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Application of Flexible Ureteroscopy Combined with Holmium Laser Lithotripsy and Their Therapeutic Efficacy in the Treatment of Upper Urinary Stones in Children and Infants

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Purpose: To investigate the efficacy and safety of retrograde intrarenal surgery (RIRS) for the treatment of pediatric patients.

Materials and Methods: A total of 45 patients with upper urinary stones treated using flexible ureteroscopy combined with holmium laser lithotripsy at our department between June 2015 and January 2017 were examined in this study.

Results: The operative success rate of treatment using holmium laser lithotripsy via flexible ureteroscopy was 97.8% (44/45); one patient (1/45, 2.2%) was converted to laparoscopic pyelolithotomy, and the calculus was successfully removed. Lithotripsy via flexible ureteroscopy was successful during the first phase in 38 patients (38/45, 84.4%), and second or third phase lithotripsy was needed for six patients (6/45, 13.3%). Intraoperative ureteral fracture in the middle and lower sections occurred in one pediatric patient who was converted to laparoscopic pyelolithotomy and ureter bladder reimplantation. This patient was discharged after recovery at 2 weeks postoperative and showed no significant renal dysfunction over the 12-month follow-up period. Severe postoperative gross hematuria occurred in one patient, who improved after hemostasis and other symptomatic treatments. High fever occurred in two patients (body temperature >39°C), who later improved. These pediatric patients were discharged after active anti-infection and other conservative treatments for 4 days. All of the included patients were followed up for 2-15 months, with an average follow-up period of 8 months. The total calculus clearance rate was 100% (45/45), with no recurrence of the calculus.

Conclusion: In this study, most upper urinary stones in children and infants were treated successfully with holmium laser lithotripsy applied via flexible ureteroscopy.

Keywords: infants and young children; upper ureteral calculi; flexible ureteroscopy; holmium laser

INTRODUCTION

The treatment of upper urinary calculi in children and infants has always been a difficult problem for urologists. Previously, treatment methods for upper urinary calculi in children and infants have generally consisted of those used in adults, including extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), ureteroscopic lithotripsy, and laparoscopic pyelolithotomy. Due to the physiological characteristics of children and infants, their renal volume is small, cardiopulmonary function is not fully developed, and their tolerance for surgery is low. The application of adult treatment methods for upper urinary stones may cause greater trauma in children. Flexible ureteroscopic lithotripsy has recently been increasingly applied to treat upper urinary stones in infants and children because of its advantages, such as its natural access to the human body, limited trauma, satisfactory repeatability, quick recovery, low incidence of complications, and excellent safety and effectiveness[1]. Therefore, we applied flexible ureteroscopic lithotripsy to treat upper urinary stones in children and infants. A total of 45 infants and children with upper urinary stones were treated with flexible ureteroscopy combined with holmium laser lithotripsy at our department between June 2015 and January 2017, and satisfactory results were achieved. These results are reported as follows.

MATERIALS AND METHODS

Study Population

After obtaining approval from the local ethics committee at our hospital. The calculi were diagnosed according to a reference[1], and diagnosis in all cases was confirmed by a color Doppler ultrasound and computed tomography (CT) examination of the urinary system. A routine preoperative urine test and mid-urine culture examination were performed, and routine intravenous antibiotics were provided to control and treat infections. Inclusion criteria: upper urinary stones, patients less than 14 years old. Exclusion criteria: kidney anomalies, uncontrolled coagulopathies, ureteral obstruction, history of previous renal surgery or SWL and renal failure (serum creatinine≥ 3 mg/dl)[2].

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Table 1. Preoperative data of the included cases.

Number of patients	45
Average age (months)	113.5 (7-175)
Boys/girls	24/21
Location of the calculi	
Unilateral upper ureteral calculus	15
Unilateral renal calculus	19
Unilateral renal calculus with ipsilateral upper ureteral calculus	7
Bilateral renal calculus	4
Size of the calculi (cm)	1.7 (0.8-3.3)
>2 cm	11

Procedures

Intravenous anesthesia was administered to all pediatric patients in the lithotomy position. After routine disinfection, an F4/5.6-F8/9.8 rigid ureteroscope was passed into the bladder via the urethra to locate the ureteral orifice, and a nickel holmium guide wire was placed in the ureter along the ureteroscope. If the ureteroscope successfully entered the upper section of the ureter (below the ureteral calculi or the ureteropelvic junction area), then the rigid ureteroscope was withdrawn, and a flexible ureteroscopy sheath (F10/12) was placed under the guidance of the pre-set guide wire. Next, an F7.5 flexible ureteroscope was placed along the flexible ureteroscopy sheath via water injection using an artificial syringe to locate the calculi. The power of the holmium laser (18-32 W/30-40 Hz) was adjusted for lithotripsy based on the size, color, and hardness of the calculus. High frequencies and low energy were used as much as possible to reduce mucosal damage and fully shatter the calculus or to remove the larger fragments of the calculus with a calculus basket. After the completion of lithotripsy, the flexible ureteroscope and its sheath were withdrawn, and an F6 DJ tube was placed with the indwelling catheter. A postoperative routine examination of the kidney, ureter, and bladder (KUB) was performed to determine the efficacy of the lithotripsy procedure and the position of the DJ tube. If a "feeling of the scope being held" (the physician felt that the ureteroscope could not be pushed proximally forward) was noted during the placement of the F4/5.6-F8/9.8 rigid ureteroscope, then the operation was terminated with the indwelling F6 DJ tube after withdrawing the scope. Second or third phase lithotripsy was conducted via flexible ureteroscopy after 2 weeks. At 1-2 months after surgery, urinary system B ultrasound and CT results were reviewed to observe the stone clearance, and the presence of stone fragments <4 mm was defined as a successful operation. Thus, the DJ tube could be removed; otherwise, additional operations were performed until the stone was completely cleared.

Table 2. Intraoperative and postoperative status.

Average operation time (min)	30 (10-60)
Length of hospital stay (d)	4.2 (3-5)
Calculus clearance rate after the first operation	38(84.4%)
Cases requiring phase II surgical lithotripsy	4 (8.9%)
Cases requiring phase III surgical lithotripsy	2 (4.4%)
Calculus clearance rate	45(100%)
Successful operation rate	44(97.8%)
Complication	
Ureter avulsion	1 (2.2%)
Severe bleeding	1 (2.2%)
Urinary sepsis	2 (4.4%)
Follow-up time (month)	8 (2-15)
Calculus composition	
Calcium oxalate calculus	13 (37.1%)
Urate calculus	4 (11.4%)
Phosphate calculus	3 (8.6%)
Calcium oxalate calculus with urate calculus	9 (25.7%)
Calcium oxalate calculus with phosphate calculus	6 (17.2%)

Statistical Analysis

The statistical analysis was performed using SPSS 21.0 software. Count data are presented as percentages (%). Quantitative data are presented as medians and interquartile ranges.

RESULTS

The 45 pediatric patients in this study included 24 boys and 21 girls, ranging in age from 7-175 months (14 years and 7 months). The average patient age was 113.5 months (9.5 years), and four patients were < 3 years old. Fifteen cases of calculi were observed in the unilateral upper ureter. Moreover, 19 cases of unilateral renal calculi, including three cases of calculi in the ureteropelvic junction, four cases in the middle and upper calyx, six cases in the lower calyx, and six cases of multiple calculi; seven cases of unilateral renal calculi with ipsilateral ureteral calculi; and four cases of bilateral renal calculi were observed. The maximum diameter of the calculi was 0.8-3.3 cm, with an average of 1.7 cm. Eleven calculi were >2.0 cm (**Table** 1). In this study, lithotripsy via flexible ureteroscopy combined with holmium laser treatment was successful in 44 of the 45 cases; the remaining patient presented with ureter avulsion and was converted to laparoscopic pyelolithotomy to successfully remove the calculus. The single operation time ranged from 10-60 min, with an average of 30 min. If the stone was large (i.e., > 2.0 cm) and the surgery could not be completed within 60 min, then lithotripsy was conducted for the remaining stone during the second or third phase. In this study, one case (1/45, 2.2%) was converted to laparoscopic pyelolithotomy to remove the calculus. Lithotripsy via flexible ureteroscopy was successful during the first phase in 38 cases (38/45, 84.4%), and second (4/45, 8.9%) or third (2/45, 4.4%) phase lithotripsy was needed in six cases (6/45, 13.3%). The major reasons for second or third phase lithotripsy were "ureteral stenosis" causing failure of scope placement in five cases (5/6, 83.3%), including three cases with the "feeling of the scope being held" (3/6, 50%). In 2 cases (2/6, 33.3%), the calculus was relatively large, and therefore, lithotripsy could not be completed in a single session (**Table 2**).

Due to the limited proficiency of the surgical operation, one 7-year, 4-month-old girl presented with a severe intraoperative complication of ureteral avulsion during the early stage of the development of this technology. The calculus in this patient, which was approximately 1.5×2 cm, was located in the left ureteropelvic junction. A conventional F6/7.5 rigid ureteroscope was intraoperatively placed; the patient presented with ureteral stenosis and a "feeling of the scope being held". After ureteral dilatation, the ureteroscope was placed in the ureteropelvic junction. After the withdrawal of the scope, we found a rupture in the middle part of the ureter. After consultation with the parents and obtaining informed consent, the patient was converted to laparoscopic pyelolithotomy, and ureter bladder reimplantation was performed. This operation, resulting in postoperative F6-DJ tube placement for 3 months, was successful. To date, the follow-up examinations

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Figure 1. Case of ureteral avulsion and Reexamination at 6 months after ureter bladder reimplantation.

including urinary system B ultrasound scans and blood biochemistry measures have shown no obvious hydronephrosis or renal dysfunction (**Figure 1**). Therefore, the operation was terminated in subsequent cases when the surgeon noted a "feeling of the scope being held" while placing the rigid ureteroscope to avoid the occurrence of ureteral avulsion and other severe complications. In all other cases, no intraoperative ureteral perforation, avulsion, or other serious complications occurred; however, different degrees of postoperative gross hematuria were observed, including severe bleeding (bright red urine and decreased hemoglobin) in one 4-year, 3-month-old with a renal calculus in the lower calyx (1/45, 2.2%), indicated by 200 ml of bright red urine in the postoperative indwelling catheter drainage. The gross hematuria gradually disappeared after timely reporting of the condition to the physician, hemostasis, and other symptomatic treatments. The urinary catheter was withdrawn without obvious gross hematuria after 3 days, and a routine urine test on the fourth day revealed occult blood (+). The patient was discharged with an improved condition. Urinary sepsis (the patient's symptoms included a temperature >38.5□, tachypnea, and a WBC count >11,000/μl) occurred in an 8-year, 6-month-old and a 13-year, 2-month-old (2/45, 4.4%). After hemostasis, active anti-infection therapy, rehydration, and other symptomatic treatments, the patients were discharged with an improved condition 4-5 days after the surgery. The remaining 41 pediatric patients did not show serious complications, and the catheter was removed 1-2 days after surgery, with a hospital stay of 3-5 days (average, 4.2 days). The postoperative follow-up period lasted 2-15 months, with an average of 8 months. The overall calculus clearance rate was 100% (45/45), and no recurrence was observed.

In addition, the composition of the calculi from the 35 pediatric patients was postoperatively analyzed. The results showed that calculi containing calcium oxalate accounted for approximately 80% (28/35) of cases, which is similar to the composition of upper ureteral calculi found in adults (**Table 2**).

DISCUSSION

Due to upgrades of the flexible scope material and improvements in the technology of auxiliary equipment, the application of flexible ureteroscopy has become increasingly common in the diagnosis and treatment of calculi in the upper urinary tract. Currently, some European and American medical centers use flexible ureteroscopy as the preferred treatment method for upper ureteral and renal calculi in children[3-8]. Cavildak et al. [9] showed that laparoscopic ureterolithotomy and flexible ureteroscopy are both effective and reliable for the treatment of proximal ureteral stones, and flexible ureteroscopy was recommended as the preferred method due to the shorter operation and hospitalization times and the ability to manage situations that require secondary interventions. However, the treatment of calculi in the upper urinary tract of children using flexible ureteroscopy has rarely been reported in China[1], which imposed a new challenge on our department regarding the implementation of this technology. First, pediatric patients in China often require flexible ureteroscopic lithotripsy after the placement of an indwelling DJ tube, which differs from one-phase flexible ureteroscopic lithotripsy involving the pre-expansion of the ureter orifice, which is commonly applied by foreign surgeons. However, the success rate of first-stage lithotripsy is not different between the two methods[3-8]. Second, because flexible ureteroscopy achieves lithotripsy and calculus removal through a natural channel of the human body, surgical trauma, bleeding, renal damage, and other complications are significantly reduced compared to PCNL, laparoscopic surgery, and open surgery, and the technique has acceptable reproducibility. In a recent study, SWL was shown to be less expensive, required a shorter hospitalization time and longer fluoroscopy time, have a similar stone-free rate, and have the same efficiency as flexible ureteroscopy for pediatric renal stones with a diameter between 10 and 20 mm[10]. However, ESWL can only be performed two times in one position because the infant's kidney is too small to be manipulated repeatedly.

Flexible ureteroscopic lithotripsy surgery has specific requirements for the ureter anatomy, location of the calculus, and urinary tract infection, and serious complications might still occur. Additionally, studies have shown that flexible cystoscopy does not require antibiotics to prevent infection before surgery[11]. However, in the case of ureteroscopic lithotripsy, preoperative antibiotic use is necessary to prevent infection because the stones are associated with high levels of bacteria. For example, two patients had calculi with a large amount of adhered pus during the surgery. Although increased preoperative and intraoperative anti-infection treatments were provided, the intraoperative renal pelvic perfusion pressure was reduced, and the operation time was shortened, postoperative urinary sepsis still inevi-

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tably occurred.
In this study, flexible ureteroscopic lithotripsy had a good therapeutic effect, and the final stone-free rate reached 100%. However, this study also had some limitations. The sample size was relatively small, with only 45 cases, and it was a single center study. In addition, the composition of the stones was only analyzed in 35 cases. These results many not accurately reflect the current status of treatment for upper urinary stones in children and infants.

CONCLUSIONS

In this study, most upper urinary stones in children and infants were treated successfully with holmium laser lithotripsy applied by flexible ureteroscopy. This method has the advantages of high efficiency, minimal invasiveness, and repeatability. The method allows successful surgical treatment for this type of calculi in clinical practice.

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CONFLICT ON INTEREST

The authors declare that they have no conflict of interest.

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