Efficacy of terazosin as a facilitator agent for expulsion of the lower ureteral stones

Mohammad G. Mohseni, MD, Seyed R. Hosseini, MD, Farshid Alizadeh, MD.

ABSTRACT

Objectives: To determine the efficacy of terazosin as a facilitator agent for the passage of lower ureteral stones.

Methods: Since February 2004 to December 2004, 64 patients with lower ureteral stones who came to the emergency department were enrolled in this study. Exclusion criteria were the presence of urinary tract infection, severe hydronephrosis, elevated serum creatinine, hypertension, history of peptic ulcer disease and history of spontaneous stone passage. Patients were randomized into 2 groups of 32. Group 1 patients received terazosin tablets, 10 mg daily and analgesic (indomethacin capsules) for a maximum of 4 weeks, but patients in Group 2 received only analgesic. In cases of incomplete pain control, intravenous pethidine was administered. The 2 groups were compared with regard to stone passage rate, time to stone passage, the amount of received pethidine and the need for intervention. Statistical analysis was performed by student t-test.

Results: The mean age of Group 1 was 44 years and Group 2 was 39 years. The median stone size was 6.9 ± 2.3 mm in Group 1 and 6.6 ± 3.1 mm in Group 2, which was not significantly different. Stone expulsion rate was 90.62% in Group 1 and 62.5% in Group 2, with a significant statistical difference (p=0.041). The mean expulsion time was 76.3 ± 60 hours and 141 ± 64 hours in Groups 1 and 2, (p=0.001). Extra analgesic (pethidine) requirement averaged 34.4 ± 12.7 mg and 62.1 ± 10.5 mg in Groups 1 and 2 (p=0.036). Seven patients in Group 1 and 15 patients in Group 2 required ureteroscopy after 4 weeks due to lack of the stone passage.

Conclusion: Terazosin is a safe and effective treatment for lower ureteral stones. By using this medication, stone passage rate increases and the time of stone passage and the need for intervention decreases.

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Urolithiasis affects about 8-15% of the population in Europe and North America. In particular, symptomatic ureterolithiasis represent the most common condition observed by urologist in an emergency room.[1] The efficacy of mini-invasive therapies, such as extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy, has been proven by several studies.[2,3] Nevertheless, these techniques are not risk-free, are problematic and are quite expensive.[4] Recently, using pharmacological therapy, which can reduce symptoms and facilitate stone expulsion,[5-11] has extended use of the watchful waiting approach. Several studies have revealed α-1 adrenergic receptors in the ureter of humans. Furthermore, α-1 adrenergic blockers have proved to inhibit basal tone, peristaltic frequency and ureteral contraction even in the intramural tract. Some authors reported improved spontaneous stone passage rate using an α-blocker agent.[9-10] On the basis of the evidences that α-1 receptors present in the lower ureter, the blockage of theses receptors could have an effect on the stone expulsion in this location.[12,13] For

From the Department of Urology, Tehran University of Medical Sciences, Sina Hospital, Tehran, *Iran*.

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Address correspondence and reprint request to: Dr. Mohammad G. Mohseni, Department of Urology, Urology Ward, Tehran University of Medical Sciences, Sina Hospital, Hassan Abad Square, PO Box 11367-46911, Tehran, *Iran*. Tel. +98 (21) 66737741. Fax. +98 (21) 66716545. E-mail: rhosseinim@yahoo.com

this reason we performed a randomized, prospective clinical trial to evaluate the safety and effectiveness of these therapies for the treatment of lower ureteral stones.

Methods. From February to December 2004, 168 patients with renal colic came to our emergency department. Of these, 79 patients had lower ureteral stone according to abdominal sonography or kidney, ureter, bladder (KUB). Exclusion criteria were presence of urinary tract infection (UTI), severe hydronephrosis, elevated creatinine, hypertension, history of peptic ulcer disease, spontaneous stone passage and any previous intervention. The stone size was not an exclusion criterion. Fifteen patients were excluded from the study according to exclusion criteria. Patients were then randomly divided into 2 groups of 32. The first group was treated with terazosin (10 mg daily) and analgesic (indomethacin capsules) and the second group was treated with analgesic alone. In cases of improper pain control, pethidine was administered intravenously. Patients were followed-up for 4 weeks with sonography and KUB. They were instructed to visit their doctor if stone passage occurred or after 4 weeks and if stone passage did not occur, ESWL or ureteroscopy was performed. The 2 groups were compared with regard to stone passage rate, time of stone passage, the amount of pethidine needed and the need for intervention.

Statistical analysis was preformed using student t-test, chi-square and Fisher exact test as indicated. The *p*-values less than 0.05 were considered significant.

Results. Group 1 included 20 males and 12 females with a mean age of 44.2 ± 12.9 (15-64) years and group 2 included 24 males and 8 females with the median age of 39.3±14.2 (18-61) years. The mean age was not significantly different between 2 groups (p=0.76). The mean stone size was 6.9± 2.3 (4-12) mm in Group 1 and 6.6± 3.1 (3.5-10) mm in Group 2, which was not significantly different (p=0.34). Stone expulsion rate was 90.62% (29 patients out of 32) in Group 1 and 62.5% (20 patients of 32) in Group 2; the relation was significant (p=0.041). The time to expulsion was 76.3±60 (8-345) hours in Group 1 and 141 ± 64 (12-428) hours in Group 2 (p=0.001). The mean amount of pethidine administered was 34.4 ± 12.7 mg in Group 1 and 62.1± 10.5 mg in Group 2 (p=0.036) (t-test). There were no significant different with regards to gender in terms of stone passage. Seven patients (21.8%) in Group 1 and 15 patients (46.8%) in Group 2 needed intervention after 4 weeks due to stone retention and were rendered stone-free afterwards. Three patients (9.3%) in Group 1 developed transient orthostatic hypotension and palpitation that improved spontaneously.

Discussion. Several studies have been conducted regarding spontaneous ureteral stone passage considering the stone size. In a study by Kinder et al[14] spontaneous stone passage occurred in 45% of stone >5 mm and 94% of stone <5 mm in diameter. Other factors implicated in spontaneous stone passage are stone location, anatomical structure of the ureter and history of spontaneous stone passage.[15, 16] The aim of medical therapy is to remove preventing factors of stone expulsion (spasm, edema and infection).[17] Recently, several drugs have been proposed as spasmolytic and facilitator of ureteral stone passage.[9,10] In a study by Kupeli et al,[9] tamsulosin, an α-blocker was proposed as a provocateur of stone passage. In this study, stone clearance occurred in 20% of patients with lower ureteral stones <5 mm who were treated expectantly, 53.3% of patients with stones <5 mm treated with tamsulosin, 33.3% of patients with stones >5mm who underwent ESWL alone and 70.8% of patients with stones >5 mm who received tamsulosin in addition to ESWL.[9] In another study by Dellabella et al,[11] tamsulosin as a spasmolytic was assessed in renal colic patients. In this study, stone expulsion rate was100% in their series of 30 patients. They demonstrated that analgesic dosage decreased the pain frequency, time of stone passage was decreased and fewer patients needed hospitalization and intervention in the treatment group.[11] Porpiglia et al[10] compared the efficacy of tamsulosin and nifedipine in terms of decreasing in time of stone passage and increasing stone expulsion rate. Both drugs were effective although tamsulosin was more effective. Yilmaz et al[18] compared the effectiveness of 3 α-blockers, tamsulosin, terazosin and doxazosin as facilitators of ureteral stone passage in a study. In this study, the effectiveness of these drugs were comparable (79.31% in tamsulosin, 78.57% in terazosin and 75.86% in doxazosin group) and all of them increased stone passage rate over the control group (53.57%). The number of pain episodes and average time to expulsion were also significantly lower in the treatment groups. Recently, Resim et al[19] evaluated the effect of tamsulosin on the stone clearance and number of colic episodes in patients with lower ureteral stones and found that although this drug dose not increase the stone-free rate, it decreases the number of colic episodes. In most of these studies, tamsulosin was chosen as the α-blocker. The reason why we chose terazosin was its lesser price in our country. We followed-up the patients for up to 4 weeks to reduce the likelihood of renal parenchymal injury

due to prolonged ureteral obstruction.[20] In our study, the efficacy of terazosin was 90.6% for lower ureteral stones and patients needed less analgesic and fewer interventions. Medical treatment is less expensive and safer compared to other methods of treatment of ureteral stone (surgery, ureteroscopy, ESWL). This method does not exert negative effect on the result of interventional procedures if fails to pass the stone; all of our patients were ultimately rendered stone free.

In conclusion, our study showed that medical treatment is a convenient method for the treatment of lower ureteral stones. Considering the maximum time to expulsion of 4 weeks, complication due to prolonged obstruction reach to minimum and less costs and complications are imposed on the patient compared to other methods (ureteroscopy, ESWL, surgery). Using this drug, stone expulsion speeds up, stone passage rate increases and the need for intervention decreases.

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