Ureteroscopy: The First-Line Treatment for Distally Located Ureteral Stones Smaller Than 10 mm

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Received July 2012
Accepted November 2012

Purpose: To compare the efficacy of different treatment strategies for distal ureteral stones smaller than 10 mm.

Material and Methods: A total 127 patient were included in the study. Based on the treatment modality, patients were divided into three groups. Patients in group 1 only received conventional treatment including daily hydration of 2500 mL, ciprofloxacin, diclofenac sodium and a spasmolytic agent; group 2 patients received conventional treatment (daily hydration of 2500 mL, ciprofloxacin, diclofenac sodium and a spasmolytic agent) and tamsulosin 0.4 mg orally daily for 4 weeks; and group 3 patients underwent ureteroscopy. Patients were further subdivided into 2 categories based on maximum stone diameter: category A (less than 5 mm) and category B (5.0-9.9 mm). Following treatment, all groups were compared in terms of stone-free rate and time to expulsion.

Results: Following treatment, the stone-free rates for groups 1, 2 and 3 were 48.7%, 59.5% and 95.6%, respectively ($P < .0001$). The mean expulsion times for groups 1, 2 and 3 were 15.3 ± 5.33, 15.1 ± 5.5 and 1.95 ± 2.2 days, respectively ($P < .001$). Compared to the other treatments, the stone-free rate and mean expulsion time in the ureteroscopy group were significantly increased and decreased, respectively.

Conclusion: There are several treatment options for distal ureteral stones. Based on our data, we conclude that ureterorenoscopy should be the standard of care for distal ureteral stones smaller than 10 mm.

Key words: drug therapy; lithotripsy; treatment options; ureteroscopy; ureteral calculi.

INTRODUCTION

Ureteral stones account for roughly 20% of all urinary calculi, and 70% of these stones are located in the distal third of the ureter. Management of ureteral stones includes observation, medical expulsive treatment, extracorporeal shock wave lithotripsy (SWL), percutaneous antegrade ureteroscopy, retrograde ureteroscopy (especially for distal ureteral stones), and open/laparoscopic ureterolithotomy.[1] Although current therapeutic options for ureteral stones include both active intervention and conservative watch and wait approaches, the endoscopic treatment of ureteral stones has a high success rate and reliably results in immediate stone removal.[2,3] Furthermore, developments in ureteroscopic instrumentation has increased operational success while decreasing severe complications.[4,5] Currently, ureteroscopy is often used as a first choice treatment option for distal ureteral stones and as an alternative method to SWL or medical treatment modalities. In the present study, we evaluated the efficacy, feasibility and success rate of endoscopy for the treatment of distal ureteral stones smaller than 10 mm. We compared this treatment modality to observation and tamsulosin therapy.

MATERIAL AND METHODS

The study was approved by the local ethic committee. This study was conducted randomized and prospectively.

Patients

A total 127 patients with distal ureteral stones that were less than 10 mm were included in the study from February 2009 to July 2011. All of the patients had been admitted to and were managed by the Gazi University and Koru hospitals' department of urology due to distal ureteral stones. All patients were diagnosed with distal ureteral stones with smaller than 10 mm based on plain abdominal X-rays and urinary tract ultrasonography as well as with helical computed tomography when necessary. A case history was obtained from all patients; additionally, they underwent a physical examination and a series of measurements, including a complete blood cell count, blood electrolyte analysis, routine urinalysis, and serum urea and creatinine analyses. Patients who were pregnant or had severe hydronephrosis, a solitary kidney, a urinary tract infection, renal failure, stones greater than 10 mm, bilateral ureteral stones, multiple ureteral stones or previous urinary tract surgery were excluded from the study. All the patients′ plain abdominal X-rays and urinary ultrasonography results were reviewed and confirmed by two experienced radiologists, and the stone diameters were measured using X-rays, computed tomography and ultrasonography. All patients signed a written informed consent, and we discussed with them in detail the potential side effects and complications prior to treatment.

Grouping

Patients were divided into three groups based on treatment (see below). They were further subdivided into 2 categories based on maximum stone diameter: category A (less than 5 mm) and category B (5.0-9.9 mm).

Group-1 (Observation)-Thirty-nine patients were included in this group. Treatment included daily hydration of 2500 mL and ciprofloxacin (500 mg orally, twice a day) for the first 7 days. During the 4-week treatment period, diclofenac sodium (50 mg orally, twice a day) and a spasmolytic agent (hyoscine butylbromide, 10 mg orally, three times a day) were given.

Group-2 (Tamsulosin)-Forty-two patients were included in this group and were given tamsulosin 0.4 mg daily orally for 4 weeks. Additionally, these patients received conventional treatment with daily hydration of 2500 mL and ciprofloxacin (500 mg orally, twice a day) for the first 7 days. Diclofenac sodium (50 mg orally, twice a day) and spasmolytic (hyoscine butylbromide, 10 mg orally, three times a day) were also given to the patients in this group.

Group-3 (Ureteroscopy)-Forty-six patients were included in this group. Ureteroscopy was performed under general anesthesia using a 9.5 Fr (Karl Storz GmbH & Co KG, Tuttlingen, Germany) semi-rigid ureteroscope and a 0.035 mm safety guide wire. Patients were covered with antibiotics prior to instrumentation. All stones were located in the distal ureter and fragmented with a Swiss lithoclast (2.4 Fr long probe; 0.8 mm thick). Stone fragmentation was continued until all fragments were < 2 mm in diameter. In the event that fragments were larger than 2 mm, extraction was performed. Fragments < 2 mm were left for spontaneous

passage. Ureteral stenting was left to the discretion of the treating surgeon. However, in the event of proximal stone migration with ureteral extravasation, a stent was placed. Post-operative treatment of this patient population included daily hydration of 2500 mL, ciprofloxacin (500 mg orally, twice a day) and an analgesic agent for the first 7 days.

Group 1 and 2 patients were followed weekly for 4 weeks, or until alternative treatment (ureteroscopy) was undertaken. Follow-up visits included plain abdominal X-rays, urinary tract ultrasonography, urinalysis, serum urea creatinine and computed tomography if needed. During each visit, stone-free condition, analgesic dose, side effects and complications were recorded. Stone-free condition was defined as the absence of stones on plain abdominal X-rays and computed tomography.

Following ureteroscopy, group 3 patients were followed with routine biochemical analysis, blood counts and urinalysis. Preoperative aerobic urine cultures were routinely performed. In the event of a urinary tract infection, the patient was treated, and urine cultures were repeated to confirm sterility. The stone-free rate was determined by plain abdominal radiography and computed tomography on postoperative days 1 and 7. If inserted, the double-J ureteral stent was removed during postoperative week 3.

Statistical analysis

All groups were compared in terms of stone-free rate and time to expulsion. All data were recorded with SPSS (statistical program for social science) Statistical analyses were performed using Pearson chi-square test, t test and Fisher's exact test using the statistical package for the social science (SPSS Inc, Chicago, Illinois, USA) version 11.0.

The Efficiency Quotient Rate (EQ) was calculated using the following formula: EQ = percentage of stone-free patients/100% + percentage of re-treatment patients rate + ancillary procedures rate.[6] $P < .05$ was considered as statistically significant.

RESULTS

Of the 127 patients included the study, 71 were male and 56 were female. The mean patient age was 30.27 ± 6.7 (range, 19-44). Four patients in group 1 (2 included category A and 2 included category B) and five patients in group 2 (1 included category A and 4 included category B) withdrew from the study due to severe renal colic, infection or fever. These patients underwent immediate ureteroscopy. In the group 3, ureteroscopy was not successful in two category A patients. In one patient, the stone was inadvertently pushed up the ureter into the upper urinary system, and in the second patient, the stone was impacted in the ureteral wall. In postoperatively, re-ureterorenoscopy were applied to two patients (in category B) for residual fragment. Ancillary procedures was not need required any patient. Re-treatment rate was 4.34 and ancillary procedures rate 0.0 for group 3. There were no minor and major complications in group 1 and 2 during treatment. In the ureteroscopy group, there were no intraoperative and major postoperative complications; however there were two postoperative minor complications. Of these patients, one (included category A) had appeared acute pyelonephritis in postoperative second days. The patient treated with antibiotic including cephalosporin. In the other patient (included category B), the ureteral stent was spontaneously fallen in postoperative five days. Additionally, no statistical difference was found for patients' age, sex distribution or stone size between groups 1, 2 and 3 (Table 1).

Table 1. Patients' characteristics in the three treatment groups and in the two stone-diameter categories.

Characteristics	Patients	Treatment groups (n = 127)			*P*
		1	2	3	
Patient, n	127	39	42	46	
Age, years	30.27 ± 6.7	29.3 ± 7.1	30.7 ± 6.4	30.6 ± 6.4	.38
Sex, n (%)					
Male	71(55.9)	23 (59.0)	25 (59.5)	23 (50.0)	.60
Female	56 (44.1)	16 (41.0)	17 (40.5)	23 (50.0)	.61
Stone location, n (%)					
Left	61(48.1)	21 (53.8)	18 (42.9)	22 (47.8)	.78
Right	66 (51.9)	18 (46.2)	24 (57.1)	24 (52.2)	.80
Stone diameter, mm	6.79 ± 2.8	6.98 ± 2.1	6.46 ± 2.1	6.92 ± 2.0	.85

The stone-free rates for groups 1, 2 and 3 were 48.7%, 59.5% and 95.6%, respectively. The Efficiency Quotient rate for group 3 was 0.91. Across treatment groups, uret-

Table 2. The comparison of patient's stone-free rates and expulsion times.

Condition	Group 1			Group 2			Group 3			*P*
	Category A	Category B	Total	Category A	Category B	Total	Category A	Category B	Total	
Stone-free rate, n (%)	52.9 (9/17)	45.5 (10/22)	48.7 (19/39)	60.8 (14/23)	57.8 (11/19)	59.5 (25/42)	95.0 (19/20)	96.1 (25/26)	95.6 (44/46)	< .0001
Expulsion time, day	12.9 ± 5.4	16.0 ± 3.8	15.3 ± 5.3	13.5 ± 3.2	16.7 ± 7.0	15.1 ± 5.5	1.65 ± 2.7	1.97 ± 2.4	1.95 ± 2.2	< .001

Category A: stone size < 5 mm, Category B: stone size between 5.0-9.9 mm.
P values are for total stone-free rates.

eroscopy was significantly more effective in terms of the stone-free rate ($P < .0001$) (Table 2). In both the patients with stones smaller than 5 mm and in those with stones larger than 5 mm, surgical treatment was also significantly more effective in terms of the stone-free rate ($P = .011$ and $P < .001$ for category A and category B, respectively). In groups 1 and 2 (groups treated non-surgically), there was no significant difference in terms of the stone-free rate ($P = .29$); furthermore, There was no significant difference between category A and B patients in either group 1 or 2.

The mean expulsion times for groups 1, 2 and 3 were 15.3 ± 5.33, 15.1 ± 5.5 and 1.95 ± 2.2 days, respectively. Compared to groups 1 and 2, the expulsion time for the ureteroscopy group (group 3) was statistically different. Ureteroscopy was also significantly more effective than other treatment modalities ($P < .001$). In group 3, no difference was observed between category A and B patients ($P = .69$).

DISCUSSION

Due to recent technological advances, there are many options for the treatment of ureteral stones. The factors that determine suitable treatment choices include stone location, number of stones, renal function, surgical experience, additional patient health factors, technological qualification, cost and the patient's decision.[1,7] In our study, we compared three different options for the treatment of distal ureteral stones smaller than 10 mm.

Observation remains an alternative to treatment. To increase the likelihood of stone passage, patients are encouraged to increase fluid intake, and these patients are followed with regular visits to assess for spontaneous passage. Location and stone size should always be considered before deciding on observation. Small stones that are distally located are more suited to spontaneous passage. Analgesics overuse, debility, frequent doctor visits and emergent urinary diversion may be required in such cases.[8] In clinical trials, stones smaller than 4 mm usually pass spontaneously. Spontaneous passage rate falls significantly for stones larger than 5 mm.[1,9-11] Morse and colleagues found that distal ureteral stones pass spontaneous 71% of the time, whereas Hübner and colleagues reported an expulsion rate of distal ureteral stones of 45%.[12] In our study, the stone expulsion rate in the observational group was 48.7%. This rate was higher in individuals with stones smaller than 5 mm (52.9%), but this rate was not significantly higher than that for stones larger than 5 mm. Therefore, our results are compatible with those reported in the literature.

Both observation and treatment of distal ureteral stones have advantages and disadvantages. For observation, the disadvantages are persistent renal colic and frequent physician visits. Furthermore, urinary diversion or urgent intervention is sometimes required. Therefore, observation as the first choice remains controversial.

Another treatment for distal stones is medical expulsive therapy (MET). The presence of a ureteral stone often causes ureteral spasm, edema, pain and infection. The purpose of MET is to relax the smooth muscle, relieve pain and decrease edema without impeding peristalsis. Drugs used for MET include non-steroidal anti-inflammatory drugs (NSAIDs), antimuscarinics, steroids, calcium channel blockers and alpha-blockers. Of these drugs, alpha-blockers are the most effective and the most widely used. Blockage

of alpha-receptors, which are located throughout the ureter but are concentrated distally, causes propulsive contractions without blocking physiologic peristalsis.[13] Various studies have shown that alpha-blockers accelerate the passage of the distal ureteral stones.[14-16]

In a meta-analysis on the treatment of ureteral stones with alpha-blockers, it was shown that the use of alpha-blockers increases the rate of spontaneous passage to as high as 44 %.10 Additionally, in a study by Küpeli and colleagues, it was shown that the addition of tamsulosin increased the rate of distal stone clearance.[15] In a study by Erturhan and colleagues, the stone-free rate in individuals with distal ureteral stones was 73.3% following treatment with tamsulosin alone.16 On the other hand, Hermanns and colleagues showed that tamsulosin treatment does not improve stone expulsion rates in patients with distal ureteral stones ≤ 7 mm.[17] In our study, the stone-free rate was 59.5% in the tamsulosin group (group 2). In patients with stones smaller than 5 mm, the stone-free rate was 60.8%, and in individuals with stones larger than 5 mm, it was 57.8%. Ureterorenoscopy was performed in 41.5% of these patients due to the failure of medical treatment. In contrast to the literature, we found no significant difference between the tamsulosin and observational groups. However, tamsulosin does accelerate the expulsion of distal ureteral stones. Thus, if the stone is likely to pass, tamsulosin accelerates this process.

As mentioned above, the addition of tamsulosin to the medical treatment of distal ureteral stones has been shown to increase expulsion rates. However, there are two parameters that remain controversial: the duration of treatment and problems such as uncontrollable pain, the development of hydronephrosis, and surgical intervention. Although tamsulosin increases the expulsion of distal ureteral stones, we think that the use of alpha-blockers should not be the standard of care due to the controversial treatment duration and the high need of surgical intervention.

Because of improvements in instrumentation coupled with ureteroscopy's quick learning curve, ureteroscopy is the best treatment for ureteral stones. Although extra SWL was historically the first choice treatment for ureteral stones, the 2010 European Association of Urology (EAU) urolithiasis guidelines now list ureteroscopy as the best choice.[18,19] Additionally, in the guidelines published by Preminger and colleagues, URS is the treatment of choice for mid and distal ureteral stones smaller than 10 mm.[1] The ureteroscopy is the treatment with the highest stone-free rate after a single procedure for distal ureteral stones.[1,18] Thus, patients with ureteral stones also prefer URS over other treatments due to immediate cessation of pain and disability. In fact, Perchel and colleagues reported patient satisfaction in 100% of ureteroscopy cases.[20]

Differing energy sources coupled with ureteroscopy have produced successful results. Ultrasonic, electrohydrolic, laser and pneumatic lithotripters are widely used methods of lithotripsy. The effectiveness of ureteroscopy is well known in the treatment of distal ureteral stones when pneumatic lithotripters are used.[1,18,21] In our study, we also used a pneumatic lithotripter that is a widely used and comparatively inexpensive. In a study by Ceylan and colleagues, they reported a 95.0% success rate for 209 distal ureteral stones (average size of 8.7 mm) treated with URS.[22] Tuğcu and colleagues reported a success rate of 96.7% in their group of patients with distal ureteral stones (average size of 9 mm).[23] In our study, the average stone size was 6.9 mm, and our success rate for ureteroscopy was 95.6%. The stone-free rate was 95.3% for cases where the stone was smaller than 5 mm and 96.1% in cases where the stone was larger than 5 mm. This result shows that ureteroscopy is more effective than observation and alpha-blockers for the treatment of distal ureteral stones smaller than 10 mm.

Stone size and localization affect ureteroscopy success.[1,24] If the location of the stones is near the distal proportion of the ureter, ureteroscopy success is more likely.[1,18,24,25] Thus, distally located stones smaller than 10 mm are more suitable for ureteroscopy. The ureteroscopy also has a lower complication rate, morbidity and mortality compared to other treatments. In addition, it is much more effective. Factors included male sex, proximal ureteral stone, large stone size, surgical inexperience and symptoms for more than three months may increase the complication rate.[26,27] In our study, there were no major or minor complications in patients treated with URS. Thus, we think that it is unnecessary to treat patients with alpha-blockers for distal ureteral stones of any size, unless the patient cannot tolerate ureter-

oscopy.

CONCLUSION

We concluded that ureteroscopy was shown to be the most effective in our study. The advantages of ureteroscopy are its low complication rate, short expulsion time, and high stone-free rate after a single application and high patient satisfaction. Therefore, we believe that ureteroscopy should be the standard of care for distal ureteral stones smaller than 10 mm.

CONFLICT OF INTERSET

None declared.

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