

# Prevention of vesicoureteral reflux in neonatal patients with intravesical ureterocele using holmium-laser



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## Prevention of vesicoureteral reflux in neonatal patients with intravesical ureterocele using holmium-laser

**AIM:** To evaluate the effectiveness of laser fenestration of intravesical ureterocele in prevention of vesicoureteral reflux.

**MATERIAL AND METHODS:** The result of intravesical ureterocele holmium laser fenestration (LF) was retrospectively analyzed in 29 neonatal patients (mean age 8.1 days, range 3-28) in comparison with 38 neonates (mean age 9.6 days, range 5-28) treated with electrosurgical incision (ES). Patients' records were reviewed for preoperative findings, endoscopic procedure description and postoperative outcomes.

**RESULTS:** Vesicoureteral reflux (VUR) was found in two patients (5.6%) in LF and in 25 patients (65.8%) in ES group after six months ( $P=0.000$ ). The patients with VUR in LF group had reflux grade III. In ES group six patients (15.8%) had reflux grade III, ten (26.3%) grade IV and nine (23.7%) grade V.

**DISCUSSION:** In our study we found that de novo VUR is several times more common in patients treated with electrosurgical incision. This is the main difference between two described endoscopic procedures. Although this is a relatively new surgical technique, and other authors had similar results, which implies the importance of laser fenestration in the prevention of VUR in neonates with ureterocele.

**CONCLUSION:** The occurrence of VUR is significantly lower in neonatal patients treated with holmium-laser fenestration, compared to standard electrosurgical incision, although both techniques are highly effective in relieving the obstruction. Since the use of this technique reduces the incidence of VUR, the need for subsequent surgery is lower in patients treated with holmium-laser.

**KEY WORDS:** Laser Reflux Prevention, Ureterocele

## Introduction

Ureterocele presents a cystic dilation of the distal segment of the ureter<sup>1</sup>. Insufficient ureteral maturation is suspected cause of the anomaly, implying the fetal process in which the developing ureteral bud separates from the mesonephric duct and moves to the bladder<sup>2</sup>. The ureterocele localization can be intravesical or extravascular, including the bladder neck and urethra, and usu-

ally is associated with duplex renal system for the upper pole<sup>3</sup>. Usually, ureterocele is without symptoms, but it can lead to difficult voiding followed by urinary tract infection (UTI) and rarely urosepsis, and in some female patients can be presented as intralabial prolapse of mucosa-covered mass causing obstruction<sup>4,5</sup>. The diagnosis is commonly prenatal with ultrasound (US). Voiding cystourethrogram (VCUG) determines intravesical status and the presence of vesicoureteral reflux (VUR). Renal function is assessed by radionuclide imaging, but the exact anatomy is confirmed by magnetic resonance imaging (MRI). Bladder function needs to be evaluated in cases of bladder outlet obstruction<sup>6-11</sup>. Cystoscopy is the final diagnostic procedure. Endoscopically the ureterocele presents as a thin-walled, cystic dilation inside the bladder<sup>1,3</sup>.

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The current ureterocele management is early and minimally invasive endoscopic treatment<sup>[12]</sup>. There are several techniques available: traditionally used electrosurgical incision, cold-knife incision and a relatively recently described the use of holmium: yttrium-aluminum-garnet (Ho: YAG) laser for ureterocele fenestration<sup>13,14</sup>.

Literature data published so far show that Ho: YAG laser is highly-effective for ureterocele decompression and as ultimate treatment. To prove this thesis, the aim of our study is to compare outcomes of endoscopic laser ureterocele puncture with commonly used electrosurgical incision, analyzing the incidence of redo surgery, and postintervention VUR in neonates.

## Material and Method

The study was conducted at national tertiary pediatric referral center. There was no need for Ethical committee approval due to retrospective study design, but all the included subjects had patient informed consents and approvals for complete diagnostics and treatment procedures, signed by caregivers. The patients were divided into two groups. In LF group we analyzed the results of laser fenestration of intravesical ureterocele in 29 neonatal patients, treated between November 2012 and February 2021. In ES group 38 neonates treated with electrosurgical incision between November 2000 and November 2012, were analyzed. Neonates with intravesical ureterocele in a single or double system were included and evaluated. Patients who were excluded had more than 28 days or had extravesical ureterocele and comorbidities that may affect the outcome of the treatment.

The diagnosis of intravesical ureterocele was confirmed with US and VCUG. Urinalysis, urine culture and kidney function tests were evaluated. Antibiotic prophylaxis was applied in all patients. All endoscopic treatments were performed under general anesthesia using 7.5 Fr cystoscope.

In LF group the source of energy for ureterocele fenestration was Ho: YAG laser with 230 and 365-microns laser probes. In ES group electrocautery was used for electrosurgical incision. The size of the probe was 3 Fr. We considered all anatomic conditions after transurethral cystoscope placing: urinary bladder mucosal appearance, its capacity, trigonal shape, ureteral orifices position and the presence of ureterocele. The ureterocele characteristics were considered: side, size, tension and urethral propagation.

**LF group:** Laser probe (micro laser fibers generating 0.2 to 1 J at a frequency of 5 Hz) was placed through the working channel of the cystoscope to the lowest and medial portion of the ureterocele, near to the bladder floor. The ureterocele wall perforation was made with 4 to 8 punctures until it had been collapsed. After the fenestration the ureteral stent was not placed. If there

was a risk of bladder neck obstruction, the Foley catheter was placed.

**ES group:** Electrocautery probe was placed through the cystoscope working channel and performed ureterocele wall incision. The sign of obstruction removal was undisturbed visualization of the ureterocele interior.

Antibiotic prophylaxis was administered postoperatively in all patients. Ultrasound examination was performed one day, one month and three months after the surgery in order to confirm the decreasing dilation of the kidneys' collecting system and ureter. To confirm the obstruction removal, three to twelve months after the surgery, depending on US finding, dynamic radionuclide renal imaging (DRI) was performed. If US dilatation persisted after three to six months, we performed DRI, otherwise DRI was performed 12 months after the surgery. Possibility of VUR was evaluated with VCUG. During the follow-up period VCUG was a mandatory procedure in all patients in ES group. VCUG was not obligatory in LF group to avoid negative impact of ionizing radiation. If there was no UTI and US was normal we performed observation only. In case of the persistence of ureterocele endoscopically re-treatment was conducted using the same procedure as the first time. Results are presented as counts (percent) or median (range). Fisher's exact test and Mann-Whitney U test were used to assess the differences between groups. For data analysis SPSS 20.0 was used. All p values less than 0.05 were considered significant.

## Results

In both groups the female/male ratio, patient's median age, median body weight, ureterocele side location and number of patients with ureterocele on single/double system were similar (Table I). Prenatal diagnosis was made in 23 patients in LF group (79.3%) and in 27 patients

TABLE I - Preoperative findings in patients.

Characteristics	LF group (n=29)	ES group (n=38)
Female	19 (65.5%)	27 (71.1%)
Male	10 (34.5%)	11 (28.9%)
Mean age, days (range)	8.1 (3-28)	9.6 (5-28)
Mean weight, kg (range)	3.4 (2.1-4.5)	3.3 (2.0-4.1)
Double system ureterocele	23 (79.3%)	30 (78.9%)
Single system ureterocele	6 (20.7%)	8 (21.1%)
Left side	18 (62.1%)	23 (60.5%)
Right side	11 (37.9%)	15 (39.5%)
Diagnosed prenatally	23 (79.3%)	27 (71.1%)
Diagnosed postnatally	6 (20.7%)	11 (28.9%)

LF - Laser fenestration group

ES - Electrosurgical incision group

n - Number of patients

TABLE II - Postoperative findings in patients.

	LF group	ES group	p value
Number of re-treatments	2/29 (6.9%)	8/38 (21.1%)	0.168
Complications	none	4/38 (10.5%)	0.127
Obstruction (after 3 month)	2/29 (5.6%)	4/38 (10.5%)	0.691
VUR (after 6 months):	2/29 (5.6%)	25/38 (65.8%)	0.000
VUR grade III	2/29 (5.6%)	6/38 (15.8%)	
VUR grade IV	none	10/38 (26.3%)	
VUR grade V	none	9/38 (23.7%)	

LF - Laser fenestration group

ES - Electrosurgical incision group

in ES group (71.1%), and postnatal in 6 (20.7%) and 11 (28.9%) patients, respectively.

Fenestration of the ureterocele with Ho: YAG laser was performed in the total number of 31 procedures in 29 patients in LF group. Electrosurgical incision of ureterocele was performed in the total number of 46 procedures in 38 patients in ES group. There were no complications in LF group, and in ES group there were four (10.5%) patients with pyelonephritis after the surgery. Obstruction was confirmed in two (5.6%) and four (10.5%) patients after three months, respectively. After six months obstruction was not found in any of the patients in both groups. Vesicoureteral reflux was found in two (5.6%) patients after laser fenestration of the ureterocele and in 25 (65.8%) patients after electrosurgical incision after six months, which was statistically significant (Table II). Two patients with VUR in LF group had reflux grade III. In ES group six (15.8%) patients had reflux grade III, ten (26.3%) patients grade IV and nine (23.7%) patients grade V.

## Discussion and Commentary

Relieving the obstruction is the main reason for the immediate treatment of patients with intravesical ureterocele due to renal function preservation<sup>3</sup>. Also, prenatal endoscopic treatment is published<sup>15,16</sup>. Many patients with ureterocele have associated anomalies of the urinary tract: duplicated ureter, renal dysplasia, renal parenchyma damage, megaureter, VUR, etc. Managing the ureterocele we manage all these conditions<sup>3-5</sup>. Endoscopic procedures for the treatment of ureterocele are electrosurgical incision, cold-knife incision and laser fenestration. The incision and fenestrations are made until ureterocele collapses. When the electrosurgical incision is performed it is very difficult to define the incision line length adequate to resolve the obstruction and at the same time preventing a VUR. During the laser fenestration there is no need for further punctures when the ureterocele collapses, any new punctures may lead to VUR.

The study conducted by Pogorelic and colleagues included 64 neonates with intravesical ureterocele treated by laser fenestration and electrosurgical incision. All the patients were divided into two groups, LF and ES, with 41 and 23 children respectively. Ureterocele laser fenestration with 6 to 8 punctures was performed with a holmium laser fiber 20 W at 6 Hz and 0.6 J. The authors stated that the optimal ureterocele decompression was achieved in all patients in LF group in contrast to 88% of those in ES group. Five patients in ES group had endoscopic re-treatment, and no patients in LF group required additional surgery. They performed US at the first postoperative day, one and six months after the surgery, and then once every year. VCUG was performed six months postoperatively or in a case of a febrile UTI. The incidence of de novo VUR was significantly lower in the LF group, and secondary procedures were required significantly more among the patients in ES group<sup>17</sup>.

Di Renzo and colleagues conducted the retrospective study comparing the outcomes of pediatric patients treated with laser fenestration and electrosurgical incision. They had 7 and 9 children in LF and ES groups, respectively. The settings of Ho: YAG laser were 6-8 Hz and 0.6-0.8 J. The laser fibers of 550 and 200 microns (for one patient) were used for 4 to 8 punctures of ureterocele. In postoperative follow-up they performed US and VCUG after 3 months in all patients, and subsequently in cases of persistent de novo VUR. There was no difference between groups in the occurrence of *de novo* VUR. Vesicoureteral reflux spontaneously resolved among the patients in LF group. In ES group the need for secondary surgeries was significantly higher<sup>18</sup>.

The study conducted by Caione and colleagues included 90 pediatric patients, divided into two groups, LF and ES, 64 and 26 patients respectively. The Ho: YAG laser settings were 0.5-0.8 J with 5-9 Hz. Laser fibers of 272 and 550 microns were used for creating 4 to 10 punctures at the ureterocele base. Decompression was achieved in 92% of the patients in both groups. Postoperative follow-up assumed US at 1, 3, 6 months and then once every year. They did not perform regular VCUG, but only for cases with proven UTI and those showing significant upper urinary tract dilatation, at 6-12 months postoperatively. The occurrences of de novo VUR, febrile UTI, and the need for re-treatment were statistically significantly lower among the patients in LF group<sup>19</sup>.

Publications on this topic show that both procedures success regarding the releasing of the obstruction is up to 90%<sup>17,19,20</sup>.

According to the above mentioned studies, our results also show no significant difference between laser fenestration and electrosurgical incision related to the obstruction. We can state that both, ureterocele laser fenestration and electrosurgical incision, are highly effective in relieving the obstruction.

Vesicoureteral reflux after the endoscopic treatment of ureterocele is well described and it ranges between 0-75%<sup>19-21</sup>. In our study we found that de novo VUR is several times more common in patients treated with electrosurgical incision. This is the main difference between two described endoscopic procedures.

As in our study, similar results have been collected by Haddad and colleagues, where the incidence of de novo VUR in the LF group was statistically significant compared to the ES group (32% vs 67%)<sup>22</sup>. Also, the study conducted by Palmer and colleagues, showed statistically significantly lower incidence of de novo VUR in LF versus ES procedures (36% vs. 88%)<sup>21</sup>.

Anand and colleagues in most recent published meta-analysis highlighted the superiority of LF over the ES technique for ureterocele decompression. The study results emphasize that the incidence of de novo VUR was significantly lower among pediatric patients who underwent ureterocele laser fenestration versus electrosurgical incision<sup>23</sup>.

As mentioned, the higher rates of de novo VUR in ES group is due to the creation of large-caliber defects in the ureterocele wall<sup>22,24</sup>. These defects tend to confront the flap-valve anti-reflux mechanism, essential in preventing the VUR during the bladder filling<sup>25</sup>. The smaller ureterocele holes created by laser fenestration do not interfere with anti-reflux mechanism. According to the published studies, the grades of de novo VUR were different between LF and ES groups<sup>17,18,26</sup>. Pediatric patients in the ES group had higher grade de novo VUR, while the patients in the LF group had lower grade VUR, which in most cases resolved spontaneously.

Reliable signs of decompression after the endoscopic treatment of ureterocele are US detected collapse of the ureterocele and decrease of the dilation of the renal collecting system on the affected side. If the ureterocele is not collapsed and dilation persists, we performed re-treatment. According to literature data the need for re-treatment is 10% to 30%<sup>10,19,21</sup>.

Our study showed the difference between the LF and RS groups of patients regarding re-treatment, but without statistical significance. In LF group re-treatment implies making a new ureterocele wall punctures until it collapses. In ES group the ureterocele incision line was extended for 3 to 4 mm. The absence of the obstruction on control US examination is the sign of decompression. But the question is: does the re-treatment increase the risk of de novo VUR?

The important parameter after the endoscopic treatment of ureterocele is the degree of VUR, and in these patients all degrees of reflux may occur, but high-grade reflux (IV and V) is more common. Initial endoscopic surgical technique of the ureterocele decompression implies prevention of VUR. It is well described that laser fenestration provides better protection of VUR<sup>21,22,27</sup>. We can state that possibility of reflux is lower after laser fenestration, although we performed our investigation in rel-

atively small group of patients. The surgeon is the one who controls the procedure and has to stop making the punctures immediately when ureterocele collapses since it is the critical moment when anti-reflux mechanism is still functional.

There are controversies about VCUG in neonates with ureterocele treated endoscopically, is it an obligatory procedure or not<sup>22</sup>. In our institution, from 2012, we decided not to perform routine VCUG after the ureterocele decompression. If there was no UTI and US and radionuclide renal scan were normal we performed observation only. Reliable signs of decompression after the endoscopic treatment of ureterocele were collapse of the ureterocele and reduction of the upper urinary tract dilation registered by US examination and dynamic radionuclide renal scan.

Considering these procedures that are performed in neonates the treatment duration is very important. Pagano and colleagues reported median duration of the endoscopic treatment of 23 minutes<sup>27</sup>. Our study in neonates showed that both LF and ES techniques allow the short general anesthesia, without significant difference. The skill of a surgeon is of great importance for adequate treatment.

After the initial endoscopic management of ureterocele there are options for subsequent surgery. Anatomy of the urinary tract determines surgical options. In a case of ureterocele with duplex system and afunctional upper pole, the most probable option is upper pole partial nephrectomy. Some authors consider that partial upper pole nephrectomy is not the best choice<sup>28,29</sup>. Our decision depends on the occurrence of VUR and UTI, if high-grade VUR occurs and patient has recurrent UTI, we consider subsequent surgery, in contrary we perform observation only. After analyzing the results of our study and published data, we can conclude that subsequent surgery is not indicated after the laser fenestration of intravesical ureterocele in majority of patients, because the occurrence of VUR is rare. Hence, laser fenestration may become the treatment of choice in patients with this anomaly.

Our study has several limitations, reflecting in retrospective design, small sample size, two groups being operated at different time periods.

## Conclusions

The occurrence of vesicoureteral reflux in neonates with intravesical ureterocele is significantly lower in patients treated with holmium-laser fenestration, compared to standard electrosurgical incision, although both techniques are highly effective in relieving the obstruction. Since the use of this technique reduces the incidence of reflux, the need for upper pole partial nephrectomy is lower in patients treated with holmium-laser fenestration. Considering all the above mentioned, laser fenes-

tration could be the treatment of choice for the management of neonates with intravesical ureterocele, but further prospective studies and meta-analysis are required.

## Riassunto

L'ureterocele è costituito da una dilatazione cistica del segmento distale dell'uretere, che può essere localizzato in sede intravesicale o extravescicale, compreso il collo vescicale e l'uretra, e di solito è associata ad una anomalia renale per duplicità del polo superiore. La diagnosi è comunemente prenatale con l'ecografia (US). Il cistoureterogramma di svuotamento (VCUG) dimostra la situazione intravesicale e la eventuale presenza di reflusso vesico-ureterale (VUR). La funzione renale viene valutata mediante imaging con radionuclidi, ma l'esatta anatomia è confermata dalla risonanza magnetica (MRI). Endoscopicamente l'ureterocele si presenta generalmente come una dilatazione cistica a parete sottile all'interno della vescica. Le opzioni per il trattamento chirurgico di fenestrazione intravesicale sono l'incisione elettrochirurgica, l'incisione con bisturi a freddo e - di impiego relativamente recente - del laser ad olmio: laser ittrio-alluminio-granato. Nel nostro studio i risultati della fenestrazione intravesicale con laser olmio (LF) sono stati analizzati retrospettivamente in 29 neonati (età media 8,1 giorni, range 3-28) rispetto a 38 neonati (età media 9,6 giorni, range 5-28) trattati con incisione elettrochirurgica (ES).

L'insorgenza di VUR nei neonati con ureterocele intravesicale è significativamente inferiore nei pazienti trattati con fenestrazione laser ad olmio, rispetto a quelli trattati con incisione elettrochirurgica standard, sebbene entrambe le tecniche siano altamente efficaci nel rimuovere l'ostacolo. Poiché l'uso di questa tecnica riduce l'incidenza del reflusso, e la necessità di eseguire una nefrectomia parziale del polo superiore è minore nei pazienti trattati con fenestrazione con laser ad olmio.

Considerando tutto quanto sopra, la fenestrazione laser potrebbe essere il trattamento di scelta per la gestione dei neonati con ureterocele intravesicale, ma sono necessari ulteriori studi prospettici e meta-analisi.

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