin EH.
Pediatr Nephrol. 2014 Dec 11. [Epub ahead of print]

**BACKGROUND:** The conclusion drawn by the authors of the Randomized Intervention for Children with Vescicoureteral Reflux (RIVUR) trial is that antimicrobial prophylaxis reduces the risk of recurrent urinary tract infection (UTI)-but not of renal scarring-in patients with vesicoureteral reflux (VUR).

**RESULTS:** A review of the findings showed that the decreased recurrent UTI rate was only present at the end of the 2-year follow-up period and was only slightly increased (12.3 %) above the 10 % cutoff for statistical significance. The difference was not observed in children younger than two years of age with VUR grade III and IV. In addition, the rate of new renal scarring was not statistically different between the prophylaxis and placebo groups (8.2 vs. 8.4 %, respectively). A high rate of uropathogen antibiotic resistance was observed in the prophylaxis group (68.4 vs. 24.6 %, respectively).

**CONCLUSION:** The analysis of the RIVUR findings questions the validity of its authors suggestion that the results may warrant reconsideration of the current recommendations by the American Academy of Pediatrics on obtaining a voiding cystourethrogram after the first febrile UTI and the use of urinary antibiotic prophylaxis in VUR patients.

Antibiotic prophylaxis in the management of vesicoureteric reflux: a randomized double-blind placebo-controlled trial.


BACKGROUND: The benefits of long-term low-dose antibiotics in preventing urinary tract infection (UTI) and renal damage in children with primary vesicoureteric reflux (VUR) are unclear.

METHODS: Children aged between 1 and 12 years with VUR grade I-IV and a microbiologically proven UTI were randomized into two groups to receive either antibiotic prophylaxis [2 mg/kg trimethoprim + sulfamethoxazole (TMP-SMX)] daily or placebo, respectively, for 12 months. Primary outcome was microbiologically confirmed symptomatic UTI. Intention-to-treat analysis using time-to-event data was performed.

RESULTS: A total of 93 children (66.7 % boys) with a median age of 4.6 years were enrolled in this study; VUR grade III-IV was present in 73.1 % of these children. At least one symptomatic UTI occurred in ten (21.3 %) patients receiving antibiotic prophylaxis and in three (6.5 %) patients receiving placebo [hazard ratio in antibiotic group 3.9; 95 % confidence interval (CI) 1-14; log rank test P=0.02]. Compared to the group receiving placebo, the antibiotic group had a 14.8 % increased risk for developing UTI (95 % CI 1-28; P=0.03). Of the total number of episodes of UTI, 58.3 % of those in the antibiotic group were caused by TMP-SMX-resistant bacteria compared to 20 % in the placebo group (P=0.15). A renal scan at 12 months revealed that six of 37 (16.2 %) patients in the antibiotic group and seven of 43 (16.3 %) patients in the placebo group had new or worsening of pre-existing scar.

CONCLUSIONS: Long-term antibiotic prophylaxis with TMP-SMX is associated with increased risk of symptomatic UTI compared to placebo in children with grade I-IV VUR.

Continuous antibiotic prophylaxis reduces the risk of febrile UTI in children with asymptomatic antenatal hydronephrosis with either ureteral dilation, high-grade vesicoureteral reflux, or ureterovesical junction obstruction.


BACKGROUND: The efficacy and utility of continuous antibiotic prophylaxis (CAP) in children with congenital antenatal hydronephrosis (ANH) is uncertain. The literature has both supportive and contradictory evidence. The growing trend not to place children with ANH on CAP has created varied clinical practice based on anecdotal individual case characteristics. Our goal was to compare individual infant characteristics between those children who were maintained on CAP to those that were not to try to determine predisposing risk factors to febrile.

METHODS: All electronic medical records (EMRs) of children referred to our institution for congenital ANH over a period from 2001 to 2011 were examined. We excluded those referred for urinary tract infection (UTI) who had a history of congenital ANH. We also excluded those with incomplete records, or follow-up less than 2 years. Children were divided into two groups: those maintained on CAP (YCAP) and those not maintained on CAP (NCAP). Our primary endpoint was febrile UTI. Follow-up was at least 24 months. Demographic, perinatal and postnatal clinical data were recorded. Statistical analysis was performed using STATA Version 11.1.

RESULTS: Of the 405 children fitting inclusion criteria, 278 (68.6%) children were maintained on CAP and 127 (31.4%) were not on CAP. The incidence of prematurity, oligohydramnios, perinatal respiratory complications, use of perinatal antibiotics, circumcision status, renal anomalies, associated medical diagnoses, and low birth weight did not differ between the two groups. Overall the incidence of febrile UTI during the follow-up period was 22.2%. The incidence of febrile UTI between the YCAP and NCAP groups was significant (YCAP = 7.9% and NCAP 18.7%, p = 0.021). Multivariate logistic regression using CAP as the dichotomous dependent variable revealed that ureteral dilation, high-grade vesicoureteral reflux (VUR), and ureterovesical junction (UVJ) obstruction were independent risk factors for febrile UTI. More specifically, children with ureteral dilation >11 mm NOT maintained on CAP had a 5.54 (OR = 5.54; CI = 3.15-7.42, p = 0.001) fold increased risk of febrile UTI compared to those maintained on CAP.

CONCLUSIONS: The presence of ureteral dilation, high grade VUR, and UVJ obstruction were independent risk factors for development of UTI in children with congenital ANH. Therefore CAP may have a significant role in reducing the risk of febrile UTI in children with ANH with those identifiable risk factors, but otherwise seems unnecessary.

Probiotics prophylaxis in infants with primary vesicoureteral reflux.


BACKGROUND: In this era of increasing bacterial resistance to antimicrobial therapy, probiotics have great potential and yet they are a harmless alternative approach. This study is a prospective randomized uncontrolled trial to investigate the preventive effect of probiotic prophylaxis in infants with primary vesicoureteral reflux (VUR) and frequently recurring urinary tract infection (UTI) during the first follow-up year.

METHODS: One hundred and twenty-eight infants (aged 1 week to 12 months) with primary VUR were prospectively randomized into a probiotic (n = 64, Lactobacillus acidophilus, 1.0 \times 10^8 CFU/g) or antibiotic (n = 64, trimethoprim/sulfamethoxazole, 2/10 mg/kg) group.

RESULTS: The incidence of recurrent UTI in the probiotic group was slightly lower than in the antibiotic group without statistical significance (32.8% [21 out of 64] vs 40.6% [26/64]) (P = 0.348). Causative organisms of recurrent UTI, resolution rate of VUR, and development of renal scarring were not different between the probiotic and antibiotic prophylaxis groups. The incidences of antibiotic resistance of causative organisms in recurrent UTI were significantly lower in the probiotic group than in the antibiotic group.

CONCLUSIONS: Probiotics could be considered a natural alternative regimen for prophylaxis in infants with primary VUR.

Compliance With Antibiotic Prophylaxis in Children With Vesicoureteral Reflux: Results From a National Pharmacy Claims Database

Copp HL, Nelson CP, Shortliffe LD, Lai J, Saigal CS, Kennedy WA and the Urological Diseases in America Project

Purpose: Antibiotic prophylaxis is commonly used for medical management of vesicoureteral reflux. Little information exists on compliance with antibiotic prophylaxis in patients with vesicoureteral reflux.

Materials and Methods: We queried the i3 Innovus (Ingenix®) pharmacy claims 2002 to 2007 database for patients 18 years old or younger with vesicoureteral reflux (ICD-9 code 593.7 plus claim for cystogram) and analyzed those with at least 1 year of followup data. Criteria for management with antibiotic prophylaxis were 2 or more 30-day supplies of antibiotic prescriptions, or 4 or more 14-day supplies of prescriptions if the antibiotic was a penicillin or cephalosporin. Antibiotic prophylaxis compliance was determined using a medication possession ratio, an estimate of the proportion of time that patients have a prescribed drug available for use. Compliance was established as a medication possession ratio of 80% or greater, meaning coverage with antibiotic prophylaxis for 80% of the year or more.

Results: Of 9,496 patients with vesicoureteral reflux 5,342 (56.3%) were treated with antibiotic prophylaxis. Most patients were female (81%) and 5 years old or younger (79%). Trimethoprim/sulfonamides were most commonly prescribed (62%) and antiseptics were next (.24%). Of patients prescribed antibiotic prophylaxis 40% were compliant. Compliance was lower for 6 to 10-year-olds (OR 0.71, 95% CI 0.61-0.83) and 11 to 18-year-olds (OR 0.56, 95% CI 0.41-0.79) compared to younger children (5 years or less). Increased compliance was associated with 1 or more hospitalizations (OR 1.70, 95% CI 1.48-1.97) and 1 or more urologist visits (OR 1.41, 95% CI 1.25-1.58).

Conclusions: Among patients with vesicoureteral reflux who are prescribed prophylactic antibiotics 40% are compliant with treatment. Young age, frequent hospitalization and specialist visits are associated with compliance. This knowledge may help to develop effective interventions to improve compliance and underscores the importance of reporting compliance in clinical studies evaluating the usefulness of antibiotic prophylaxis in vesicoureteral reflux management.

Outcome after discontinuing prophylactic antibiotics in children with persistent vesicoureteral reflux.


Purpose: Treatment for vesicoureteral reflux remains controversial. Lacking an evidence-based treatment protocol, we offered the option of terminating prophylactic antibiotics in otherwise healthy patients with persistent vesicoureteral reflux at age 5 years or greater. We report outcomes with respect to the urinary tract infection incidence and to whether surgical intervention was eventually done.

Materials and Methods: We obtained institutional review board approval to retrospectively review the records of all children with vesicoureteral reflux from December 1999 to February 2009. Of this group we selected children 5 years old or older who had been taken off prophylactic antibiotics. We assessed children with primary vesicoureteral reflux in detail.

Results: The records of 1,217 that we reviewed showed that antibiotics were discontinued in 185 patients, including 160 girls (89%) and 25 boys (11%), at an average age of 6.2 years. Average followup was 2.0 years with recorded follow up up to 8 years off prophylaxis. In 50 girls (91%) and 5 boys (9%), urinary tract infection developed after discontinuing prophylaxis. Correction was done in 57 patients, including open repair in 34 and endoscopic injection in 23. Two patients underwent intervention at parent request after an average of 0.7 years of uneventful observation. We identified no parameter predicting patients at risk for urinary tract infection.

Conclusions: Urinary tract infection develops in 29% of patients 5 years old or older with persistent vesicoureteral reflux within 2 years after the cessation of prophylaxis. Most of these cases are febrile. Discontinuing antibiotics is reasonable but a prospective, randomized, long-term, multi-institutional trial is required to determine whether this approach is beneficial.

Part 4: Considerations regarding the medical management of VUR: what have we really learned?

Koyle MA, Caldamone AA.

In the treatment of vesicoureteral reflux (VUR), the use of prophylactic antibiotics is most often the first treatment option in children with grades I-IV VUR. Both the overuse and misuse of antimicrobials have accelerated the appearance and spread of antibiotic resistance. There is a lack of controlled studies that address the role and efficacy of prophylactic antibiotic use in the VUR population. Physicians may also be pressured to prescribe antibiotic therapy by patients even in the absence of appropriate indications for use. However, patient reported compliance is often far lower than clinically documented compliance. The associated disadvantages of prophylactic antibiotic use include the development of antimicrobial resistance and patient noncompliance which begs for a re-evaluation of current management patterns of VUR

Considering questionable evidence supporting the use of traditional therapies, new innovations, including endoscopic injection, should be considered as an alternative.

Comparison of Therapies

New contralateral vesicoureteral reflux after unilateral ureteral reimplantation: predictive factors and clinical outcomes.


PURPOSE: Although unilateral ureteral reimplantation for vesicoureteral reflux is highly successful, new contralateral reflux will develop postoperatively in some patients. We examined predictors and clinical outcomes of postoperative contralateral vesicoureteral reflux.

MATERIALS AND METHODS: We reviewed patients who underwent nontapered unilateral reimplantation for primary vesicoureteral reflux graded on a 3-point scale at our institution from January 1990 to December 2002, and identified those with subsequent contralateral vesicoureteral reflux. We analyzed the association of patient/procedure characteristics with incidence, and time to resolution of contralateral reflux and postoperative urinary tract infection. Multivariable models controlled for variables associated with incidence and time to resolution of contralateral reflux.

RESULTS: A total of 395 patients (77.2% female, median age 5.3 years) underwent ureteral reimplantation for vesicoureteral reflux. Preoperative reflux was grade 1 in 2.8% of patients, grade 2 in 56.6% and grade 3 in 40.6%. Technical success was 95.4%. After reimplantation 39 patients (9.9%) had new contralateral reflux (grade 1 in 7, grade 2 in 27 and grade 3 in 5). Median followup was 51.8 months. On multivariate analysis younger age (less than 6 years, OR 3.7, p = 0.006) and low observed bladder capacity as percent of predicted bladder capacity (less than 50% of predicted capacity, OR 6.3, p = 0.02) were significant predictors of contralateral reflux. Contralateral reflux resolved in 21 of 27 patients (77.8%) on subsequent cystography at a median of 21.5 months. Two patients underwent reimplantation for persistent contralateral reflux. Four of 39 patients (10.3%) with contralateral reflux had postoperative febrile urinary tract infections at a median of 26 months, with spontaneous resolution of contralateral reflux in all.

CONCLUSIONS: Younger patients and those with low observed vs predicted bladder capacity may be at increased risk for postoperative contralateral vesicoureteral reflux. A majority of contralateral reflux will resolve spontaneously, and the clinical course is typically benign.

Postoperative ureteral obstruction after endoscopic treatment of vesicoureteral reflux with polyacrylate polyalcohol copolymer (Vantris®).


PURPOSE: To investigate the incidence and presentations of ureteral obstruction following periureteral injection of polyacrylate polyalcohol copolymer (PPC) for the treatment of vesicoureteral reflex (VUR).

MATERIALS AND METHODS: From Jan 2010 to Dec 2012, 88 patients (28 male, 60 female) with 128 renal refluxing units (RRU), 131 ureters and a mean age of 6.7 ± 5.9 years (range: 4 months to 32 years) underwent endoscopic correction of their VUR, using PPC. Exclusion criteria were dysmorphic appearing distal ureter, extravesical position of the ureteral orifice, persistent urethral obstruction (e.g. after previous valve ablation) and severe bladder trabeculation, making ureteral orifice unidentifiable. Patients were followed up by ultrasound one month after the injection and then every three months. Cystography was performed 3 months post-operation. Mean follow-up time was 13.1 ± 6.8 months (range: 3-27 months).

RESULTS: Two patterns of obstruction were observed: early, during the first 3-4 days post-operation, in four patients (4 ureters; 3%) which was associated with transient hydroureteronephrosis (HUN) in 2 patients (2 ureters; 1.5%); and late-onset obstruction in 3 patients (4 ureters; 3%) which appeared 3 months to 1 year after surgery. It manifested itself by urinary tract infection and uremia in one patient with bilateral obstruction but was asymptomatic in the other two. Early obstruction was managed expectantly and resolved in 3-12 months; however, late-onset obstruction needed catheter placement or open ureteroneocystostomy.

CONCLUSIONS: Patients who undergo endoscopic treatment for their VUR using PPC need long-term follow up until the safety of this substance is confirmed.

Outcomes of targeted treatment for vesicoureteral reflux in children with nonneurogenic lower urinary tract dysfunction


PURPOSE: There is a known association between nonneurogenic lower urinary tract conditions and vesicoureteral reflux. Whether reflux is secondary to the lower urinary tract condition or coincidental is controversial. We determined the rate of reflux resolution in patients with lower urinary tract dysfunction using targeted treatment for the underlying condition.

MATERIALS AND METHODS: Patients diagnosed and treated for a lower urinary tract condition who had concomitant vesicoureteral reflux at or near the time of diagnosis were included. Patients underwent targeted treatment and antibiotic prophylaxis, and reflux was monitored with voiding cystourethrography or videouro dynamics.

RESULTS: Vesicoureteral reflux was identified in 58 ureters in 36 females and 5 males with a mean age of 6.2 years. After a mean of 3.1 years of treatment reflux resolved with targeted treatment in 26 of 58 ureters (45%). All of these patients had a history of urinary tract infections before starting targeted treatment. Resolution rates of vesicoureteral reflux were similar for all reflux grades. Resolution or significant improvement of reflux was greater in the ureters of patients with dysfunctional voiding (70%) compared to those with idiopathic detrusor overactivity disorder (38%) or detrusor underutilization (40%).

CONCLUSIONS: Vesicoureteral reflux associated with lower urinary tract conditions resolved with targeted treatment and antibiotic prophylaxis in 45% of ureters. Unlike the resolution rates reported in patients with reflux without a coexisting lower urinary tract condition, we found that there were no differences in resolution rates among grades I to V reflux in patients with lower urinary tract conditions. Patients with dysfunctional voiding had the most improvement and greatest resolution of reflux. Additionally grade V reflux resolved in some patients.

Primary vesicoureteral reflux
Stein R1, Ziesel C, Rubenwolf P, Beetz R.
Urologe A. 2013 Jan;52(1):39-47

The never ending discussion about the diagnostics and treatment of vesicoureteral reflux (VUR) now includes arguments for diagnostic nihilism as well as invasive diagnostics and therapy, which is reminiscent of the debate on prostate cancer in adulthood. The common goal of all currently competing diagnostic strategies and approaches is the prevention of renal scars by the most effective and least burdensome approach. There is a difference between acquired pyelonephritic scars with VUR (acquired reflux nephropathy) and congenital reflux nephropathy (primary dysplasia) which cannot be influenced by any therapy. The VUR can be verified by conventional radiological voiding cystourethrography (VCUG), by urosonography, radionuclide cystography or even by magnetic resonance imaging (MRI). The guidelines of the European Association of Urology/European Society for Paediatric Urology (EAU/ESPU) recommend radiological screening for VUR after the first febrile urinary tract infection. Significant risk factors in patients with VUR are recurrent urinary tract infections (UTI) and parenchymal scarring and the patients should undergo patient and risk-adapted therapy. Infants with dilating reflux have a higher risk of renal scarring than those without dilatation of the renal pelvis. Bladder dysfunction or dysfunctional elimination syndrome represents a well-known but previously neglected risk factor in combination with VUR and should be treated prior to any surgical intervention as far as is possible. Certainly not every patient with VUR needs therapy. The current treatment strategies take into account age and gender, the presence of dysplastic or pyelonephritic renal scars, the clinical symptoms, bladder dysfunction and frequency and severity of recurrent UTI as criteria for the therapy decision. The use of an antibacterial prophylaxis as well as the duration is controversially discussed. Endoscopic therapy can be a good alternative to antibacterial prophylaxis or a surveillance strategy in patients with low grade VUR. In patients with dilating VUR and given indications for surgery, endoscopic treatment can be offered. However, parents should be completely informed about the significantly lower success rate of endoscopic therapy compared to open surgical procedures. The open surgical techniques guarantee the highest success rates and should be used in patients with a dilating VUR and high risk of renal damage.

Interventions for primary vesicoureteric reflux (Review)

Nagler EVT, Williams G, Hodson EM, Craig JC.

BACKGROUND: Vesicoureteric reflux (VUR) results in urine passing retrograde up the ureter. Urinary tract infections (UTI) associated with VUR have been considered a cause of permanent renal parenchymal damage in children with VUR. Management of these children has been directed at preventing UTI by antibiotic prophylaxis and/or surgical correction of VUR. The optimum strategy is not clear.

OBJECTIVES: To evaluate the benefits and harms of different treatment options for primary VUR.

SEARCH STRATEGY: In August 2010 we searched CENTRAL, MEDLINE and EMBASE and screened reference lists of papers and abstracts from conference proceedings.

SELECTION CRITERIA: RCTs in any language comparing any treatment of VUR including surgical or endoscopic correction, antibiotic prophylaxis, non-invasive non-pharmacological techniques and any combination of therapies.

DATA COLLECTION AND ANALYSIS: Two authors independently searched the literature, determined study eligibility, assessed quality, extracted and entered data. We expressed dichotomous outcomes as risk ratios (RR) and their 95% confidence intervals (CI) and continuous data as mean differences (MD) and their 95% CI’s. Data were pooled using the random effects model.

MAIN RESULTS: Twenty RCTs (2324 children) were included. Long-term low-dose antibiotic prophylaxis compared to no treatment/placebo did not significantly reduce repeat symptomatic UTI (846 children: RR 0.68, 95% CI 0.39 to 1.17) or febrile UTI (946 children: RR 0.77, 95% CI 0.47 to 1.24) at two years. There was considerable heterogeneity in the analyses and only one study was adequately blinded. At one to three years, antibiotic prophylaxis reduced the risk of new or progressive renal damage on DMSA scan (446 children: RR 0.35, 95% CI 0.15 to 0.80). Side effects were infrequent when reported, but antibiotics increased the likelihood of bacterial drug resistance threefold (132 UTIs: RR 2.94, 95% CI 1.39 to 6.25). When long-term antibiotic prophylaxis was compared with surgical or endoscopic correction of VUR plus antibiotics for one to 24 months (10 studies, 1141 children), the risk of symptomatic UTI was not significantly different at any time point. Combined surgical and antibiotic treatment caused a 57% reduction in febrile UTI by five years (2 studies, 449 children: RR 0.43, 95% CI 0.27 to 0.70) but did not decrease the risk of new or progressive renal damage at any time point. Postoperative obstruction was seen in 0% and 7% of children in two surgical studies and 0% in one endoscopic study.

AUTHORS’ CONCLUSIONS: Compared with no treatment, use of long-term, low-dose antibiotics did not significantly reduce the number of repeat symptomatic and febrile UTIs in children with VUR. Considerable heterogeneity in the analyses and inclusion of only one adequately blinded study, made drawing firm conclusions challenging. Antibiotic prophylaxis significantly reduced the risk of developing new or progressive renal damage, but assuming an 8% baseline risk, 33 children would need long-term antibiotic prophylaxis to prevent one more child developing kidney damage over the course of two to three years. The added benefit of surgical or endoscopic correction of VUR over antibiotic treatment alone remains unclear. Eight
children would require combined surgical and antibiotic treatment to prevent one additional child developing febrile UTI by five years, but it would not cause fewer children developing renal damage.

Therapy for Vesicoureteral Reflux: Antibiotic Prophylaxis, Urotherapy, Open Surgery, Endoscopic Injection, or Observation?

Elder JS

Vesicoureteral reflux (VUR) refers to the retrograde flow of urine from the bladder into the ureter and renal pelvis. It generally results from congenital maldevelopment of the ureterovesical junction, although VUR may develop in individuals with abnormally high detrusor pressure. VUR increases a child’s susceptibility to pyelonephritis and renal scarring. Treatment goals include the prevention of pyelonephritis, reflux nephropathy, and other complications of reflux. Treatment alternatives include antibiotic prophylaxis, urotherapy (correction of voiding dysfunction), and surgical correction (open, injection therapy, or laparoscopic). Recent studies have challenged the presumed benefit of prophylaxis in children with VUR, while long-term retrospective studies have documented a high rate of hypertension in adults with reflux nephropathy. In addition, the risk of persistent VUR in adulthood is unresolved. These reports have stimulated a reevaluation of the role of various treatment options in children with VUR.

Traditional viewpoints regarding the role of antibiotic prophylaxis in the management of VUR are being challenged. Nevertheless, long-term studies demonstrate that individuals with reflux nephropathy are at significant risk for hypertension. Whether the recent advances in open, endoscopic, and laparoscopic surgical techniques justify an earlier role in children with VUR remains to be determined.

Interventions for primary vesicoureteric reflux


BACKGROUND: Vesicoureteric reflux (VUR) results in urine passing, in a retrograde manner, up the ureter. Urinary tract infections (UTIs) have been considered the main cause of permanent renal parenchymal damage in children with reflux. Management of these children has been directed at preventing infection by antibiotic prophylaxis and/or surgical correction of reflux. Controversy remains as to the optimum strategies.

OBJECTIVES: To evaluate the benefits and harms of different treatment options for primary VUR.

SEARCH STRATEGY: Randomised controlled trials (RCTs) were identified from the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, reference lists of articles and abstracts from conference proceedings. Date of last search: June 2006

SELECTION CRITERIA: Any treatment of VUR including surgery, antibiotic prophylaxis of any duration, non-invasive techniques and any combination of therapies.

DATA COLLECTION AND ANALYSIS: Two authors independently searched the literature, determined study eligibility, assessed quality, extracted and entered data. For dichotomous outcomes, results were expressed as relative risk (RR) and 95% confidence intervals (CI). Data were pooled using the random effects model.

MAIN RESULTS: Eleven studies (1148 children) were identified. Seven compared correction of VUR (by surgery or endoscope) plus antibiotics for 1-24 months with antibiotics alone, two compared antibiotics with no treatment and two compared different materials for endoscopic correction of VUR. Risk of UTI by 2, 5 and 10 years was not significantly different between surgical and medical groups (2 years RR 1.07, 95% CI 0.32 to 2.09; 5 years RR 0.99, 95% CI 0.79 to 1.26; 10 years RR 1.06, 95% CI 0.78 to 1.44). Combined treatment resulted in a 50% reduction in febrile UTI by 10 years (RR 0.54, 95% CI 0.55 to 0.92) but no concomitant reduction in risk of new or progressive renal damage by 10 years (RR 1.03, 95% CI 0.53 to 2.00). In two small studies no significant differences in risk for UTI (RR 0.75, 95% CI 0.15 to 3.84) or renal damage (RR 1.70, 95% CI 0.36 to 8.07) were found between antibiotic prophylaxis and no treatment.

AUTHORS’ CONCLUSIONS: It is uncertain whether the treatment of children with VUR confers clinically important benefit. The additional benefit of surgery over antibiotics alone is small at best. Assuming a UTI rate of 20% for children with VUR on antibiotics for five years, nine reimplantations would be required to prevent one febrile UTI, with no reduction in the number of children developing any UTI or renal damage.

Clinical Significance of Primary Vesicoureteral Reflux and Urinary Antibiotic Prophylaxis After Acute Pyelonephritis: A Multicenter, Randomized, Controlled Study


OBJECTIVES: To evaluate the role of primary vesicoureteral reflux (VUR) in increasing the frequency and severity of urinary tract infections (UTIs) and renal parenchymal damage among patients with acute pyelonephritis and to determine whether urinary antibiotic prophylaxis reduces the frequency and/or severity of UTIs and/or prevents renal parenchymal damage among patients with mild/moderate VUR.

METHODS: Patients 3 months to 18 years of age with acute pyelonephritis, with or without VUR, were assigned randomly to receive urinary antibiotic prophylaxis or not. Patients were monitored every 3 months for 1 year. Dimercaptosuccinic acid renal scans were repeated at 6 months or if there was a recurrence of febrile UTI. Urinalysis and urine culture were performed at each clinic visit. Renal ultrasound scans and voiding cystourethrogram were repeated at the end of 1 year of follow-up monitoring.

RESULTS: Of the 236 patients enrolled in the study, 218 completed the 1-year follow-up monitoring. Groups were similar with respect to age, gender, and reflux grade distribution for those with VUR. No statistically significant differences were found among the groups with respect to rate of recurrent UTI, type of recurrence, rate of subsequent pyelonephritis, and development of renal parenchymal scars.

CONCLUSIONS: After 1 year of follow-up monitoring, mild/moderate VUR does not increase the incidence of UTI, pyelonephritis, or renal scarring after acute pyelonephritis. Moreover, a role for urinary antibiotic prophylaxis in preventing the recurrence of infection and the development of renal scars is not supported by this study.

Treatment of vesico-ureteric reflux: a new algorithm based on parental preference.


OBJECTIVE: To assess parental preference (acknowledged in treatment guidelines as important when choosing therapy) about treatments for vesico-ureteric reflux (VUR, commonly associated with urinary tract infection and which can cause long-term renal damage if left untreated), as at present there is no definitive treatment for VUR of moderate severity (grade III).

SUBJECTS AND METHODS: The parents of 100 children with grade III reflux (38 boys and 62 girls, mean age 4 years, range 1–15) were provided with detailed information about the three treatment options available for treating VUR (antibiotic prophylaxis, open surgery and endoscopic treatment), including the mode of action, cure rate and possible complications, and the practical advantages and disadvantages. They were then presented with a questionnaire asking them to choose their preferred treatment.

RESULTS: Most parents preferred endoscopic treatment (80%), rather than antibiotic prophylaxis (5%) or open surgery (2%); 13% could not decide among the three options and endoscopic treatment was recommended.

CONCLUSION: Given the strong preference for endoscopic treatment we propose a new algorithm for treating VUR; endoscopic treatment would be considered as the first option for persistent VUR, except in severe cases where open surgery would still be recommended.


Stenburg A, Hensle TW, Läckgren G

Vesicoureteral reflux (VUR) affects about 1% of all children and carries an increased risk of pyelonephritis and long-term renal impairment. There are several approaches to the treatment of VUR: antibiotic prophylaxis (conservative treatment), open surgery, and endoscopic treatment. For many patients, endoscopic treatment cures VUR with a single procedure, eliminating the need for long-term antibiotic treatment and avoiding the trauma of a major surgical procedure.

The choice of material for endoscopic treatment is of key importance, and, until recently, all available materials were associated with concerns regarding safety and efficacy. Emerging data demonstrate that dextranomer/hyaluronic acid (Dx/HA) copolymer has good long-term safety and efficacy in treating VUR. A new treatment algorithm is, therefore, proposed.

Several different options are available for the treatment of VUR. There is ample evidence of the advantages of endoscopic implantation over both open surgery and prolonged antibiotic prophylaxis, provided that the chosen bulking agent has proven long-term safety and efficacy. Until recently, all available materials for an endoscopic injection were associated with significant safety and/or efficacy concerns. The latest evidence indicates that patients with VUR treated endoscopically with Dx/HA copolymer are unlikely to relapse in the long term and that there are no safety concerns with this substance. Thus, the 1997 AUA treatment guidelines for VUR may now be outdated because endoscopic treatment was not considered to be a viable treatment option at the time. Therefore, a new treatment algorithm for the treatment of VUR has been proposed, involving endoscopic treatment with Dx/HA copolymer as first-line therapy for patients with persistent VUR (ie, after 1 year’s therapy with antibiotic prophylaxis and, if appropriate, bladder training). It is anticipated that this algorithm may form the basis of future updates to VUR treatment guidelines.

Cost Analysis

The demographics and costs of inpatient vesicoureteral reflux management in the USA.


This study evaluates the impact of vesicoureteral reflux (VUR) on the economy and inpatient healthcare utilization in the USA.

A retrospective analysis was performed on children ≤ 18 years of age, hospitalized with the principal discharge diagnosis of VUR between 2000 and 2006, using the Healthcare Cost and Utilization Project Kids’ Inpatient Database.

The results are stratified as follows. First, by hospitalizations: between 2000 and 2006, 6,655 ± 720 (standard error) children/year were hospitalized with VUR. Since 2003, both the length of each hospitalization and the number of hospitalizations have decreased. Second, by related procedures/diagnoses: ureteral reimplantation was the most common procedure, accounting for 89% of hospitalizations. Congenital genitourinary anomalies, disorders of the kidney/ureter/bladder, and urinary tract infections (UTI) were the most common related diagnoses. Thirdly, by hospital economics: since 2000, hospital charges for VUR increased despite decreased lengths of hospitalization. By 2006, hospital charges rose to $18,798/hospitalization, and aggregate national charges exceeded $100 million.

Our results indicate that fewer children with VUR are requiring inpatient management. Children with VUR are often hospitalized for ureteral reimplantation or the management of related diagnoses. Since 2000, hospital charges for inpatient VUR management have increased. More efforts are needed to evaluate cost-effective strategies for the evaluation and management of VUR.

The cost-effectiveness of dextranomer/hyaluronic acid copolymer for the management of vesicoureteral reflux. 1: substitution for surgical management.
Benoit RM, Peele PB, Docimo SG.
Urol 2006; 176: 1588-92

PURPOSE: We examined the cost-effectiveness of dextranomer/hyaluronic acid copolymer injection in patients who would otherwise undergo ureteral reimplantation.

MATERIALS AND METHODS: A model for managing vesicoureteral reflux has previously been created. We now update the model to compare the costs of treating vesicoureteral reflux using standard methods (ie ureteral reimplantation after failed medical therapy) with the costs of dextranomer/hyaluronic acid injection.

RESULTS: In the first scenario created dextranomer/hyaluronic acid injection is substituted for ureteral reimplantation when surgical intervention would be performed for treatment of breakthrough infection or failure of the reflux to resolve. For dextranomer/hyaluronic acid injection to have equal cost-effectiveness compared to ureteral reimplantation in this scenario success rates for dextranomer/hyaluronic acid injection would need to be 57.8% per ureter for patients with unilateral reflux and 75.3% per ureter for patients with bilateral reflux. However, if increasing grades of reflux require increasing volumes of dextranomer/hyaluronic acid, success rates would need to be 72.5% for patients with unilateral reflux and 93.8% for patients with bilateral reflux. In the second scenario created dextranomer/hyaluronic acid injection is repeated if it fails to resolve the reflux after the first injection. Success rates to obtain equal cost-effectiveness for the repeat dextranomer/hyaluronic acid injection would need to be 0%, 11.4% and 60.3% in patients with unilateral reflux if the respective success rates of the initial injection were 85%, 70% and 55%. Success rates for the second dextranomer/hyaluronic acid injection would need to be 0%, 29.1% and 76.7% per ureter in patients with bilateral reflux if the respective success rates of the initial injection were 85%, 70% and 55%. If increasing volumes of dextranomer/hyaluronic acid were required for increasing grades of reflux, a second dextranomer/hyaluronic acid injection would not be a viable option.

CONCLUSIONS: Based on our results, dextranomer/hyaluronic acid injection may be more cost-effective than ureteral reimplantation for children who meet standard criteria for surgical therapy, especially for lower grades of reflux. If increasing grades of reflux require an increased volume of dextranomer/hyaluronic acid, then injection would likely be cost-effective only for grades I and II unilateral and bilateral reflux, and perhaps unilateral grade III reflux.

Cost-analysis of management strategies for children with vesicoureteric reflux

Nicklasson L, Högård S.

This study is an economic evaluation of three treatment strategies for vesico-ureteric reflux in children: neo-implantation; subureteric injection; and antibacterial prophylaxis.

Cost-analysis was used to compare the strategies, implying that the differences in benefits between them were not measured. Direct and indirect costs are included, taking the analytical viewpoint of the community. For the surgical strategies, data from four different hospitals in Sweden were used, and for the prophylactic strategy, data was gathered through a survey of 31 hospitals.

The treatment strategies were ranked in the following order (bilateral reflux in parentheses): (i) subureteric injection SEK 25,000-28,000 (26,000-36,000); (ii) antibacterial prophylaxis SEK 16,000-36,000; and (iii) neo-implantation SEK 65,000-90,000 (72,000-95,000).

The injection and prophylactic treatments are apparently less expensive than the neo-implantation, but as we have compared only the costs we cannot draw further conclusions.

**Diagnostic**

The reliability of VCUG performed within 24 hours after injection of dextranomer/hyaluronic acid in patients with vesico-ureteral reflux.


OBJECTIVE: To assess the reliability and negative predictive value of voiding cystourethrogram (VCUG) performed within 24 hours postoperatively.

Forty patients (56 ureters) who underwent first injection of dextranomer/hyaluronic acid (Dx/HA) because of vesicoureteral reflux (VUR) were enrolled. Patients with previous reflux operation or neurogenic disorders were excluded. All patients underwent the hydrodistention implantation technique (HIT). Patients underwent VCUG within 24 hours postoperatively and after 6 months. Grade 0 and grade 1 were considered to be cured. Negative predictive values of VCUG performed within 24 hours postoperatively were assessed.

RESULTS: The mean age of the patient was 98 ± 45.8 months. Twenty-seven patients were male and 13 patients were female. The number of refluxing ureters was 4, 12, 14, 12, and 14 in ascending order of VUR grade. Overall success rate of single injection therapy was 66.07%. Only 2 ureters with grade IV and 1 patient with grade V VUR showed failure on 24-hour VCUG. The success rates on 6 months VCUG were 100%, 83.3%, 78.57%, 50%, and 42.85% according to ascending order of VUR grade. The negative predictive value of 24-hour VCUG were 100%, 83.3%, 78.57%, 60.0%, and 46.15% according to ascending order of VUR grade. VUR grade was the only factor associated with the discrepancy. Positive but weak correlation was noted between the preoperative grade of VUR and the rate of discrepancy on Spearman correlation analysis (Spearman correlation coefficient = 0.303, P value = .018).

CONCLUSION: Twenty-four hour VCUG cannot replace follow-up VCUG usually performed beyond 3 months postoperatively. Further studies are needed for confirmation of cure.

Upper tract changes in patients with neurogenic bladder and sustained pressures >40 cm following bladder neck surgery without augmentation.


OBJECTIVE: We report new hydronephrosis or VUR (vesicoureteral reflux) in patients with end filling pressures >40 cm for at least 1 year after bladder neck surgery without augmentation for neurogenic incontinence.

MATERIALS: Consecutive children with neurogenic sphincteric incompetency had bladder neck surgery without augmentation. Postoperative renal sonography and fluoroscopic urodynamics were done at 6 months, 12 months, and then annually. Those with sustained end fill pressures >40 cm for ≥1 year were included as participants in the study.

RESULTS: Of 79 patients, 17 (22%) had end fill pressures >40 cm for at least 1 year despite anticholinergics, with follow-up a mean of 39 months. New hydronephrosis or VUR developed in six (35%). All new hydronephrosis resolved with medical treatment, as did two out of three new VUR cases. The other patient with VUR had successful Dx/HA (dextranomer hyaluronic acid) injection.

CONCLUSIONS: Despite sustained pressures >40 cm, upper tract changes developed in only 35% of patients, and resolved with medical management or minimally invasive interventions. End pressures should not be used as an independent indication for augmentation.

Role of endoscopic treatment of vesico-ureteric reflux in downgrading renin angiotensin system activation.

Verma A, Panda SS, Bajpai M.

OBJECTIVES: The objective of this study was to assess the role of endoscopic treatment of vesico-ureteric reflux (VUR) in downgrading renin angiotensin system (RAS) activation.

METHODS: Of 115 patients diagnosed and treated for VUR, 63 underwent hyaluronic acid/dextranomer (deflux) injection in a total of 99 ureteric moieties. Patients were monitored for urinary tract infection (UTI), glomerular filtration rate (GFR), plasma renin activity (PRA), renal scarring, persistence, or appearance of contra-lateral reflux.

RESULTS: Grade III VUR was most common (38%), and the most common cause of VUR was primary (60%). Analysis of patient characteristics at presentation revealed increased PRA in most cases (68%). Grade I VUR showed the most avid decrease in serum PRA levels after single injection. Serum PRA levels were sustainably low in patients of grade I and II VUR, whereas in patients of grade III values kept rising after reaching nadir. This increase in PRA levels correlated well with persistence of symptoms and reappearance of VUR in some patients.

CONCLUSION: PRA levels can be used as an indicator to initiate treatment of VUR. They can also be used for monitoring the progress of the disease and efficacy of the treatment given.

Childhood vesicoureteral reflux studies: registries and repositories sources and nosology.


Despite several recent studies, the advisability of antimicrobial prophylaxis and certain imaging studies for urinary tract infections (UTIs) remains controversial. The role of vesicoureteral reflux (VUR) on the severity and re-infection rates for UTIs is also difficult to assess. Registries and repositories of data and biomaterials from clinical studies in children with VUR are valuable. Disease registries are collections of secondary data related to patients with a specific diagnosis, condition or procedure. Registries differ from indices in that they contain more extensive data. A research repository is an entity that receives, stores, processes and/or disseminates specimens (or other materials) as needed. It encompasses the physical location as well as the full range of activities associated with its operation. It may also be referred to as a biorepository. This report provides information about some current registries and repositories that include data and samples from children with VUR. It also describes the heterogeneous nature of the subjects, as some registries and repositories include only data or samples from patients with primary reflux while others also include those from patients with syndromic or secondary reflux.

The Value of PIC Cystography in Detecting De Novo and Residual Vesicoureteral Reflux after Dextranomer/Hyaluronic Acid Copolymer Injection.

Palmer BW, Hemphill M, Wettengel K, Kropp BP, Frimberger D.

The endoscopic injection of Dx/HA in the management of vesicoureteral reflux (VUR) has become an accepted alternative to open surgery. In the current study we evaluated the value of cystography to detect de novo contralateral VUR in unilateral cases of VUR at the time of Dx/HA injection and correlated the findings of immediate post-Dx/HA injection cystography during the same anesthesia to 2-month postoperative VCUG to evaluate its ability to predict successful surgical outcomes.

The current study aimed to evaluate whether an intraoperatively performed cystogram could replace postoperative studies. But a negative intraoperative cystogram correlates with the postoperative study in only 80%.

Considering the 75-80% success rate of Dx/HA implantation, the addition of intraoperative cystograms cannot replace postoperative studies. In patients treated with unilateral VUR, PIC cystography can detect occult VUR and prevent postoperative contralateral new onset of VUR.

Risk Factors for Breakthrough Infection in Children With Primary Vesicoureteral Reflux

Shiraishi K, Yoshino K, Watanabe M, Matsuyama H, Tanikaze S.
J Urol. 2010 Oct;184(4):1574-5;

Purpose: Despite the widespread application of endoscopic therapy and the debate surrounding the use of prophylactic antibiotics to treat children with vesicoureteral reflux, many pediatric urologists still favor medical management. Breakthrough infection is one of the absolute indications for surgery. Data to predict breakthrough infection are warranted to manage cases of primary reflux.

Materials and Methods: We reviewed medical records of 72 girls and 138 boys (mean SD age at diagnosis 2.66 3.23 years) with primary vesicoureteral reflux who were followed with antibiotic prophylaxis at Aichi Children’s Health and Medical Center. We examined multiple factors by univariate/multivariate analysis to elucidate risk factors for breakthrough infection.

Results: Breakthrough infection developed in 59 children (28%). On univariate analysis higher reflux grade (p 0.05) and abnormal renal scan determined by 99mtechnetium dimercapto-succinic acid (p 0.0001) were significantly associated with breakthrough infection. On multivariate analysis abnormal renal scan was an independent risk factor for breakthrough infection (OR 11.08, 95% CI 0.76–1.72, p 0.0001).

Conclusions: Abnormal renal scan is an independent risk factor for breakthrough infection. Parents and physicians should remain aware that these patients are at high risk for breakthrough infection, which potentially could lead to renal damage.

Postoperative cystography and endoscopic treatment of low-grade vesicoureteral reflux.


INTRODUCTION: The endoscopic subureteral injection of tissue-bulking agents has become an established alternative to long-term antibiotic prophylaxis and open surgery with a high success rate, especially for low-grade reflux (>90%). Though it is recognized that a routine postoperative voiding cystourethrography (VCUG) is unnecessary following a ureteroneocystostomy, most teams perform one after an endoscopic treatment.

MATERIALS AND METHODS: In this paper, we report on our experience with the endoscopic correction of vesicoureteral reflux in 72 ureteral units, for whom no routine postoperative cystography was performed.

DISCUSSION: Two children presented with postoperative recurrent febrile urinary tract infections (UTIs), which were not correlated with cystography findings. Postoperative VCUGs after a ureteroneocystostomy are invasive and expose the child to radiation, they are associated with a substantial cost, and most of all, they do not allow the identification of those patients at risk of recurrent febrile UTIs. Further, the endoscopic subureteral injection of tissue-bulking agents have been used for several years, and numerous studies, set in various clinical settings, have since been published, confirming excellent long-term results for low-grade reflux.

CONCLUSIONS: We feel that postoperative cystograms should be reserved for children who present with recurrent UTIs, new sonographic abnormalities, or who were treated for high-grade reflux.

The role of intraoperative cystography following the injection of dextranomer/hyaluronic acid copolymer.

Palmer LS.
J Urol. 2008 Mar;179(3):1118-20;

PURPOSE: Dextranomer/hyaluronic acid copolymer has become a popular bulking agent for subureteral injection in the treatment of vesicoureteral reflux. The success rates are lower compared to ureteral reimplantation, and, therefore, postoperative voiding cystourethrography is required. We sought to determine if post-injection intraoperative cystography can be useful in improving the success rate of injection and replacing the need for the 3 to 4-month postoperative voiding cystourethrogram.

MATERIALS AND METHODS: Dextranomer/hyaluronic acid copolymer was injected subureterally by a single surgeon until the orifice was crescentic at the dome of the bolus. Contrast material was instilled by gravity into the bladder until capacity was reached and was monitored fluoroscopically. No voiding phase was obtained. The procedure was deemed successful only in the absence of reflux. Postoperative voiding cystourethrography performed at 3 to 4 months postoperatively was used to determine whether antibiotic administration should be discontinued. The results of the 2 cystograms were compared.

RESULTS: A total of 41 patients (64 ureters) underwent subureteral injection. We sought to determine if post-injection intraoperative cystography can be useful in improving the success rate of injection and replacing the need for the 3 to 4-month postoperative voiding cystourethrogram. Intraoperative post-injection cystogram documented reflux eradication after a single injection in 96.9% of ureters and 95.1% of patients. Two boys had persistent reflux and 1 girl had new contralateral reflux after a single injection. In these cases additional bulking agent was injected and the reflux was confirmed by a second cystogram. There were 32 patients (52 ureters) who underwent intraoperative post-injection cystography plus postoperative voiding cystourethrography at 3 to 4 months. Postoperative voiding cystourethrography documented a 77% ureteral and 69% patient success rate. None of the patients with post-injection reflux had postoperative reflux at 3 to 4 months.

CONCLUSIONS: Intraoperative cystography following dextranomer/hyaluronic acid copolymer injection may help to determine immediate success and identify cases of new contralateral reflux. However, there is insufficient correlation with the standard 3 to 4-month postoperative cystogram to advocate replacing the current standard postoperative voiding cystourethrography with an intraoperative cystogram.

Management

Physician preference is a major factor in management of vesicoureteral reflux.


BACKGROUND: Known factors affecting the management of vesicoureteral reflux (VUR) include reflux grade, infection frequency, age and gender. We hypothesized that provider preference is highly associated with management.

METHODS: Utilizing the national billing database, Faculty Practice Solutions Center, a multivariable logistic regression model, was applied to analyze the association of pediatric urologist treatment patterns, patient age, gender, uni- or bilateral disease, insurance type, presence of nephropathy and race with the type of VUR treatment a patient would receive.

RESULTS: We identified 59 pediatric urologists who managed 7,882 new reflux patients from 2009 to 2011. Over this 3-year period there was wide variation in surgical utilization between surgeons (mean 50 %) but minimal change for each surgeon (5 %). For every 100 new reflux patients, median utilization of reimplantation surgery and injection of dextranomer/hyaluronic acid copolymer (Deflux) was 26 and 20 %, respectively. Age ranked highest in predicting surgical versus non-surgical management, while a surgeon’s historic Deflux utilization rate ranked highest in predicting surgery type. Older age, female gender and white race also increased the odds of Deflux utilization over reimplantation.

CONCLUSIONS: A surgeon’s historic Deflux utilization was the most important predictor of VUR surgery type. Although data on reflux grade were not available, analysis of patient and surgeon characteristics suggests that surgeon preference is the first or second most critical factor in determining a patient’s treatment.

Outcomes of a minimally invasive surgical approach to manage persistent high-grade vesicoureteric reflux post successful augmentation cystoplasty of patients with non-compliant bladder.


PURPOSE: To assess the outcome of a minimally invasive surgical approach in management of persistent high-grade vesicoureteric reflux (VUR) in patients with non-compliant bladders after augmentation cystoplasty.

MATERIALS AND METHODS: Between 2001 and 2011, 24 patients (13 male and 11 female, mean age 7.62 years) with non-compliant bladders and 44 high-grade refluxing units, (40 bilateral and 4 unilateral, grades 3-5), underwent augmentation cystoplasty without ureteric re-implantation. Of the 24 patients, 17 underwent augmentation ileocystoplasty and 7 underwent ureterocystoplasty. Of the 44 refluxing units, 7 were used for ureterocystoplasty, and 1 was excised. For those who did not show resolution of VUR and had recurrent breakthrough febrile urinary tract infections (UTI) despite antibiotic prophylaxis, interval endoscopic correction was initiated.

RESULTS: Of the 36 remaining refluxing units, 21/36 (58.3%) showed complete resolution in the first follow-up cystogram, and 1 showed complete resolution after 1 year. Two patients, each with single refluxing unit, received repeat augmentation cystoplasty because of inadequate bladder capacity post ureterocystoplasty and demonstrated complete resolution postoperatively. Of the remaining 12 refluxing units, 10 underwent interval endoscopic intervention. VUR resolved in 8 of the refluxing units after the first trial and in another 2 after the second trial. Parents of the patient with the remaining 2 refluxing units preferred to continue on conservative management.

CONCLUSION: Augmentation cystoplasty without ureteric re-implantation with interval endoscopic management if needed is an effective and adequate treatment for high-pressure, non-compliant bladders as well as high-grade persistent VUR when conservative management fails. In our study, a VUR resolution rate of 94% (34/36) was achieved by combining conservative and minimally invasive approaches without ureteric re-implantation at the time of augmentation cystoplasty.

Lopez PJ, Celis S, Reed F, Zubieta R.

Vesicoureteral reflux (VUR) is a disorder that has been studied since the early days of pediatric urology. From 1893, when it was first documented in humans by Pozzi, the research and clinical management of VUR has been marked by pendulum swings through the decades. Initially, the vesicoureteral junction was the main subject of study, whereas current practice takes into account the bladder and bowel dynamics. The primary objective, however, is unchanged: preservation of the kidney and its function. Management of the condition has included open surgery, minimally invasive surgery, endoscopic treatment, antibiotic prophylaxis, and watchful waiting. In this article, we will attempt to cover every angle of this complex pathology and its current management in children.

Vesico-ureteric reflux (VUR) management and screening patterns: are paediatric urologists following the 2010 American Urological Association (AUA) guidelines?


OBJECTIVE: To evaluate the current practice patterns of vesico-ureteric reflux (VUR) management and screening among paediatric urologists and their relationship with the current American Urological Association (AUA) guidelines in managing and treating VUR.

SUBJECTS AND METHODS: A 17-question survey was sent out to 476 paediatric urologists who are members of the Society for Pediatric Urology (SPU). In all, 133 respondents answered the survey and results were included for all questions.

RESULTS: Paediatric urologists who were surveyed were consistent with the 2010 AUA guidelines in the initial evaluation of children with VUR, continuous antibiotic prophylaxis for the child aged < or >1 year, and follow-up evaluation in children with VUR. Most paediatric urologists do not obtain a serum creatinine on initial screening of children with VUR. The new guidelines address screening of siblings of patients with VUR and most paediatric urologists were consistent with these recommendations. Almost one third of responders screened all neonates diagnosed with prenatal hydronephrosis regardless of clinical history or findings on imaging despite the recommendations of the new guidelines.

CONCLUSION: We conclude that based on our present sample, most paediatric urologists follow the 2010 AUA guidelines on VUR management.

The management of vesicoureteral reflux in the setting of posterior urethral valve with emphasis on bladder function and renal outcome: a single center cohort study.

Urology. 2014 Jan;83(1):199-205

OBJECTIVE: To represent our experience in the management of posterior urethral valves and concomitant vesicoureteral reflux (VUR).

METHODS: A total of 326 children with posterior urethral valve who had underwent valve ablation/bladder neck incision were studied, and those who had persistent VUR and were categorized under 3 main groups were followed up. Group 1 (n = 71) received prophylactic antibiotic, group 2 (n = 50) underwent Deflux injection (2a) (n = 28): Deflux injection alone, group 2b (n = 22) Deflux with concomitant autologous blood injection (HABIT), and group 3 (n = 19) underwent ureteroneocystostomy before referral and was followed up conservatively. VUR resolution, incidence of urinary tract infections (UTI), and bladder function were assessed.

RESULTS: Mean duration of follow-up was 3.8 years; VUR resolution occurred in 66.1%, 86.0%, and 94.0% of groups 1-3, respectively (P = .013). Resolution rate in group 2b was significantly higher than group 2a (90.9% vs 78.5%). Patients in group 2 experienced a longer UTI-free period compared with others (P <.05). Urodynamic studies demonstrated significant decrease in maximum voiding detrusor pressure and detrusor overactivity in all groups (P <.001). Children in group 3 ended up with lower compliance compared with others (P <.001). After toilet training, only 2.8%, 21.4%, 13.6%, and 27% children were diagnosed with lower urinary tract dysfunction in groups 1-3, respectively (P = .027). Myogenic failure developed only in 3 boys in group 3.

CONCLUSION: Ablation/bladder neck incision leads to significant improvement in VUR status in part because of improvement in bladder function. After successful valve removal, conservative therapy can be regarded as the mainstay of reflux treatment, whereas HABIT is recommended for high grade VUR associated with febrile UTI or deterioration in renal function.

The RIVUR trial: profile and baseline clinical associations of children with vesicoureteral reflux.


Vesicoureteral reflux (VUR) is diagnosed in ~30% to 40% of children who have imaging studies after urinary tract infections (UTIs). Our goal is to characterize children enrolled in the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial and to compare our study cohort with those from previously published studies.

METHODS: RIVUR investigators from 19 pediatric sites in the United States recruited 607 children with grade I through IV VUR. Children were enrolled after a first or second UTI. This cross-sectional report of baseline data includes extensive clinical, parental report, and imaging study results.

RESULTS: RIVUR recruited 607 children (558 girls, 49 boys) with grade I (11%), II (42%), III (38%), or IV (8%) reflux. The median age was 12 months, and most children (91%) were enrolled after their first UTI. The UTI leading to enrollment was both febrile and symptomatic for 323 children, febrile only in 197 children, and symptomatic only in 86. Renal involvement at baseline as documented by a (99m)Tc dimercaptosuccinic acid scan was uncommon with cortical defects identified in 89 (15%) children. Bladder and bowel dysfunction was identified in 71 (56%) of 126 toilet-trained subjects assessed.

VUR is associated with recurrent and febrile UTI as well as renal damage. The optimum approach to managing the condition remains controversial, but non-treatment appears inappropriate for most patients except those with reflux grade I II and normal kidney

Individualizing management of vesicoureteral reflux.

Cooper CS

BACKGROUND: Approaches to the management of vesicoureteral reflux (VUR) in children have changed rapidly in recent years. Multiple studies published over the last decade have contributed to these changes by challenging the dogma that all children with reflux require and benefit from continuous antibiotic prophylaxis. The advent and wide acceptance of endoscopic treatment for VUR has also contributed to these changes. Although new guidelines for VUR management have recently been proposed, they are broad and relatively non-specific. Many physicians and parents remain unsure which children are at risk from their VUR, and which would benefit from antibiotic prophylaxis or surgical intervention.

MATERIALS AND METHODS: A literature search, followed by an additional search based on bibliographies, was performed for articles reporting on VUR and the utility of antibiotic prophylaxis for its treatment, as well as the chance of spontaneous resolution.

RESULTS: Articles selected for review included those that provided information to assist physicians in determining if a child with VUR is at increased risk of pyelonephritis or persistent VUR, and would benefit from intervention. Particular emphasis was placed on recent prospective, randomized trials in children with VUR.

CONCLUSIONS: Because of the multiple factors affecting risk in a child with VUR, specific guidelines for intervention cannot be provided. However, an accurate understanding of these risk factors will help the physician and parents to develop a more individualized management plan for a child with VUR.

Quality of life in children with vesicoureteral reflux.

Kiddoo DA, Ajamian F, Senthilselvan A, Morgan CJ, Pinsk MN.

Vesicoureteral reflux (VUR) is commonly diagnosed in children presenting with urinary tract infections. Antibiotic prophylaxis and ureteric surgery are standard treatments for these children. Our aim was to investigate whether health-related quality of life (HRQOL) was altered in children treated for VUR. Children aged 1-5 years with grade III or higher VUR were identified through electronic records at the Stollery Children’s Hospital. Parents of these children were mailed the TNO-AZL Netherlands Organisation for Applied Scientific Research Academic Medical Centre Quality of Life (TAPQOL) questionnaire. QOL scores for this group were compared with normative controls from the instrument’s creators using the Mann-Whitney U test. Thirty-two of the 96 (33%) mailed surveys were returned. Eight children had surgery, and 19 were treated with antibiotic prophylaxis. When comparing the VUR group with the control group, we found that anxiety and social functioning scores were significantly better in patients with VUR (p < 0.01). The VUR group had worse scores in problem behavior, stomach complaints, and communication (p < 0.01). This study reveals that children with VUR have a reasonable QOL when compared with controls. However, the diagnosis of VUR and its management does have an impact on gastrointestinal complaints, behavior, and communication, which may occur as a result of chronic medical intervention.

Deflux™ Supporting Evidence

Vesicoureteral Reflux (VUR)

EAU guidelines on vesicoureteral reflux in children.

CONTEXT: Primary vesicoureteral reflux (VUR) is a common congenital urinary tract abnormality in children. There is considerable controversy regarding its management. Preservation of kidney function is the main goal of treatment, which necessitates identification of patients requiring early intervention. To present a management approach for VUR based on early risk assessment.

EVIDENCE ACQUISITION: A literature search was performed and the data reviewed. From selected papers, data were extracted and analyzed with a focus on risk stratification. The authors recognize that there are limited high-level data on which to base unequivocal recommendations, necessitating a revisiting of this topic in the years to come.

EVIDENCE SYNTHESIS: There is no consensus on the optimal management of VUR or on its diagnostic procedures, treatment options, or most effective timing of treatment. By defining risk factors (family history, gender, laterality, age at presentation, presenting symptoms, VUR grade, duplication, and other voiding dysfunctions), early stratification should allow identification of patients at high potential risk of renal scarring and urinary tract infections (UTIs). Imaging is the basis for diagnosis and further management. Standard imaging tests comprise renal and bladder ultrasonography, voiding cystourethrography, and nuclear renal scanning. There is a well-documented link with lower urinary tract dysfunction (LUTD); patients with LUTD and febrile UTI are likely to present with VUR. Diagnosis can be confirmed through a video urodynamic study combined with a urodynamic investigation. Early screening of the siblings and offspring of reflux patients seems indicated. Conservative therapy includes watchful waiting, intermittent or continuous antibiotic prophylaxis, and bladder rehabilitation in patients with LUTD. The goal of the conservative approach is prevention of febrile UTI, since VUR will not damage the kidney when it is free of infection. Interventional therapies include injection of bulking agents and ureteral reimplantation. Reimplantation can be performed using a number of different surgical approaches, with a recent focus on minimally invasive techniques.

CONCLUSIONS: While it is important to avoid overtreatment, finding a balance between cases with clinically insignificant VUR and cases that require immediate intervention should be the guiding principle in the management of children presenting with VUR.

Is availability of endoscopy changing initial management of vesicoureteral reflux?

Nelson CP, Copp HL, Lai J, Saigal CS; Urologic Diseases in America Project.
J Urol. 2009 Sep;182(3):1152-7

PURPOSE: The optimal management of vesicoureteral reflux continues to be controversial. Since dextranomer/hyaluronic acid copolymer implants were approved in 2001 for endoscopic antireflux surgery, the perception that endoscopy is less morbid than open surgery, combined with concerns over potential adverse effects of prophylactic antibiotics, has led some to advocate endoscopy as initial therapy for reflux. We examined whether the availability of endoscopy has changed the management of reflux.

MATERIALS AND METHODS: The i3 Innovus database (Ingenix, Eden Prairie, Minnesota) contains longitudinal claims data on more than 39 million patients spanning a 5-year period. We analyzed children diagnosed with vesicoureteral reflux (ICD-9 code 593.7, plus claim for radiographic or nuclear cystogram within 90 days) and at least 1 year of followup. We assessed patient characteristics, and diagnostic and therapeutic interventions. We evaluated surgical trends, including the changing use of endoscopic vs open antireflux surgery.

RESULTS: Among 9,496 children meeting inclusion criteria 1,998 (21%) underwent antireflux surgery during the study period (2002 to 2006). Median followup for surgical cases was 894 days. Of patients undergoing antireflux surgery 1,046 (52.4%) underwent an open procedure and 952 (47.6%) underwent endoscopy. Females were more likely to undergo endoscopy (52% vs 33% of males, p <0.0001), as were children older than 5 years (53% vs 45% of those younger, p = 0.0002). Of patients undergoing surgery 1,234 (62%) were treated early (within 12 months of diagnosis). During the study period the rate of newly diagnosed reflux cases managed by early surgery increased from 12.0% to 17.3% (Mantel-Haenszel chi-square test p <0.0001). This increase was primarily due to a more than doubling of patients undergoing early endoscopy (4.2% in 2002 vs 9.7% in 2006, p <0.0001). The rate of newly diagnosed cases managed by early open surgery did not change significantly (p = 0.3446).

CONCLUSIONS: During a 5-year period after dextranomer/hyaluronic acid was introduced for endoscopic therapy the number of children newly diagnosed with vesicoureteral reflux treated with early antireflux surgery increased primarily due to increased use of endoscopy. This finding suggests that despite the lack of evidence of benefit, endoscopy is increasingly viewed as first line therapy for reflux.

Part 1: Vesicoureteral reflux treatment: the past, present, and future

Hensle TW, Grogg AL.
Curr Med Res Opin. 2007 Sep;23 Suppl 4:S1-5.

The purpose of this manuscript is to provide clinicians with highlights of key findings pertaining to our current understanding and treatment of the condition of vesicoureteral reflux (VUR). This includes a review of the disease, patient characteristics, current treatment options, challenges for managed care and patients, and opportunities for improvements in care. This is not intended as a comprehensive review of VUR. This manuscript does, however, serve to introduce three additional manuscripts contained within this supplement.

The first article in this series is designed to provide the clinician with real-world data pertaining to treatment patterns and outcomes in patients with VUR (Examining pediatric vesicoureteral reflux: a real-world evaluation of treatment patterns and outcomes: Hensle TW, Hyun G, Grogg AL, Eaddy M). The second article considers the efficacy of prophylactic antibiotics in reducing the likelihood of urinary tract infections (UTIs) when compared with endoscopic injection with dextranomer/hyaluronic acid (Endoscopic injection versus antibiotic prophylaxis in the reduction of urinary tract infection in patients with vesicoureteral reflux: Elder JS, Shah MB, Batiste LR, et al.). The third article explores the role medication noncompliance plays in contributing to antibiotic resistance, the consequences associated with resistance (longer lasting illness and costs), and the difficulties with resistance specific to UTI pathogens in children (Considerations regarding the medical management of VUR: what have we really learned?: Koyle MA, Caldamone A).

This supplement is intended to provide the clinician with valuable information regarding the treatment patterns, the role of compliance, and the efficacy of treatments for pediatric patients with VUR.

Conclusion: This supplement in its entirety, and each of these studies individually, provides insight into the current medical and surgical modalities of VUR, typical clinical practice patterns, adherence to published treatment guidelines, and treatment outcomes within a real-world environment. Compliance, in particular, is an outcome that is most appropriately studied outside the constraints of a clinical trial. The use of large administrative claims databases allows results to be stratified by gender, age, and other relevant demographics. Assessing compliance through administrative claims databases allows for the analysis of real-world medication-taking behaviors not subjected to the biases involved with patients who are knowingly being measured for compliance. Lastly, with the increasing use of endoscopic injection as an alternative to long-term antimicrobial prophylaxis and open surgery, it is essential to better understand the current treatment paradigm for VUR and evaluate the relevant clinical outcomes associated with endoscopic injection compared to prophylactic antibiotics.

Part 2: Examining pediatric vesicoureteral reflux: a real-world evaluation of treatment patterns and outcomes.


OBJECTIVE: Vesicoureteral reflux (VUR) occurs in 1% of infants and children. Upon diagnosis, patients are often placed on prophylactic antibiotics to prevent urinary tract infections (UTIs) and potential renal damage. The objective of this study was to assess current diagnosis and treatment patterns for patients diagnosed with VUR, focusing on compliance with antibiotic therapy and the occurrence of UTIs.

METHODS: This is a retrospective study of children less than 11 years of age diagnosed with VUR. Data were obtained from a national managed care database with over 45 million lives. Patients were followed for up to 6 months prior to their diagnosis and 1 year after. All were required to be eligible for medical and pharmacy services for 1 year after diagnosis. Outcome measures included the use of and compliance with prophylactic antibiotics, rates of curative treatment (surgery and endoscopic injections), and diagnoses of UTIs.

RESULTS: There were 35,450 patients meeting inclusion criteria. After being diagnosed with VUR, 76.5% of patients were placed on prophylactic antibiotics, 1.5% had open surgery, and 0.38% had an endoscopic injection with dextranomer/hyaluronic acid copolymer (Dx/HA). Only 17% of patients on prophylactic antibiotics were adherent to therapy, with mean patient compliance equaling 41.4%. Of patients on prophylactic antibiotic therapy, 58% still had a diagnosis for a UTI within 12 months of VUR diagnosis.

LIMITATIONS: Adherence to VUR-related antibiotic therapy may be overestimated as the data used in the analysis represents prescriptions acquired but not necessarily consumed. This study lacked detailed clinical information, such as VUR-resolution rates and VUR grade.

CONCLUSIONS: Only 17% of pediatric VUR patients on prophylactic antibiotics were compliant with therapy. Of patients on prophylactic therapy, 58% had a diagnosis of a UTI within 1 year of treatment.

The evolution of vesicoureteral reflux management in the era of dextranomer/hyaluronic acid copolymer: a pediatric health information system database study.

Lendvay TS, Sorensen M, Cowan CA, Joyner BD, Mitchell MM, Grady RW

PURPOSE: Since Food and Drug Administration approval of Deflux, injection therapy for vesicoureteral reflux has increased. Little data exist on the effect that injection therapy has had on the incidence of ureteral reimplantation and total vesicoureteral reflux procedures. We used the Pediatric Health Information System database to define practice trends for vesicoureteral reflux therapy.

MATERIALS AND METHODS: From 2002 to 2004 we extracted data on 0 to 19-year-old patients with International Classification of Diseases-9 diagnosis codes for vesicoureteral reflux, and procedure codes for ureteral reimplantation and subureteral injection therapy. Of 37 hospitals enrolled in Pediatric Health Information System 18 submitted ambulatory surgery and inpatient data. Data on the total number of patients who underwent reimplantation and injection were analyzed using linear regression analysis for trend.

RESULTS: We identified a total of 4,570 procedures performed in 1,948 patients treated with injection therapy and in 2,483 treated with reimplantation. The mean number of injections per institution yearly increased from 17 to 66 from 2002 to 2004 or 288%, while the mean number of reimplantations yearly was not statistically different from 2002 to 2004 (p = 0.02 and 0.09, respectively). In addition, the annual mean number of vesicoureteral reflux procedures per institution increased from 75 to 116 or 55% (p <0.05), primarily due to the increased number of injections.

CONCLUSIONS: With the introduction of a new, minimally invasive procedure for reflux therapy the number of procedures for reflux has increased, while open surgery rates have remained stable. This may be explained by public and clinician acceptance of a newer injection material that is safe and increasingly successful. To our knowledge this represents the largest series of patients treated for vesicoureteral reflux in the United States.

Spontaneous Reflux Resolution

**Vesicoureteral reflux index (VURx): A novel tool to predict primary reflux improvement and resolution in children less than 2 years of age.**

Kirsch AJ1, Arlen AM2, Leong T3, Merriman LS4, Herrel LA4, Scherz HC4, Smith EA4, Srinivasan AK4.


**PURPOSE:** Surgical correction of vesicoureteral reflux (VUR) is influenced by recurrent urinary tract infection (UTI) risk and the likelihood of spontaneous resolution. We aimed to identify factors associated with VUR resolution in children less than 2 years of age and to design a simple scoring tool to predict improvement and resolution.

**MATERIALS AND METHODS:** Children less than 2 years old with primary VUR were identified. Patient demographics, voiding cystourethrogram (VCUG) findings and clinical outcomes over time were assessed. Multivariate analysis with time to resolution was performed to identify factors predictive of VUR improvement and resolution. A random forest model was used to confirm the VUR index (VURx) with normalized importance.

**RESULTS:** Two-hundred and twenty-nine children met all inclusion criteria. Mean age at initial VCUG was 0.46 ± 0.43 years. Median clinical follow-up was 1.6 years (range 0.5-4.4 years). Children with grade 4-5 reflux, complete ureteral duplication or periureteral diverticula, and filling phase VUR, as well as female gender, had significantly (p < 0.01) longer time to improvement or resolution on multivariate survival analysis. VURx 1 to 5-6 had improvement/resolution rates of 89%, 69%, 53%, 16% and 11%, respectively.

**CONCLUSIONS:** Female gender, high-grade VUR, ureteral anomalies, and filling reflux are associated with longer time to improvement and non-resolution. VURx reliably predicts resolution of primary reflux in children less than 2 years of age.

Primary vesicoureteral reflux: conservative therapy or surgical intervention

Teixeira CB, Cançado MA, Carvalhaes JT.

The relationship between urinary tract infections and primary vesicoureteral reflux may lead to permanent renal damage. In the literature an increasing number of spontaneous cure of vesicoureteral reflux in children and the significant decrease in surgical therapy has been observed.

OBJECTIVE: To study the evolution of primary vesicoureteral reflux associated with recurring urinary tract infections settings in patients of the Pediatric Nephrology department of our institution, evaluating cases in which cure was achieved through conservative therapy only and those in which surgical intervention was required.

METHODS: We analyzed records and collected data refers to parameters: sex, age upon the diagnosis of primary urinary infection, age upon diagnosis of vesicoureteral reflux, number of urinary tract infections, vesicoureteral reflux grade; renal function, renal scaring, other malformation of urinary tract, and surgical or conservative intervention. Statistical analysis was descriptive and conducted with the SPSS program.

RESULTS: Within the subgroup of patients with grade IV and V, 63.6% of the cases evolved to surgical intervention and 36.4% to conservative intervention. In those with grades I, II, and III, 38.5% evolved to surgical treatment against 61.5% for conservative approach. Among those with bilateral vesicoureteral reflux, 72.7% had to undergo surgical intervention. No relationship was observed between the vesicoureteral reflux grade and the presence of renal scaring.

CONCLUSION: Patients with low grade vesicoureteral reflux and recurring urinary tract infections tend to experience spontaneous reflux resolution with good renal evolution in the long term in a way that surgical intervention becomes limited to high grade reflux or when followed by other clinical issues.


BACKGROUND/AIM: To evaluate the spontaneous resolution rate in infants and young children with vesicoureteral reflux (VUR).

PATIENTS AND METHODS: Paediatric patients with VUR treated in our hospital from January 2000 to December 2010 were retrospectively analyzed. Only patients with pretreatment and follow-up voiding cystourethrogram were included into the study. Treatment success was defined as complete VUR resolution.

RESULTS: The resolution rate for infants less than 1 year of age was 38.6% (17 of 44 renal units). Renal units with mild-moderate VUR (I-III) had a resolution rate of 40% (12 of 30 renal units) compared to 35.7% (5 of 14 renal units) with severe grade (IV-V) VUR. The resolution rate for children over 1 year of age was 39.1% (9 of 23 renal units). Renal units with mild-moderate VUR (I-III) had a resolution rate of 42.9% (9 of 21 renal units) compared to 0% (0 of 2 renal units) with severe grade (IV-V) VUR.

CONCLUSION: Infants less than 1 year of age with nonsymptomatic, mild, moderate or severe VUR have a spontaneous resolution rate of more than 35% and therefore should receive a primary conservative therapy. Children over 1 year of age with nonsymptomatic mild-moderate VUR (I-III) have a spontaneous resolution rate of about 40% and should receive primary conservative treatment as well.

Predictive Factors for Resolution of Congenital High Grade Vesicoureteral Reflux in Infants: Results of Univariate and Multivariate Analyses

Sjöström S, Sillén U, Jodal U, Sameby L, Sixt R, Stokland E.

Purpose: We studied variables with impact on cessation of congenital high grade vesicoureteral reflux in univariate analyses and provide a multivariate model for prediction of reflux resolution.

Materials and Methods: A total of 80 male and 35 female infants (median age 2.7 months) were included in this prospective observational study. Of the cases 71% were diagnosed after urinary tract infection and 26% after prenatal ultrasound. Reflux was bilateral in 70% of the patients and maximum grade was III in 16%, IV in 45% and V in 39%. The study protocol included repeat videocystometries, renal scintigrams, chromium edetic acid clearances and free voiding observations. Median followup was 36 months.

Results: Overall spontaneous reflux resolution, including cases downgraded to grade I to II, was 38%. Variables significantly negatively correlated to resolution were breakthrough febrile urinary tract infection, bladder dysfunction, higher grade of reflux at inclusion, renal abnormality, subnormal renal function, increased bladder capacity, residual urine and passive occurrence of reflux. Multivariate Cox proportional hazard model with stepwise selection identified 3 independent predictors—renal abnormality (hazard ratio 0.45, 95% CI 0.31–0.64, p 0.0001), bladder dysfunction (hazard ratio 0.43, 95% CI 0.29–0.64, p 0.0001) and breakthrough urinary tract infection (hazard ratio 0.38, 95% CI 0.18–0.78, p 0.009). Performance of the model was evaluated by the receiver operating characteristic curve, with a calculated area under the curve of 83%.

Conclusions: Overall resolution rate in congenital high grade vesicoureteral reflux is high during the first years of life. By multivariate analyses renal abnormality, bladder dysfunction and breakthrough febrile urinary tract infection were identified as strong independent negative predictive factors for reflux resolution.

Spontaneous resolution of high grade infantile vesicoureteral reflux.

Sjöström S, Sillén U, Bachelard M, Hansson S, Stokland E.
J Urol. 2004 Aug;172(2):694-8

PURPOSE: We studied the spontaneous resolution rate in a group of infants with high grade vesicoureteral reflux (VUR). The influence of gender, prenatal or postnatal diagnosis, recurrent urinary tract infections (UTIs) and bladder dysfunction on the resolution rate was also evaluated.

MATERIALS AND METHODS: This prospective study comprised 115 infants (80 boys and 35 girls) with high grade VUR (grades III to V). Bilateral reflux was seen in 70% of cases. The majority of patients (71%) were diagnosed after UTI during infancy and only 26% were prenatally diagnosed. Median age at diagnosis was 2.7 months. Patients were followed according to a program of repeat video cystometry and noninvasive 4-hour voiding observations. Median followup was 39 months.

RESULTS: The overall spontaneous resolution rate to grade II or less for all grades was 39% with no difference between boys and girls. However, when comparing the more severe grades IV and V, we found a significantly higher resolution rate in boys during the infant year. No difference in VUR disappearance could be detected when comparing the groups according to presentation, prenatal ultrasound or pyelonephritis. Breakthrough UTIs were seen in 47% of cases despite antibacterial prophylaxis and they significantly correlated with VUR nonresolution. Bladder dysfunction was found in 37% of patients and it also significantly correlated with nonresolution.

CONCLUSIONS: The spontaneous resolution rate for high grade (grades IV and V) congenital VUR was high in boys during the infant year (29%), whereas in girls and boys after the infant year the resolution rate was 9% yearly during followup. Negative prognostic factors for resolution were recurrent UTIs and bladder dysfunction.

Spontaneous resolution of vesicoureteral reflux: a 15-year perspective.

PURPOSE: The spontaneous resolution rate of vesicoureteral reflux is helpful for determining the need for surgical intervention and the proper followup schedule in patients on antibiotic prophylaxis. We determined the resolution rate by patient rather than by ureter and analyzed the effects of laterality, gender, age and dysfunctional voiding.

MATERIALS AND METHODS: We retrospectively reviewed the records of 179 girls and 35 boys who presented between 1981 and 1984 with urinary tract infection and were diagnosed with primary vesicoureteral reflux. Mean age at presentation was 4.2 years and median followup was 3 years. Of the patients 107 (50%) had bilateral reflux and 60 had dysfunctional voiding. In 146 children (68%) reflux spontaneously resolved during the study. Patients were categorized by the worst grade of reflux, maintained on antibiotic prophylaxis and underwent voiding cystourethrography yearly until reflux resolved. Kaplan-Meier curves were constructed to define the resolution rate.

RESULTS: Grades I to III reflux resolved at 13% yearly during the initial 5 years of followup and then at 3.5% yearly during subsequent followup. Grade IV to V reflux resolved at 5% rate yearly. Bilateral reflux resolved more slowly than unilateral reflux and it resolved more rapidly in boys than in girls. Untreated dysfunctional voiding had no effect on overall resolution.

CONCLUSIONS: Grades I to III primary vesicoureteral reflux diagnosed after urinary tract infection resolve at identical rates and significantly more rapidly than grades IV to V. Early repair of grade IV to V reflux should be considered after age 18 months.
