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Original Article

Minimally-invasive stone removal in urinary calculi patients during pregnancy: clinical therapeutic effects and low complications

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Abstract: Purpose: To study the clinical effect of minimally-invasive surgery to treat urinary calculi and the prevention of surgery-associated complications during pregnancy. Methods: A retrospective analysis of the clinical data of 96 pregnant urinary calculi patients admitted to our hospital from April 2017 to April 2018 was conducted. The patients were randomly divided into a study group and a control group, with 48 patients in each group. The control group was given extracorporeal shock wave lithotripsy (ESEL), and the study group underwent minimally-invasive percutaneous nephrolithotomies (MPCNL). The clinical efficacy and the complications associated with the two treatments were compared. Results: The two groups' BUN and SCr levels were significantly decreased after the treatment ($P < 0.05$), with more significant reductions in the study group than in the control group ($P < 0.001$). There were marked reductions in the IL-6 and ET-1 levels in the two groups of patients post-treatment ($P < 0.001$), with greater decreases in the study group than in the control group ($P < 0.001$). The post-treatment CA and GLU levels were significantly lower than their pre-treatment values ($P < 0.001$), with greater decreases in the study group than in the control group ($P < 0.001$). Moreover, the patients' pain scores in the study group at post-surgery days 1, 3, and 5 were significantly lower than the post-surgery pain scores in the control group ($P < 0.001$). There were no significant differences in the stone removal rates between the two groups ($P > 0.05$). The Incidence of postoperative complications in the study group was significantly lower than the incidence in the control group ($P < 0.05$). Conclusion: The use of MPCNL for patients with urinary calculi during pregnancy effectively improves renal function, decreases the inflammatory and stress responses, and lowers the postoperative pain. Therefore, this treatment merits clinical application.

Keywords: Urinary calculi, pregnancy, minimally-invasive stone removal, treatment outcomes, reduced complications

Introduction

Urinary calculi during pregnancy is a rarely-seen disease clinically. Calculi whether in the ureter, renal pelvis, or bladder affects pregnancy. In addition, calculi can cause *qi stagnation* in the parturient and block the urethra [1, 2]. The surge in the secretions of estrogens and progesterone during pregnancy in women of childbearing age leads to a decline in urinary function, resulting in decreased ureteral peristalsis. This causes the retention of a large amount of crystals in the urine, forming calculus [3]. Some scholars believe that pregnancy increases the secretion of parathyroid hormone, enhances the absorption of calcium ions in the gastrointestinal tract, and promotes calcium urine [4]. The clinical symptoms of maternal urinary calculi depend on factors such as the location, size, infection, and obstruction of the internal calculus. If it is a kidney stone, it may cause back pain when the stone moves, and the pain is usually either paroxysmal or permanent. If it is a urethral stone, it causes difficulty or pain in urination, leading to urinary tract infections. Bladder stones are typically manifested as pain during urination or as lower abdomen pain [5-7]. Urinary calculi cause severe renal colic in the parturient, in which uterine contractions occur under the stimulation of inflammation, a condition which can easily lead to the premature rupture of membranes and miscarriage. For this reason, the timely diagnosis and treatment of the disease are extremely necessary. Extracorporeal shock wave lithotripsy (ESEL) uses X-rays to locate the stones in the patient's body. The stones are broken down with shock waves, thereby enhancing their discharges through the urine. However, apart from resulting in the unsatisfactory removal of stones, this method is affected by many factors such as the doctor's skills and the equipment parameters, and it is associated with many complications [8, 9]. The emergence of MPCNL has led to a qualitative leap in the treatment of urinary tract diseases. This technology can theoretically treat most stones. With the development of holmium laser technology and the constant accumulation of surgical experience, this minimally-invasive treatment technology has been widely applied in clinics [10]. Based on this, the present study was designed to investigate the effect of MPCNL on the treatment of urinary calculi during pregnancy.

Materials and methods

General information

A retrospective analysis of the clinical data of 96 pregnant patients with urinary calculi admitted to our hospital from April 2017 to April 2018 was conducted. The patients were randomly divided into a study group and a control group, with 48 patients in each group.

Inclusion criteria

Pregnant women who met the diagnostic criteria for urinary calculi during pregnancy, patients who met the ESEL and MPCNL treatment indications, and pregnant women who had unilateral calculi were included in this study.

Exclusion criteria

Patients in the following categories were excluded: patients who had recently received stone-removal treatment, patients with immune disease or systemic bleeding, and patients who had other diseases of the urinary system. In addition, patients with mental or other cognitive disorders or speech communication disorders.

The study was approved by the ethics committee of our hospital. The aim of the study and the processes involved were clearly explained to the included patients and their family members, prior to our obtaining signed informed consent forms from them.

Methods

The patients in the control group were subjected to ESEL using An XY-K-MEDICAL extracorporeal shock wave therapy machine (Zhengzhou Orrick Technology Co. Ltd.). Each patient was placed in a prone position, and the stones were explored. The lithotripter button was adjusted to display internal images of the stones, and the distance between the epidermis and the stones was measured prior to the lithotripsy. The applied voltage was increased appropriately, (the usual voltage range is 7-13 KV) based on the patient's clinical tolerance, 40-50 times/min, and the number of single impulses was 850-1100 times (as appropriate) for crushing the stones. The interval for lithotripsy was maintained at 7-30 days. For patients with multiple stones, anti-infective treatment was implemented after the impulses were administered. If the patient's stones were in the upper or middle section of the ureter, the internal lesions were examined with the patient placed in a supine position, and the probe was placed on the affected side at the same time. A CT examination was performed 2-3 weeks after the operation to assess the extent of the stone removal.

The study group underwent MPCNL under epidural anesthesia. The patient was placed in the lithotomy position, and a sterile drape was laid. Then, an Fr5 catheter was inserted retrograde into the affected ureter, and a pressurized infusion set was connected to form artificial hydronephrosis. Thereafter, in the prone position, a puncture was made under the 11^{th} intercostal or under the 12^{th} rib with the aid of ultrasound, and a puncture needle was used to assess the surface of the stone. The needle core was pulled out after entering the renal collecting system, the guide wire was inserted after the urine flowed out, and the skin was freed layer by layer. A fascia dilator was used for layer-by-layer expansion, and the Fr16 catheter was placed in a peelable sheath to establish a percutaneous renal passage.

The ureteroscope was inserted through the sheath into the renal collection system. Upon

Table 1. The two groups' general clinical data

	Control (n=48)	Study (n=48)	t/χ^2	P
Age ($\overline{x}$±s, years)	27.68±2.41	27.65±2.39	0.061	0.951
Gestational age ($\overline{x}$±s, weeks)	26.73±1.42	26.71±1.39	0.070	0.945
Stone types			0.849	0.839
Kidney stones	19	21		
Ureteral stones	13	11		
Urethral stones	10	12		
Bladder stones	6	4		
Stone diameter ($\overline{x}$±s, cm)	1.75±0.18	1.78±0.16	0.863	0.390

locating the stones, a holmium laser was used for the lithotripsy, and the broken stones were flushed using high-pressure water flow, while the larger stones were taken out directly using forceps. When the stones were cleared, an Fr5 double J tube was inserted, with an in-dwelling Fr16 nephrostomy tube for drainage. A kidney, ureter and bladder (KUB) X-ray was performed on the day after the operation to assess the treatment effect and the position of the double J tube, prior to the removal of the urinary catheter. After the operation, the patient's vital signs, lumbar symptoms, and urine color were closely monitored, and the nephrostomy tube was removed 3 to 6 days later. A CT examination was performed 2-3 weeks after the operation to determine the effectiveness of the stone removal and to determine the appropriate time to remove the double J tube.

Outcome indices

Determination of the renal function indices: Fasting venous blood (3 mL) was collected from each patient before and after the treatment. After centrifugation, the serum samples were used to complete an assay of the serum creatinine (SCr) and the blood urea nitrogen (BUN) using an BIOELAB Automatic Biochemical Analyzer (Nanjing Beiden Medical Co. Ltd.).

Assay of levels of the inflammatory factors: The serum interleukin (IL-6) and endothelin (ET-1) expression levels, as well as the serum catecholamine (CA) and plasma glutamate (GLU) levels were determined using the enzyme-linked immunosorbent assay (ELISA) kits provided by Elabscience Biotechnology Co., Ltd. (Cat. no. E-EL-H0102c, E-EL-H0064c, E-EL-H5735c, and E-EL-H2237c).

Determination of pain score: The physical pain levels in each of the two groups of patients at days 1, 3, and 5 post-surgery were evaluated using the Numerical Rating Scale (NRS) with a maximum score of 10 points [11]. The higher the score, the more severe the pain felt by the patient.

The stone removal and postoperative complication rates: The stone removal and postoperative complications rates in the two groups of patients were determined and statistically compared.

Statistical analysis

The count data are expressed as numbers (n) and percentages (%)] and were statistically analyzed using x^2 tests. The measurement data were expressed as the mean ± standard deviation (SD), and were compared using *t*-tests. All the statistical analyses were processed by SPSS version 20.0, and all the figures were drawn using GraphPad Prism 8.0. *P* < 0.05 was considered statistically significant.

Results

Comparison of the two groups' general data

The clinical data of the two groups of patients were comparable (*P* > 0.05). These results are presented in **Table 1**.

Comparison of the renal function before and after the treatment

There were significant decreases in the BUN and SCr levels in the two groups of patients after the treatment, with more significant decreases in the BUN and SCr levels in the study group than in the control group (*P* < 0.05). These results are presented in **Figures 1** and **2**.

Comparison of the inflammatory factor levels before and after the treatment in the two groups

The IL-6 and ET-1 levels in the two groups were significantly reduced after the treatment (*P* < 0.05). Again, there were greater reductions in

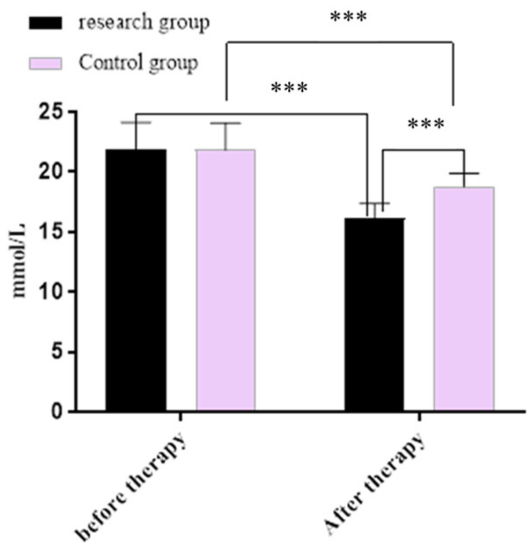

Figure 1. Comparison of the BUN levels between the two groups before and after the treatment. The data are presented as the mean ± SD. The abscissa indicates the data before and after the treatment, and the ordinate indicates the BUN levels (mmol/L). The BUN levels of the patients in the study group before and after the treatment were 20.29±3.17 and 15.23±1.77 mmol/L, respectively, while the BUN levels of the patients in the control group before and after the treatment were 20.27±3.14 and 18.02±1.52 mmol/L, respectively. ***represents P < 0.001.

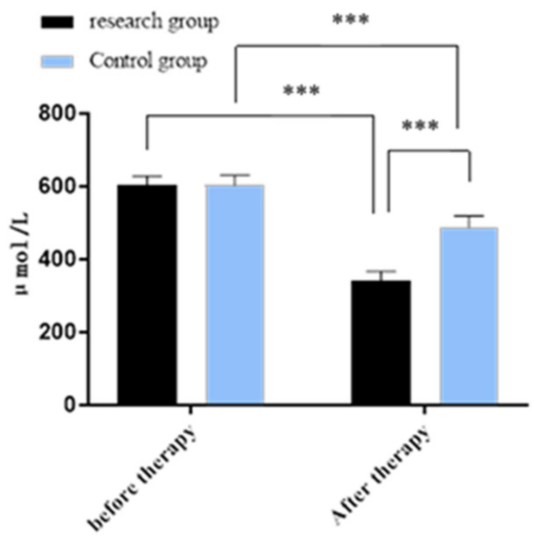

Figure 2. Comparison of the SCr levels before and after the treatment between the two groups of patients. The results are expressed as the mean ± SD. The abscissa indicates the data before and after the treatment, and the ordinate indicates the SCr levels (μmol/L). The SCr levels of the patients in the study group before and after the treatment were 586.23±35.45 and 321.44±37.47 μmol/L, respectively, and the SCr levels of the patients in the control group before and after the treatment were 586.27±36.24 and 467.68±42.26 μmol/L, respectively. ***represents P < 0.001.

the study group than in the control group ($P < 0.05$). These results are shown in **Table 2**.

Comparison of the systematic stress responses before and after the treatment

As shown in **Table 3**, the post-treatment CA and GLU levels in the two groups of patients were significantly lower than the corresponding pre-treatment values, with a greater reduction in the study group than in the control group (P < 0.05).

Comparison of the body pain levels at days 1, 3, and 5 post-operation

The pain scores of the patients in the study group were significantly lower than the pain scores in the control group at days 1, 3, and 5 after the surgery ($P < 0.05$). These results are shown in **Table 4**.

Comparison of the stone removal and postoperative complication rates

There was no significant difference in the stone clearance rates between the two groups ($P > 0.05$). However, the postoperative complication rate was significantly lower in the study group than it was in the control group ($p < 0.05$). These results are presented in **Table 5**.

Discussion

Due to the delicate nature of the uterus, conservative and minimally-invasive treatments should be the methods of choice for managing pregnancy-related problems [12]. With the constant improvements in minimally-invasive treatment technology, there have been many successful cases involving MPCNL. Clinical practice has fully confirmed that MPCNL effectively reduces intraoperative hemorrhaging and minimizes damage to the renal cortex, with the additional advantage of low pain levels and high success rates [13, 14]. However, MPCNL may inevitably cause complications such as perforations and small intestine and liver injuries, all of which compromise its efficacy. Therefore, there is a need for effective measures aimed at minimizing the MPCNL complications in order to improve its efficacy.

Table 2. Comparison of the IL-1 and ET-1 levels before and after the treatment in the two groups

Group	n	IL-6 (pg/ml)		ET-1 (ng/l)	
		Before treatment	After treatment	Before treatment	After treatment
Study	48	28.14±0.42	8.63±0.25	70.18±3.26	55.77±3.41
Control	48	28.17±0.38	17.95±0.23*	70.20±3.25	65.46±3.17*

The data are expressed as the mean ± SD. The IL-6 and ET-1 levels in the two groups of patients after the treatment were significantly lower than their corresponding levels before the treatment (*$P < 0.05$).

Table 3. Comparison of the systemic stress responses before and after the treatment in the two groups

Group	n	CA (ng/l)		GLU (mmol/l)	
		Before treatment	After treatment	Before treatment	After treatment
Study	48	354.72±22.63	173.48±19.84	6.17±0.83	2.43±1.05
Control	48	354.68±22.65	209.84±18.37*	6.15±0.80	4.12±1.06*

The data are presented as the mean ± SD. The CA and GLU levels in the two groups after the treatment were significantly lower than their levels before the treatment (*$P < 0.05$).

Table 4. Comparison of the pain levels after the operations in the two groups (points)

Group	n	1 day after operation	3 days after operation	5 days after operation
Study	48	6.21±0.54	2.65±0.68	1.13±0.31
Control	48	7.06±0.84	5.14±0.73	3.13±0.48
t		5.897	17.292	24.250
p		< 0.001	< 0.001	< 0.001

The data are the mean ± SD.

Perforation is a common complication of MP-CNL surgery. It arises as a result of the susceptibility of the peelable sheath to extravasation or perforation outside the renal collection system. This results in the retention of a large amount of fluid in the retroperitoneal cavity, with a small amount of fluid in the abdominal cavity. Breathing difficulties may arise, and if the fluid is absorbed, it causes electrolyte disturbances and induces intestinal obstruction [15, 16]. Therefore, if the patient has difficulty breathing or distress during the treatment, and the intestinal infarction does not resolve on its own, puncture and fluid extraction should be performed under ultrasound guidance. Once perforation occurs, the operation should be stopped immediately. In addition, appropriate channel expansion techniques should be selected. The peelable sheath is controlled in the renal collection system, and the insertion and removal of the nephrostomy tube is carried out under the guidance of the fluoroscopy system to avoid perforation.

Small intestine injuries are another complication associated with MPCNL. Small intestine injuries are likely to occur during surgery due to the closeness of the duodenum to the right renal pelvis [17, 18]. Thus, a diagnosis of small intestine injury is confirmed by the appearance of the duodenal contents during the operation. If the small intestine is severely damaged, open surgery is required. However, if the damage is small, conservative treatment can be selected, usually involving gastrointestinal decompression and the use of antibiotics.

Liver enlargement in patients increases the risk of liver injuries to a certain extent. Therefore, a CT-assisted puncture should be performed for this class of patients. If a liver injury occurs after surgery, an in-dwelling renal fistula tube should be used for 7-10 days to establish a sinus. Thereafter, it should be removed carefully, but if there is massive bleeding, it should be re-inserted immediately.

Minimally-invasive percutaneous nephrolithotomy (MPCNL) not only clears the stones, it also effectively reduces the patient's systematic stress response. The present study found that the CA levels of the patients in the study group after treatment were significantly lower than the CA levels in the control group. The main physiological role of CA is to excite the α-receptors of the tube, resulting in renal vasoconstriction, an increased perfusion pressure of the coronary blood vessels, an increased heartbeat, higher blood pressure, and an electrolyte

Table 5. Comparison of the stone removal and postoperative complication rates in the two groups of patients [n (%)]

Group	n	Stone removal	Complications			Total incidence
			Perforation	Liver injury	Small intestinal injury	
Study	48	100.00 (48/48)	0 (0.00)	1 (2.08)	1 (2.08)	4.17 (2/48)
Control	48	93.75 (45/48)	2 (4.17)	4 (8.33)	3 (6.25)	18.75 (9/48)
x^2		3.097				5.031
p		0.078				0.025

imbalance [19]. Sighinolfi *et al*. [20] reported that when MPCNL was used to treat urinary calculi, the patients' postoperative CA levels were significantly lower than the corresponding levels in the ESEL group. Thus, it was suggested that MPCNL is less traumatic to patients in the treatment of urinary calculi, and the stress response is lower, and this results in an improvement in the patient tolerance levels. However, the following limitations were identified in this study. It was a retrospective study with a small number of participants and a short follow-up. A randomized controlled, multicenter, double-blind study with a large sample is needed to confirm this conclusion further.

Conclusion

The use of the minimally-invasive percutaneous nephrolithotomy (MPCNL) procedure for the treatment of urinary calculi during pregnancy results in an effective improvement in renal function, a reduction in the inflammation and stress responses, and a reduction in the pain levels. Therefore, MPCNL should be used clinically for the treatment of urinary calculi in pregnant women.

Disclosure of conflict of interest

None.

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References

[1] Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Doizi S, Traxer O and Tiselius HG. Kidney stones. Nat Rev Dis Primers 2016; 2: 16008.

[2] Prochaska M, Taylor EN and Curhan G. Menopause and risk of kidney stones. J Urol 2018; 200: 823-828.

[3] Kmietowicz Z. Sixty seconds on ... kidney stones. BMJ 2018; 362: k3190.

[4] Letavernier E and Daudon M. Vitamin D, Hypercalciuria and Kidney Stones. Nutrients 2018; 10: 366.

[5] Ferraro PM, Taylor EN, Gambaro G and Curhan GC. Vitamin B6 intake and the risk of incident kidney stones. Urolithiasis 2018; 46: 265-270.

[6] Tangren JS, Powe CE, Ecker J, Bramham K, Ankers E, Karumanchi SA and Thadhani R. Metabolic and hypertensive complications of pregnancy in women with nephrolithiasis. Clin J Am Soc Nephrol 2018; 13: 612-619.

[7] Gamal W, Moursy E, Hussein M, Mmdouh A, Hammady A and Aldahshoury M. Supine pediatric percutaneous nephrolithotomy (PCNL). J Pediatr Urol 2015; 11: 78, e1-5.

[8] Wei C, Zhang Y, Pokhrel G, Liu X, Gan J, Yu X, Ye Z and Wang S. Research progress of percutaneous nephrolithotomy. Int Urol Nephrol 2018; 50: 807-817.

[9] Patwardhan SK, Shelke UR, Patil BP and Pamecha YR. Laparoscopic assisted percutaneous nephrolithotomy in chronic kidney disease patients with ectopic pelvic kidney. Urol Ann 2017; 9: 257-260.

[10] Zhao Z, Fan J, Liu Y, de la Rosette J and Zeng G. Percutaneous nephrolithotomy: position, position, position! Urolithiasis 2018; 46: 79-86.

[11] Senocak C, Ozbek R, Bozkurt OF and Unsal A. Predictive factors of bleeding among pediatric patients undergoing percutaneous nephrolithotomy. Urolithiasis 2018; 46: 383-389.

[12] Senocak C, Ozbek R, Yildirim YE, Bozkurt OF and Unsal A. Predictive ability of Guy's stone score in pediatric patients undergoing percutaneous nephrolithotomy. J Pediatr Urol 2018; 14: 437.e1-437.e7.

[13] Falahatkar S and Teimoori M. Re: percutaneous nephrolithotomy-position, position, position! Urolithiasis 2018; 46: 501.

[14] Lee AS, Bowen DK, Vatsky S, Zderic SA and Tasian GE. Percutaneous nephrolithotomy in an 8-week-old infant. Can J Urol 2018; 25: 9363-9365.

[15] Reesink DJ, Scheltema JMW, Barendrecht MM, Boeken Kruger AE, Jansonius A, Wiltink J and van der Windt F. Extracorporeal shock wave

lithotripsy under intravenous sedation for treatment of urolithiasis. Scand J Urol 2018; 52: 453-458.
[16] Brad AB, Ferro M, Vartolomei MD, Tătaru S, Anton-Păduraru DT, Simion C, Martha O, Pricop C, Porreca A and Negru I. Particularities and efficacy of extracorporeal shock wave lithotripsy in children. Urol Int 2019; 103: 318-325.
[17] Liu T, Shindel AW, Lin G and Lue TF. Cellular signaling pathways modulated by low-intensity extracorporeal shock wave therapy. Int J Impot Res 2019; 31: 170-176.
[18] Basulto-Martínez M, Klein I and Gutiérrez-Aceves J. The role of extracorporeal shock wave lithotripsy in the future of stone management. Curr Opin Urol 2019; 29: 96-102.
[19] El-Nahas AR, Taha DE, Elsaadany MM, Zahran MH, Hassan M and Sheir KZ. Hospital admission for treatment of complications after extracorporeal shock wave lithotripsy for renal stones: a study of risk factors. Urolithiasis 2018; 46: 291-296.
[20] Sighinolfi MC, Sandri M, Eissa A, El Sherbiny A, Micali S, Bianchi G and Rocco B. The safety of extracorporeal shock wave lithotripsy: an undervalued issue. Int Urol Nephrol 2019; 51: 457.