

PEDIATRIC VESICoureTERAL REFLUX: CURRENT DIAGNOSIS AND TREATMENT

Essay

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللَّهِ عَلَيْكَ
عَظِيمًا

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List of Abbreviations

<i>Abb.</i>	<i>Full term</i>
AAP	American Academy of Pediatrics
APD	Anteroposterior renal pelvic diameter
APN	Acute pyelonephritis
AUA	American Urology Association
BBD	Bladder bowel dysfunction
BT-UTI	Breakthrough urinary tract infection
CAP	Continuous antibiotic prophylaxis
CKD	Chronic kidney disease
CRF	Chronic renal failure
DMSA	Dimercaptosuccinic acid
DRC	Direct radionuclide cystography
DVSS	Dysfunctional voiding symptom score
DX/HA	Dextranomer hyaluronic acid
EAU	European Association of Urology
EI	Endoscopic injection
ESRD	End-stage renal disease
FDA	Food and Drug Administration
FUTI	Febrile urinary tract infection
HIT	Hydrodistension implantation technique
HN	Hydronephrosis
IMRVC	Interactive magnetic resonance voiding cystourethrography
LUTD	Lower urinary tract dysfunction
LUTS	Lower urinary tract symptoms
MCDK	Multicystic dysplastic kidney

<i>MRU</i>	Magnetic resonance urography
<i>PNH</i>	Prenatal hydronephrosis
<i>PTFE</i>	Polytetrafluoroethylene
<i>PUVS</i>	Posterior urethral valves
<i>RBUS</i>	Renal bladder ultrasonography
<i>RIVUR</i>	Randomized intervention of VUR
<i>RN</i>	Reflux nephropathy
<i>RNC</i>	Radionucleide cystography
<i>RU</i>	Refluxing ureter
<i>SF6</i>	Sulphur hexafluoride
<i>SFU</i>	Society of fetal urology
<i>STING</i>	Subureteral transurethral injection technique
<i>TDA</i>	Top down approach
<i>Teflon</i>	Polytetrafluoroethylene
<i>TMP/SMZ</i>	Trimethoprim /sulfamethoxazole
<i>UGS</i>	Urogenital sinus
<i>US</i>	Ultrasonography
<i>USCA</i>	Ultrasound contrast agent
<i>UTI</i>	Urinary tract infection
<i>UVJ</i>	Ureterovesical junction
<i>VCUG</i>	Voiding cystourethrography
<i>VUR</i>	Vesicoureteral reflux
<i>VUS</i>	Voiding urosonography

INTRODUCTION

 Vesicoureteral reflux is characterized by retrograde flow of urine from the bladder up the ureter towards the kidney. It is the most common urologic finding in children, occurring in as high as 30-40 % in children with febrile urinary tract infection (*Nguyen and Herndon, 2010*).

Children with vesicoureteral reflux are predisposed to acute pyelonephritis which is a morbid event that may lead to renal scarring (i.e reflux nephropathy), which may progress to further renal damage with subsequent hypertension, decreased renal function, proteinuria, and end-stage renal disease (ESRD) (*Swerkersson et al., 2010*).

The main radiologic studies for evaluation and diagnosis of vesicoureteral reflux are voiding cystourethrography and renal ultrasonography. These two imaging modalities should be done in all children between 2 months and 2 years of age following first febrile urinary tract infection, as the prevalence of vesicoureteral reflux and risk of renal scarring following pyelonephritis is highest in this age group (*Cohen et al., 2011*).

Technetium- 99m labeled dimercaptosuccinic acid scintigraphy (DMSA scan) is the gold standard technique for detection and evaluation of acute pyelonephritis and

renal scarring. DMSA Scan can be performed at the time of infection with sensitivity and specificity for detecting pyelonephritis of 92% and 95% respectively, also DMSA scan can be performed at 6 month follow up with sensitivity and specificity, for detecting renal scarring, of 96% and 98% respectively (*Montini and Zucchetta, 2009*).

A new diagnostic strategy for evaluation of childhood urinary tract infection, named the "top-down" approach (TDA), in contrast to traditional "bottom-up" approach, in which the initial diagnostic test is voiding cystourethrography. The "top-down" approach focuses first on detecting pyelonephritis via DMSA scan at the time of infection, and recommends voiding cystourethrography only in children with abnormal DMSA scan (*Herz, 2010*).

Treatment of pediatric vesicoureteral reflux includes medical treatment by using long-term suppressive antibiotics which decreases the incidence of pyelonephritis and subsequent renal scarring. Although, this approach avoids surgical intervention, a risk of breakthrough infections are reported in 30%-40% of children over a 5 year period of long-term suppressive antibiotics, which is related to poor compliance or resistant bacteria (*Craig et al., 2009*).

Other therapeutic option in treatment of vesicoureteral reflux is surgical intervention, in which ureteral reimplantation is done. Open surgery carries risk of

complications such as postoperative bleeding, bladder dysfunction, contralateral reflux, ureteral obstruction, and recurrent reflux (*Elder, 2009*).

Recently, endoscopic treatment of pediatric vesicoureteral reflux with injection of dextranomer microspheres in a stabilized hyaluronic acid-based gel of non-animal origin (DxH gel), is minimally invasive, well tolerated technique and can be used in persistent, complicated cases of pediatric vesicoureteral reflux (grades II- V) with cure rates approaching those of open surgery reaching about 90% (*Stenberg and Lackgren, 2010*).

The cure rate of pediatric vesicoureteral reflux following endoscopic injection of (DxH gel) can be optimized by using the hydrodistension implantation technique (HIT), which is a modified version of the original subureteral transurethral injection (STING) technique. By using this technique the cure rates have been reported to be increased reaching about (89%), compared with the standard STING method (71%) (*Kirsch et al., 2011*).

Comparative appraisal of these treatment options has led to the conclusion that endoscopic treatment is generally the most favorable of these options for managing vesicoureteral reflux in children (*Capozza et al., 2011*).

AIM OF THE WORK

The aim of this work is to review and highlight the current diagnosis and management of vesicoureteral reflux in pediatric age group.

INCIDENCE OF PEDIATRIC VESICoureTERAL REFLUX

Vesicoureteral reflux (VUR) is believed to be present in 1% or less of general pediatric population, although the incidence is likely to vary depending on the age of screening because VUR often resolves over time, most cases of VUR are diagnosed after occurrence of a urinary tract infection (UTI). In children with UTI, the reported frequency of VUR varies from 30% to 40%. Pediatric clinical practice guidelines recommend screening children for VUR after a UTI (*Cooper et al., 2009*).

Evidence supporting the heritability of VUR is strong, however, its mode of inheritance and phenotypic expression are widely variable, not the same across different families, and further confounded by environmental factors. Given the high prevalence of familial VUR, it is suggested to perform routine screening of VUR in asymptomatic populations with positive family history (*Williams et al., 2008*).

Siblings and offsprings

Familial VUR has an autosomal dominant mode of transmission. Whereas VUR is thought to be present in 1% of the general pediatric population, the average prevalence of VUR is 27% among siblings of children with VUR and

36% among offspring of parents with VUR (*Skoog et al., 2010*).

Because of this increased likelihood of VUR, the EAU recommends screening asymptomatic siblings of VUR patients based on the assumption that if sibling VUR is diagnosed early, measures can be implemented to prevent future UTI and renal scarring (*Tekgul et al., 2011*).

AUA recommendations are similar: Parents should be informed about the increased risk of VUR, and RBUS can be offered to siblings (particularly those who are not yet toilet-trained), although the ability of RBUS to detect VUR is limited. If RBUS reveals any abnormality, VCUG is recommended. If parents choose not to screen, then prompt treatment of febrile episodes or presumptive UTI is required, followed by a complete investigation for VUR (*Skoog et al., 2010*).

Age

Younger children are more prone to vesicoureteral reflux (VUR) because of the relative shortness of the submucosal ureters. This susceptibility decreases with age as the length of the ureters increases as the children grow. In children under the age of 1 year with a febrile urinary tract infection, 70% will have VUR. This number decreases to 15% by the age of 12 year (*Peters et al., 2010*).