

CHINESE MEDICAL SCIENCES JOURNAL

SHORT COMMUNICATION

Effect of Tamsulosin in Medical Expulsive Therapy for Proximal Ureteral Calculi After Ureteroscopic Holmium Laser Lithotripsy

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THE technical achievements during the past decade have changed the modalities for the removal of ureteral calculi. The introduction of small-caliber semirigid ureteroscopes, as well as the development of holmium: yttrium-aluminum-garnet (Ho:YAG) laser and NTrap stone occlusion device, has improved the stone-free rate of ureteroscopy and reduced the incidence of complications. Recently, medical expulsive therapy has shown encouraging results in facilitating spontaneous passage of lower ureteral calculi and fragments after shock wave lithotripsy for renal/ureteral calculi. Tamsulosin has been proven to increase the stone-free rate, improve stone expulsion after shock wave lithotripsy, and decrease the expulsion time. In this randomized prospective study, we evaluated the efficacy of tamsulosin in promoting spontaneous clearance of stone fragments after ureteroscopic Ho:YAG laser lithotripsy in patients with proximal ureteral calculi.

PATIENTS AND METHODS

Patients

A prospective randomized study was conducted at Shouguang

Hospital of Traditional Chinese Medicine from June 2007 to June 2012. The inclusion criteria were: (1) symptomatic stone, (2) 10-15 mm in size, (3) located in the proximal ureter (between the ureteropelvic junction and sacroiliac joint), and (4) associated with moderate hydronephrosis. The presence and location of the stone were confirmed with ultrasound and/or kidney, ureter, and bladder (KUB) X-ray. The stone sizes were measured based on the KUB film. Exclusion criteria were: fever, leukocytosis, presence of ureteral stricture distal to the stone, co-existence of a kidney stone on ultrasound, and proximal stone migration during ureteroscopic Ho:YAG laser lithotripsy.

A total of 94 patients with proximal ureteral calculi undergoing ureteroscopic Ho:YAG laser lithotripsy were included in the study. All the patients were diagnosed as having proximal ureteral calculi based on KUB, ultrasound, and CT. Additionally, a series of data were collected, including case history, physical examination findings, complete blood cell count, blood electrolytes, and routine urinalysis as well as serum urea and creatinine.

The study protocol was approved by the ethics committees of Shouguang Hospital of Traditional Chinese Medicine, and written informed consents were obtained from the included patients.

Surgical procedures

The patients were placed in the asymmetric lithotomy

position under general or regional anesthesia. All the procedures were performed using semirigid ureteroscopes (8F/9.8F, Richard Wolf GmbH, Knittlingen, Germany) combined with the lithoclast (60W Coherent Medical Systems, Santa Clara, CA, USA). The stones were fragmented using a 550 μ m holmium laser fiber until small enough (approximately 2-3 mm). At the end of the procedure, a double-J ureteric stent (5F) was routinely placed in each patient. All the procedures were performed by a single endourologist. Operative time was recorded from the insertion of ureteroscope through the urethra to the withdrawal of the ureteroscope. The double-J ureteric stent was removed after 2 weeks by cystoscopy. Sixteen-French catheter was routinely placed and removed 1-3 days postoperatively.

Grouping and treatments

After operation, the patients were randomly divided into 2 groups, the tamsulosin group and the control group, using a random number table. The tamsulosin group received oral tamsulosin 0.4 mg/d in the morning after breakfast. The control group underwent careful observation and nursing in addition to conventional treatment.

All the patients received the conventional treatment with 2000-3000 ml/d hydration. The patients were advised to filter their urine, and those who had passed their stones were asked to stop the medication. During the 6-week treatment period, diclofenac (75 mg) was given to the patients when needed for pain relief.

Follow-up

All the patients were followed up weekly at clinic. At each visit, ultrasonography and KUB X-ray were performed to confirm stone expulsion and residual fragments localization. The primary outcome was the stone-free rate at 3 and 6 weeks. Stone expulsion was defined as no fragments or presence of a smaller than 3-mm clinically insignificant and asymptomatic residual. The secondary outcomes were episodes of ureteric colic during the 6-week period and expulsion time. An episode of flank pain requiring emergency treatment, narcotic use, or inpatient admission was defined as a colicky episode. The expulsion time is the period from random allocation to stone expulsion.

Statistical analysis

Statistical analysis was performed with SPSS 19.0 software. Quantitative data were expressed as means $\pm$ SD and compared with unpaired *t* test. Categorical data were expressed as number (percentage) and compared with Chi-squared test. $P < 0.05$ was considered statistically significant.

RESULTS

General information

Of the 94 randomized patients, 48 were in the tamsulosin group and 46 in the control group. The data of 3 patients from the tamsulosin group and 2 from the control group were not included in the final analysis for failure of timely follow-up visit, inadequate data for failure, and postural hypotension associated with tamsulosin. Age, sex, stone size, and operative time of the 2 groups were all comparable (all $P > 0.05$).

Follow-up results

The stone-free rate after 3 and 6 weeks were higher in tamsulosin group than in the control group (95.56% *versus* 79.55%, $P = 0.018$; 97.78% *versus* 93.18%, $P = 0.285$). The ureteral colic rate in the tamsulosin group was significantly lower than that in the control group (4.44% *versus* 22.73%, $P = 0.028$). The mean time of fragment expulsion was 7.86 ± 4.99 days in the tamsulosin group, significantly shorter than that in the control group (11.54 ± 9.89 days, $P = 0.032$).

Dizziness occurred in 2 patients and nausea in 1 patient, which were all tolerable.

DISCUSSION

For ureteral stones > 10 mm, ureteroscopy was recommended for its high stone-free rate. The success rate of proximal ureteral stone clearance after ureteroscopic lithotripsy has been elevated to 98%, while the rate of associated complications has fallen to 3%-9%. Ureteroscopic Ho:YAG laser lithotripsy has therefore become a standard procedure for the treatment of large proximal ureteral calculi.

The success of ureteral calculi treatment depends on the passage of the stone fragments. Stone passage from the ureter is basically influenced by ureteral peristalsis above the stones, spasm and edema at the location of the stone. Drugs have been used to facilitate stone expulsion *via* increasing hydrostatic pressure proximal to the calculus and relaxing the ureter around the stone. Those effects can be achieved with alpha-receptor antagonists and calcium channel blockers. Tamsulosin, an alpha-adrenergic receptor antagonist, was applied in this study, which could reduce the frequency and amplitude of ureteral peristalsis of the ureter and increase the flow of urine. The results of this study suggest that tamsulosin may help in early clearance of proximal ureteral calculi.

The most common complication after ureteroscopy is ureteral colic. The causes may be the increase in intraluminal

pressure resulting from lithic obstruction and the production of lactic acid due to smooth muscle spasm. Tamsulosin acts on smooth muscles of the ureter to prevent spasm, and blocks pain conduction to the central nervous system. In this study, tamsulosin significantly reduced the incidence of colic compared with the control group. The common side effects of tamsulosin are dizziness, nausea, diarrhea, headache, and abnormal ejaculation. The adverse effects

observed in this study were dizziness and nausea.

In conclusion, this study demonstrated that tamsulosin after ureteroscopic Ho:YAG laser lithotripsy could shorten stone expulsion time and reduce the occurrence of colic episodes. After 6 postoperative weeks, there was no statistically significant difference in terms of stone-free rate between the tamsulosin group and the control group.