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Comparative retrospective study for surgically treated primary VUR in pediatric patients

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Abstract

Introduction

Vesicoureteral reflux have incidence of about 1% in pediatric population. It is a very common pediatric condition. Anomalies of the ureter, the dynamics of the bladder, and the anatomy of the ureterovesical junction can lead to abnormal valve mechanisms and vesicoureteral reflux.

Aim

The purpose of this study is to evaluate the effectiveness of open and endoscopic urethral reimplantation in relation to the severity of the vesicoureteral reflux and renal function.

Materials and Methods

We retrospectively analyzed 53 children treated for primary vesicoureteral reflux at the Clinic of Pediatric Surgery in Skopje in the period from 2017 to 2020. Endoscopic treatment was done using subureteric Teflon injection "STING" technique. Operative treatment (open procedure) was used in higher grade vesicoureteral reflux (3 or 4). The evaluation of the results of the treatment was done mainly according to the following criteria: reduced grade of reflux, maintaining renal function, absence of urinary infection and postoperative complications. These outcomes were compared between the two techniques.

Results and Discussion

The endoscopic procedure was shown to be superior for lower grade vesicoureteral reflux. The open procedure is preferable in cases of higher vesicoureteral reflux or after failure with the endoscopic procedure.

Conclusion

Treatment of vesicoureteral reflux with the endoscopic procedure is always preferable due to fewer days of hospitalization and as a minimally invasive approach. Both procedures proved to be effective in reflux correction, and successfully reduce the occurrence of febrile urinary tract infections.

Key words: pediatric urology, VUR, STING procedure, endoscopic treatment, surgery treatment

Introduction

Vesicoureteral reflux (VUR), one of the most frequent pediatric urological anomalies, is characterized by the regurgitation of urine from the bladder up the ureter into the kidneys collecting system (Figure 1). Atypical valve function and VUR can result from a number of irregularities that affect the ureter's structural integrity, the dynamics of the bladder, and the anatomy of the ureterovesical junction (UVJ).

The ureter enters the bladder wall at an angle, passes through the detrusor muscle, and continues as a submucosal channel between the bladder mucosa and the detrusor muscle before entering the bladder lumen. The ureter is compressed against the detrusor backing by the flap-valve mechanism, which works by stretching-distensioning and thinning the intramural section of the ureter and the bladder wall when the bladder fills. Reflux can occur when the passage between the submucosa and the detrusor muscle is too short, is missing, or has insufficient support. The ratio of the length of the ureters' submucosal tunnel to their diameter, which is typically between 4:1 and 5:1, is disturbed or decreasing in this circumstance. The decrease in this ratio suggests that the urethra has a greater diameter, the submucosal tunnel is shorter, or/and the ureters' insertion is lateralized to the typical trigone of the bladder. The physiological valve mechanism that prevents reflux is therefore insufficient. Typically, the degree of the malformation at the uretero-vesical junction corresponds to that proportion. Around 1% of children have VUR, which is a somewhat common condition.-

Urinary tract infections (UTIs) will affect one-third of these patients. Acute pyelonephritis brought on by VUR can result in renal scarring, which can then progress to reflux nephropathy, a chronic/end-stage kidney conditions. Although low grade VUR often resolves by adulthood, in some instances it can progress to severe renal dysfunction and injury.[2]

VUR can be divided into two categories according on the causes. The most common type of VUR, called primary VUR, is caused by an abnormality in how the ureter enters the bladder. It tends to self-resolve when the uretero-vesical circuit matures. On the other hand, secondary VUR is brought on by obstructions that prevent the urine from leaving the bladder, such as a double ureter, neurogenic bladder, myelomeningocele, spine injuries, an ectopic ureter, a sub-vesical blockage, or a back valve ureter.

Prenatal ultrasound diagnostics, a cystourethrogram, direct radioisotope voiding cystography, echo tomography, radioisotope techniques static DMSA scan and a dynamic DTPA renal scan—urodinamic tests, CT, and MRI—are all used to make the diagnosis.[3]

Starting with a precise diagnosis based on heteroanamnestic data, pre-clinical, radiological, radio isotopic, and laboratory tests, treatment necessitates a multidisciplinary approach. The best course of action for the affected child should be decided upon individually. Active surveillance, ongoing antibiotic prophylaxis, and surgical treatment are the three basic modes of treatment (endoscopic treatment and ureteroneocystostomy-ureter reimplantation).[4]

The purpose of this study is to evaluate and compare the effectiveness of open urethral reimplantation and endoscopic minimally invasive procedure in relation to the severity of the VUR and renal function.

Materials and Methods

Patient selection

53 children who had surgical treatment for primary VUR at the Clinic of Pediatric Surgery in Skopje between 2017 and 2020 were retrospectively examined (60 ureters). The diagnosis was made *via* direct radioisotope voiding cystography, voiding cystourethrogram, or prenatal ultrasound diagnostics. From the 53 patients, VUR grade I had 16 patients, VUR II had 10 patients, VUR III had 13 patients, VUR IV 12 patients and VUR V 2 patients. A decision was taken regarding whether to use an endoscopic or open approach based on the examination, the clinical presentation of VUR, the grade of VUR, and the recurrence of UTI. 32 children (36 urethras) had endoscopic therapy

using the "STING" subureteric Teflon injection technique. Patients' age ranged from 4 to 8 years (mean age of 6 years). From 32 patients, VUR I had 16 patients, VUR II 10 patients, VUR III 4 patients and VUR IV 2 patients. A total of 22 right and 14 left urethras were treated endoscopically. 4 patients out of the 32 had bilateral VUR. These patients spent an average of 1.5 days in the hospital.

Following were taken into consideration as endoscopic indications:

1. A VUR grade below VUR grade II and VUR grade III are the most optimized to treat with this procedure
2. More modest clinical manifestation and minimal UTI incidence
3. Renal functioning is unaffected (no renal scarring)

The open method was used to treat 21 patients (24 urethras), with an average age of 7.3 years and 13 female and 8 male patients. From third through fifth grades, every patient had VUR. Nine children with VUR grade III, ten with VUR grade IV, and two with VUR grade V, underwent surgery. Thirteen right and eleven left urethras were treated using this method. Three of the twenty-one children developed bilateral VUR. One patient was found to have hypoplasia of the left kidney in addition to grade IV VUR of the left ureter (Table 1).

	Total	Endoscopic treatment	Open procedure
Total number of patients	53	32	21
VUR I	16	16	/
VUR II	10	10	/
VUR III	13	4	9
VUR IV	12	2	10
VUR V	2	/	2

Table 1

The following are generally recognized indications for surgical treatment:

1. Serious reflux
2. The renal parenchyma developing more lesions or developing new scars.
3. Recurrent polynephrotic syndrome
4. Urinary infections coupled with feverish episodes when taking antibiotics as preventative measures
5. The cautious course of treatment is ineffective.

Endoscopic treatment

Patients were given premedication, put in the lithotomy position, and given general anesthesia. The operational field was cleaned and isolated around the genitalia and perineum. The introduction of the cystourethroscope was followed by the subtrigonally positioned application of Deflux® with a specially made cannula. The puncture was located in the 6 o'clock position, 2-3 mm below the ureter's entrance. A silicon-coated 5F, 33 cm cystoscope needle was utilized for injection, and between 0.3 and 1.5 ml of material was administered. A biocompatible and biodegradable implant, Deflux® is a sterile, highly viscous gel of dextranomer microspheres (50 mg/mL) in a carrier gel of non-animal stabilized hyaluronic acid (15 mg/mL). The average size of the dextranomer microspheres, which range in size from 80 to 250 microns, is about 130 microns. Hyaluronic acid that has been stabilized serves primarily as a carrier, leaving the dextran microspheres at the implant site. The plunger, tip cap, and plunger rod are all included with the syringe filled with Deflux®. Submucosal injections of Deflux® are administered next to the ureteral opening of the urine bladder. The coaptation of the distal ureter during bladder filling and contraction is made possible by the injection of Deflux, which increases tissue bulk. The connective tissue of the host gradually envelops the dextranomer microspheres (Figure 2).[5]

For grade four reflux, a different application method called intrauretrical technique was employed, and the insertion needle was placed near the base of the intravesical portion of the ureter. The intervention took place on average for 15 minutes. Patients are catheterized following the surgery. The patients are released from the hospital either that day or the following day after experiencing multiple spontaneous urinations. The typical length of stay for these individuals was 1.5 days.

Open surgical technique

The length of the intravesical ureter was extended using an open surgical method. The ureter was reinserted intravenously into the bladder wall for all individuals. The Politano-Leadbetter approach was used. The operating protocol for this method is as follows:
On the operating table, the patient is positioned on their back and given general endotracheal anesthetic. The operating field is cleansed and segregated according to procedure from the area beneath the umbilicus to the genitalia and perineum. Just above the pubic bone, a Pfannenstiel incision is created in the lower abdomen. The ureters and

bladders can be seen. Bladder walls are fixed on either side. Fixed urethral catheter is implanted. Circumferential cut is made around the entrance of the urethra. The urethra is prepared. A tiny hole is made over the urethra's opening. A surgical thread was sifted through the new hole and pulled through, and a prior suture at the mouth of the ureter, which is now movable, holds it in place. The free end of the surgical thread is pulled out of the freshly created hole. Submucosal canal connects the old and new openings. The distal ureter is transposed beneath the mucosa. Fixation of the new entrance is made and uretostomy is placed. Retrovesical drain is inserted and the wound is closed layer-by-layer with dressing of sterile bandage (Figure 3).[6] For unilateral reflux, the average intervention time was 90 minutes, and for bilateral reflux, the surgery took 120 minutes. Nearly all patients received at least one unit of blood or blood derivatives during the procedure.

Surgical intervention was limited to one act for 18 individuals with VUR. Three cases had uretero-cutano-stoma therapy for the first time. In situations where there were bilateral uretero-cutano-stomas, reimplantation was done separately for each ureter in two subsequent steps. Due to the presence of severe hydronephrosis, extreme ureteral lumen expansion, or poor general health, two acts of treatment were recommended.

The desired outcome was the achievement of the ratio of 4-5:1 for the length of the ureter's submucosal tunnel to the ureter. These patients spent an average of 9 days in the hospital (ranging from 5 to 13 days).

Evaluation

All patients' reflux severity was categorized into 5 groups in accordance with the International Reflux Study Committees.[7] A voiding cystourethrogram is performed after which the severity of the reflux is evaluated. Surgery was used to treat children with high grade VUR, lesions progressing in the renal parenchyma and/or causing new arterial hypertension as a result of kidney changes, recurrent pyelonephritis, urinary tract infections accompanied by febrile episodes while receiving antibiotic prophylaxis, and patients who did not respond to or cooperate with conservative treatment.

Biological samples were collected throughout the preoperative period for laboratory tests, such as urine culture, blood tests, blood group identification, serum C-reactive protein, degradation products (urea and creatinine), and study of urinary sediment (color, odor density, proteinuria, leukocituria, and bacteriuria). The collected data were essential, together with the other medical histories of the patient, for building a broad picture of the patient's health status and assessing the anesthesiological risk of the surgery.[8] There was no requirement for postoperative antibiotic treatments or analgesics during endoscopic treatment. Blood and/or blood derivatives were not needed. Before starting treatment, antibiotic prophylaxis was provided. Due to the potential to lower the risk of infection and attenuate the symptoms of dysfunctional voiding, patients receiving anticholinergics continued their therapy.

All patients received double antibiotic therapy following open surgery. Analgesics were required for three to four days. All of the children also had hematuria, which lasted for three to five days. A second unit of blood or blood derivatives was administered to the majority of children. The urinary catheter was removed on the sixth postoperative day. The following day, the retro-vesical drain was withdrawn. On average, the eighth postoperative day was the removal of the ureteric stent. Control ultrasonography was carried out after the stents were removed. Every other day, a complete blood count was performed along with renal function tests that looked at urea and creatinine levels as well as urine sediment.

After leaving our facility, all patients underwent follow-up ultrasonography reviews. For endoscopic procedures, seven days after surgery (to confirm the existence of a bolus), two weeks following open procedures, as well as six weeks after the intervention (to determine the extent of possible hydronephrosis). Six months following the operation, radio isotopic cystography was carried out as well as a voiding cystourethrogram in cases where the result was ambiguous.[9]

Results

In individuals who underwent endoscopic treatment, the goal was to reduce the original degree of VUR by 2 degrees, often from grade IV to grade II or I. Reduction of the severity of reflux, maintenance of renal function, lack of urinary infection, and postoperative complications were the key criteria used to assess the treatment's effectiveness (contralateral reflux, ureteral obstruction, additional disorders, and dysfunctional bladder).[10]

With the use of a VUR endoscopic technique, a reduction of 1 to 2 grades was noted. In 22 out of 32 individuals, or 68.75% of the patients, endoscopy unquestionably resolved the issue. Three children experienced postoperative issues. Re-urethrocystoscopic surgery was required for three patients. Re-endoscopy was used to successfully

treat them. Three kids were diagnosed with VUR grade 2 following an endoscopic procedure when they were 2 and 3 years old, but it went away on its own by the time they were 4 years old. Four patients still required a traditional laparatomy for uretroreimplantation due to recurrent UTI.[11]

The open operation likewise showed remarkable success rates; out of 21 patients, 19 had their VUR drop by three grades (92.71%). In patients who underwent open surgery, the expected outcome indicated a reduction of 3 degrees from the initial degree of VUR, often from Grade V to Grade II or I. Two of the patients (one with VUR grade 5 and one with VUR grade 4) treated with this procedure had VUR grade 3 after the operation, but it resolved to VUR grade 2 in the following year.

Discussion

Endoscopic therapy is a relatively common treatment option due to its low invasiveness and high success rates. Studies show that endoscopic treatment has substantially greater overall success rates than antibiotic prophylaxis and open surgery, however there is a clear learning curve that must be considered.[12]

The success of the endoscopic procedure depends on how safe and effective the injectable medication is over the long term. For this aim, a number of bulking agents have been developed, including polytetrafluoroethylene, bovine collagen, polyacrylate-polyalcohol copolymer, polydimethylsiloxane, calcium hydroxyapatite, and dextranomer/hyaluronic acid, which is administrated in our patients (Deflux ®).[13]

After endoscopic therapy, the most common complications include new contralateral VUR, ureteral obstruction, which requires ureteral stent implantation or surgical correction, and treatment failure. A number of minor issues with no long-term consequences were also mentioned, including temporary hydronephrosis, febrile UTI, hematuria, flank pain, and emesis.[14]

The advantages of the minimally invasive endoscopic treatment are considerable, but according to Minky Baek and colleagues' study, which was published in the Korean Journal of Urology in 2013, antireflux open surgery is the safest and best alternative for treating higher VUR grades IV and V. Our research and years of expertise both support the findings from Minky. The results from their study from open surgery is 95.1% per patient and also ours is 92.71%. The average success rates of injection therapy for primary VUR in children according to reflux grade have been reported to be 79% for grade II VUR, 72% for grade III, 63% for grade IV, and 51% for grade V on the basis of their meta-analyses. Our findings were similar. ith higher grade of VURs, success was more questionable for the endoscopic method. Our median success rate was 68.75%. When

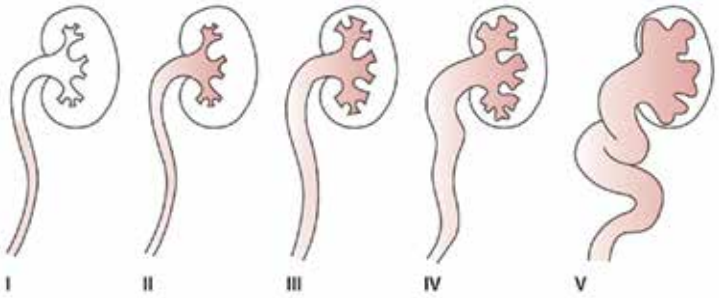

Figure 1: Representation of grading VUR and correlating urethral dilatation

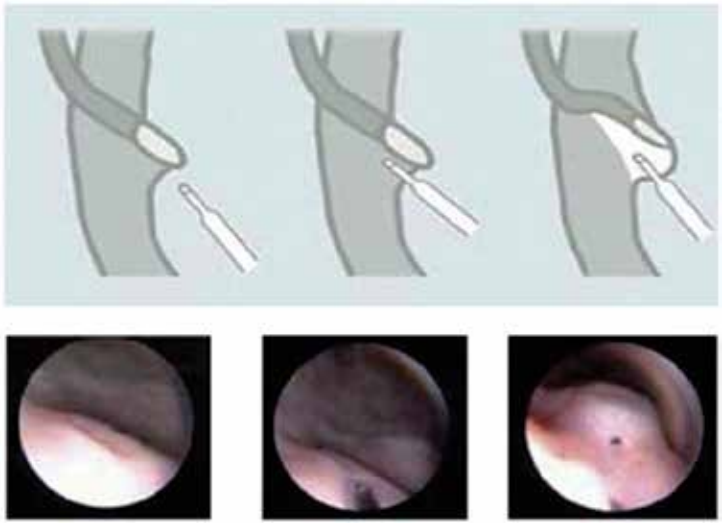

Figure 2: Endoscopic procedure

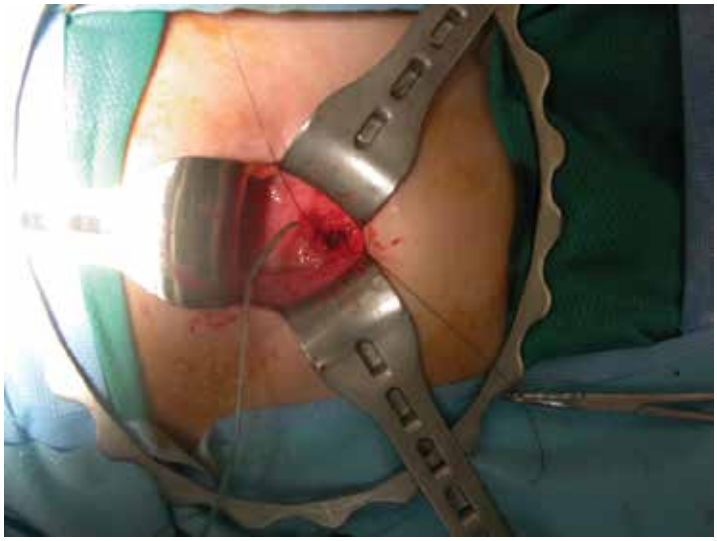

Figure 3: Open procedure for urethral reimplantation

selecting the proper treatment for VUR grades III and IV, we must use extreme caution. Our findings and their study demonstrated that when the VUR grade increases, the success percentage of endoscopic procedures decreases.[15]

The first-line treatment for VUR is the endoscopic procedure because of its effectiveness over the long term, affordability, and safety. The bulking product's high cost is offset by the shorter hospital stay and lower associated costs. Antibiotic prophylaxis should not be used long-term since it increases bacterial resistance and offers little protection against urinary tract infections.[9] Future advancements in endoscopic procedures and newly created bulking agents will expand the scope of applications for this treatment. Ureteroneocystostomy is still only used in situations where injectable treatment has failed or when there are serious anatomical anomalies. Only individuals with more complex VUR cases (grade IV–V) and those who have had unsuccessful endoscopic procedures should have open surgery. This surgical approach offers more satisfying results than other alternatives. The expense of this method is increased by the patient verticalization period, the necessity for further pharmacological therapy, the length of operation, and the anesthetic.[16]

Conclusion

Although statistics indicate that endoscopic surgery is not superior to open surgery, endoscopy has shown to be more effective in terms of patient verticalization time, the need for further medication therapy, blood loss during surgery, and operation time. But since both operational procedures, in our opinion, have their indicational areas in the proper developmental stage of VUR, we are unable to choose one over the other.[13] For every child, a patient assessment and choice regarding the method to be employed should be made.[17]

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