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Analysis of the safety and efficacy of combined extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy for the treatment of complex renal calculus

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Abstract. – **OBJECTIVE:** To investigate the safety and efficacy of extracorporeal shock wave lithotripsy (ESWL) combined with percutaneous nephrolithotomy (PCNL) for treatment of complex renal calculus.

PATIENTS AND METHODS: Seventy-eight patients diagnosed with complex renal calculus and who accepted treatment in our hospital were consecutively selected. Patients were divided randomly into the observation group (n=40) treated by combined ESWL and PCNL and the control group (n=38) treated by PCNL. The effect of treatment between the two groups was compared.

RESULTS: The stone-free rate at 3 months after surgery was higher in the observation group than in the control group. There were no differences in the rates of complications (including infection, hemorrhage, collection system perforation and laceration, peripheral organ impairment, and urination extravasation). There were gradual decreases of serum creatinine in the observation group at 4 weeks after extubation of the double J catheter and at 3 months after surgery, while there were no apparent decreases in the control group. The levels of cysteine protease inhibitor and neutrophil gelatinase-associated lipocalin in both groups increased at 4 weeks after extubation of the double J catheter, and decreased at 3 months after surgery. The decreases were more apparent in the observation group compared with the control group, and the differences were statistically significant ($p<0.05$).

CONCLUSIONS: Combined use of ESWL and PCNL to treat complex renal calculus can improve the stone-free rate and renal function, and does not increase the complication rate. It is, therefore, safe and effective.

Key Words:

Extracorporeal shock wave lithotripsy (ESWL), Percutaneous nephrolithotomy (PCNL), Complex renal calculus, Cysteine protease inhibitor (Cys-C), Neutrophil gelatinase-associated lipocalin (NGAL).

Introduction

Urinary tract calculus is a common clinical disease, characterized by rapid onset and extreme pain. It occurs secondary to other diseases such as urinary tract infection and renal injury[1]. Presently, percutaneous nephrolithotomy (PCNL) is the first choice for treatment of renal calculus, and is safe and effective[2]. However, regarding complex renal calculi, the use of PCNL alone cannot achieve the desired stone-free rate, with 30-35% residual stone rate, and 10-20% stone recurrence rate[3]. With the advantages of being noninvasive and reproducible, extracorporeal shock wave lithotripsy (ESWL) is effective for small stones located in the upper urinary tract, especially at the junction of the upper ureter and renal pelvis[4]. We achieved a favorable treatment effect by adopting combined therapy with ESWL and PCNL for complex renal calculi. We aimed to provide a reference for the proper selection of clinical treatment. The report is as follows.

Patients and Methods

Patients

Seventy-eight patients diagnosed with complex renal calculi for the first time who were admitted to our hospital from January 2014 to January 2016 and accepted treatment were consecutively selected. Plain film X-ray, B ultrasound, and intravenous or retrograde pyelography were performed for diagnosis. The selected patients met the diagnostic criteria for recurrent renal calculus and had no history of use of antiplatelet or anticoagulant drugs such as Aspirin within 2 weeks before examination. The exclusion criteria were as follows: 1. Patients with infections, renal tumors, renal inadequacy, re-

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nal atrophy, abnormal development or position of kidneys, solitary kidney, or transplanted kidney; 2. Obesity with distance between the skin and kidney over 20 cm, which made it difficult to build a passage; 3. Basic diseases such as severe organ dysfunctions of the heart, liver, lung, and brain; 4. Patients unable to complete the treatment process, and with incomplete medical history.

After patients or their families signed the informed consent, patients were randomly divided into two groups, with 40 cases in the observation group and 38 cases in the control group. There were 27 males in the observation group, with mean age of 42.8 ± 8.7 years (range: 20-68 years). There were 10 cases with multiple renal calculi, 12 cases with calculi with diameter > 3.5 cm, 10 cases with staghorn calculi, eight cases were accompanied with ureteral calculi, and 12 cases were accompanied with hydronephrosis. There were 25 males in the control group, with mean age of 43.7 ± 10.2 years (range: 24-70 years). There were nine cases with multiple renal calculi, 13 cases with calculi with diameter > 3.5 cm, 11 cases with staghorn calculi, five cases were accompanied with ureteral calculi, and 10 cases were accompanied with hydronephrosis. Comparing these data between the two groups, the differences were not statistically significant ($p>0.05$).

Treatment Methods

Urine bacterial culture and drug sensitivity tests were performed, and antibiotic control treatment was applied. Surgery could not be performed until the urine culture results became negative. PCNL was applied in the control group, and the main steps were as follows: 1) Spinal-epidural anesthesia was performed, and the patient was placed in the lithotomy position. Retrograded ureteral catheterization was performed at the affected side. The patient was connected to the infusion apparatus, and artificial hydronephrosis was created; 2) The patient was placed in the prone position, and the renal abdominal region was elevated. Under the guidance of ultrasonography, the region between the 12th rib and infrascapular region at the affected side was used as the puncture point. The PCNL passage was established (16-22F), the 8/9.8F ureteroscope was placed in the passage, and the processes of rinsing and stone-crushing were performed under coordination with the pneumatic lithotripsy infusion pump; 3) Once a favorable effect was achieved, the 6-7F double J catheter was inserted through the urethra or the PCNL passage. Bladder examination was adopted via the ureter to confirm the lower side of the double J catheter was in the bladder. The nephrostomy catheter was reserved according to the needs of the patient. The double J catheter could be extubated at 3-6 weeks after surgery. Patients were followed-up at 4 weeks after extubation of the double J catheter.

The ESWL method was combined with PCNL in the observation group, and it was provided to patients of the observation group 1-2 times according to the treatment effect 1 week before surgery. It was performed one more time after the operation according to the condition of patients. A domestic electromagnetic extracorporeal lithotripsy machine was used for ESWL, and the patient was recommended to be placed in the supine position. The power of stone crushing was usually 10-12 W, with beating time no more than 2.000, the number of stone crushing times no more than 3, and the interval between two rounds of stone crushing was 2 weeks.

Observational Indexes

The kidneys, ureters, and bladder were rechecked at 3 months after surgery to compare the stone-free rate and complication rate. The levels of serum creatinine, cysteine protease inhibitor (Cys-C), and neutrophil gelatinase-associated lipocalin (NGAL) were compared preoperatively, 4 weeks after extubation of the double J catheter, and 3 months after surgery. Conventional biochemical methods were adopted to measure serum creatinine, and double antibody sandwich ELISA was used to measure the levels of Cys-C and NGAL. The kits were from Sigma-Aldrich (Co. St. Louis, MO, USA) and used according to the manufacturer's instructions.

Statistical Analysis

SPSS22.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Quantitative data are presented as mean ± standard deviation. The independent-sample *t*-test was adopted for comparisons between groups and the repeated measurement analysis of variance was adopted for intragroup comparisons between different time points. Enumeration data are presented as rate and a χ^2-test was used for intergroup comparisons. $p<0.05$ was considered statistically significant.

Results

Comparison of Stone-free Rate and Surgical Complication Rate

The stone-free rate in the observation group was significantly higher than in the control group, and there was no difference between the two groups in complication rate ($p>0.05$) (Table I).

There was a gradual decrease of serum creatinine in the observation group at 4 weeks after extubation of the double J catheter and 3 months after surgery, but no apparent decrease in the control group. The levels of urinary Cys-C and NGAL at 4 weeks after extubation were increased compared with before treatment, and decreased at 3 months after surgery. The levels in the observation group were significantly lower in the control group ($p<0.05$) (Table II).

Discussion

Presently, the treatment methods for renal calculus mainly include laparoscopic or traditional open nephrolithotomy, PCNL, ESWL, and retrograde ureterphylogram lithotripsy. Clinically, the surgical method is selected according to the specific condition of the patient. Complex renal calculus is characterized by calculi over 3.0 cm in diameter, with multiple calculi, staghorn calculi, abnormally positioned renal calculi, infected calculi, horseshoe kidney calculi, and solitary calculi[5]. PCNL is the primary choice for treatment of complex renal calculus, which creates small wounds, has a wide range of stone clearance, allows for more thorough treatment, causes fewer complications, allows for rapid recovery, and causes less bleeding. As complex renal calculus mainly involves complete or incomplete staghorn calculi, which fill the renal pelvis and several of the calyces, single use of PCNL or ESWL cannot completely remove stones from the kidney[6]. To increase the stone-free rate, the establishment of more passages is required and reservation of the nephrostomy catheter to perform a second stage operation is needed, which can cause large wounds and more complications[7]. ESWL cannot achieve the desired effects for renal calculi of large diameter, and repeated lithotripsy is required. Repeated lithotripsy easily causes steinstrasse formation and extends the stone removing process, which can increase the patient's pain and lead to long-term hydronephrosis and decreased kidney function, and lower the stone-free rate of renal calculus[8].

We adopted combined ESWL and PCNL in this study to treat complex renal calculus. ESWL was adopted before the application of PCNL, rather than using it as postoperative assistant treatment, which could reduce the volume of calculi and increase stone loosening, and allow the stones to be crushed through the nephroscope passage successfully and removed smoothly[9]. The study showed that the 3-month postoperative stone-free rate in the observation group was significantly higher than in the control group, while the complication occurrence rate was not statistically different between the two groups. Renal calculus infection was the major complication during the treatment process and the major cause of recurrence of renal calculi[10]. The applications of strict sterile surgical procedures, thorough antimicrobial therapy, acidification of urine, and urease inhibition can decrease the occurrence of infection[11]. Operative and postoperative hemorrhages were common complications with PCNL, which were caused by an excessive number of puncture passages and excessively large expansion passages[12]. It was confirmed in a previous study[13] that combined application of ESWL and PCNL could decrease the puncture passages in nephrolithotomy, shorten operative time, and shorten the indwelling time of the nephrostomy catheter and double J catheter. The crucial steps to prevent collection system perforation and laceration were accurate puncture location during surgery, and the indwelling of the double J catheter and nephrostomy catheter after surgery[14].

Table I. Comparison of stone-free rate and surgical complication rate [n (%)].

Group	Case	Stone-free rate	Infection	Hemorrhage	Collection system perforation and laceration	Peripheral organ impairment	Urination extravasation	Total occurrence rate
Observation group	40	36 (90.0)	1	1	1	0	1	4 (10.0)
Control group	38	27 (71.1)	1	1	1	1	2	6 (15.8)
χ^2		4.504						0.181
p		0.034						0.670

Table II. Comparison of levels of serum creatinine, Cys-C, and NGAL.

Group	Creatinine (µmol/l)			Cys-C (µg/l)			NGAL (µg/l)		
	Pretreatment	4 weeks after extubation	3 months after surgery	Pretreatment	4 weeks after extubation	3months after surgery	Pretreatment	4 weeks after extubation	3 months after surgery
Observation group	203.5±23.6	156.4±15.7	132.6±13.4	268.3±32.6	289.2±35.7	234.7±25.8	1.6±0.5	2.3±0.8	1.5±0.6
Control group	195.8±25.7	236.4±23.6	178.2±24.0	256.9±35.4	342.5±33.9	265.8±26.9	1.5±0.4	2.8±0.9	2.3±0.7
t	0.126	4.527	4.123	0.234	4.629	4.237	0.254	4.527	4.230
p	0.965	0.023	0.027	0.765	0.020	0.026	0.786	0.022	0.026

Note: Cys-C refers to urine cysteine protease inhibitor; NGAL refers to neutrophil gelatinase-associated lipocalin.

There was a gradual decrease of serum creatinine in the observation group at 4 weeks after extubation and 3 months after surgery, while there was no apparent decrease in the control group. The levels of Cys-C and NGAL in both groups increased at 4 weeks after extubation of the double J catheter, and decreased at 3 months after surgery. Compared with the control group, the levels of these indicators in the observation group were lower, and the differences were statistically significant ($p<0.05$), which indicated that the combined treatment could decrease the loss of renal function. As an endogenous marker of early impairment of renal function, Cys-C is metabolized by the kidney, reabsorbed by cells of the proximal tubules, and completely and rapidly degraded within epithelial cells[15]. As a newly identified secretary protein, NGAL plays an important role in immunity, inflammation, cellular differentiation, apoptosis, tissue remodeling, and the occurrence and development of various tumors[16]. NGAL can promote the development and growth of early primitive renal epithelial cells, but is not involved in the process of transformation[17]. As a damage induced transferrin, NGAL is produced in the thick ascending limb of Henle's loop and collecting duct, and is secreted in the urine. The concentration of urinary NGAL correlates with the degree of acute renal impairment[18]. Studies have shown that urinary NGAL was a more sensitive marker of renal injury than other indexes such as kidney injury molecule-1 and β_2-microglobulin, and can be detected before serum creatinine increases[19]. Urinary NGAL was highly related with Cys-C, and was significantly negatively correlated with glomerular filtration rate[20].

Conclusions

Combined use of ESWL and PCNL to treat complex renal calculus can improve the stone-free rate and renal function, and does not increase the complication rate. It is, therefore, safe and effective.

Conflict of interest

The authors declare no conflicts of interest.

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