Is There a Role for Tamsulosin in Shock Wave Lithotripsy for Renal and Ureteral Calculi?

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Purpose: We evaluated the effect of the α-blocker tamsulosin on stone clearance, analgesic requirements and steinstrasse in shock wave lithotripsy for solitary renal and ureteral calculus.

Materials and Methods: A prospective, double-blind, randomized placebo controlled study was performed during 1 year involving 60 patients with a solitary renal or ureteral calculus undergoing shock wave lithotripsy. The control group (30) received 0.4 mg tamsulosin and the study group (30) received placebo daily until stone clearance or for a maximum of 30 days. An oral preparation of dextropropoxyphene hydrochloride and acetaminophen was the analgesic used on an on-demand basis. The parameters assessed were stone size, position, clearance time, effect on steinstrasse and analgesic requirement.

Results: The overall clearance rate was 96.6% (28 of 29) in the study group and 79.3% (23 of 29) in the control group ($p = 0.04$). With larger stones 11 to 24 mm the difference in the clearance rate was significant ($p = 0.03$) but not so with the smaller stones 6 to 10 mm ($p = 0.35$). The average dose of analgesic used was lower with tamsulosin than with controls, without statistical significance. Steinstrasse resolved spontaneously in the tamsulosin group whereas 25% (2 of 8) required intervention in the placebo group. There was no difference between the 2 groups with regard to age, stone size or location.

Conclusions: The α-blocker tamsulosin seemed to facilitate stone clearance, particularly with larger stones during shock wave lithotripsy for renal and ureteral calculus. It also appeared to improve the outcome of steinstrasse. Tamsulosin may have a potential role in routine shock wave lithotripsy.

Key Words: lithotripsy, tamsulosin, kidney, ureter, calculi

Shock wave lithotripsy has revolutionized the noninvasive treatment of renal and ureteral calculi. For larger renal calculi, SWL has a vital role as an adjunct to percutaneous lithotripsy as sandwich therapy. The success of this procedure is determined by 2 factors, fragmentation and clearance. The former is dependant on the type of lithotripter and the nature of the calculus. In a renal calculus, the clearance may be influenced by the configuration of the calix. Once the fragments enter the ureter, their management is similar to ureteral calculi on conservative treatment. Various factors like edema and infection determine the passage through the ureterovesical junction, the narrowest part of the ureter. The concept that relaxation of the ureterovesical junction can facilitate stone passage is not new, and several drugs like prostaglandins, parasympatholytics, calcium channel blockers and antihistamines have been tried. The detection of α1 receptors in the lower ureter initiated the use of specific α-blockade alone or in combination to accelerate stone passage through the ureterovesical junction. This study was performed to assess the effect of tamsulosin, an α1A and α1D-blocker on the outcome of shock wave lithotripsy for renal and ureteral calculi.

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MATERIALS AND METHODS

This was a placebo controlled, randomized, double-blind study performed prospectively during September 2004 to July 2005. A total of 60 patients who were to receive SWL for a single radiopaque renal 6 to 24 mm or ureteral 6 to 15 mm calculus, were included. Exclusion criteria were recent open or endoscopic surgical intervention, radiolucent calculus, past unsuccessful SWL, renal impairment (creatinine greater than 1.5 mg/dl), poorly functioning kidney, recurrent calciuria, urinary tract infection, those on calcium channel blockers and or α1-adrenergic antagonists, congenital urinary anomalies, history of pyeloureteral surgery and children. Institutional ethical clearance was obtained. The side effect profile was explained and informed consent was taken in all. Blood investigations included packed cell volume, random blood sugar and serum creatinine along with routine urine and culture sensitivity. The mode of imaging was excretory urography. The sample size of 60 was based on the power of the study 90% to detect a difference of 30% or more between 2 groups, allowing a 2-sided type 1 error of 5%. Block randomization was performed with even distribution, using computer generated numbers. The patients were randomized into either placebo or study group. Group 1 (30) received placebo and group 2 (30) received 0.4 mg tamsulosin, with once daily Proxyvon (65 mg dextropropoxyphene hydrochloride and 400 mg acetaminophen) orally used for analgesia as required. If there was severe pain to warrant admission to the emergency room or to the ward,

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injectable diclofenac or pethidine was given. A minimum of 2.5 l fluids was advised. Treatment was started on the first day of SWL and continued until complete stone clearance or a maximum of 30 days. All patients were required to record the number of analgesic capsules taken, side effects of the drugs if any, and to strain the urine for stone fragments. They were advised to report to the emergency department if there was severe pain, hematuria, vomiting or fever.

SWL was given using the Dornier Compact S Lithotriptor with electromagnetic shock wave generator with the patient under intravenous analgesia (injections of 50 mg pethidine and 25 mg promethazine) with electrocardiogram and pulse oximeter monitoring. A total of 1,500 shocks were given at 14 to 15 KV at the rate of 70 per minute per session. Stone fragmentation was monitored fluoroscopically and by plain x-ray of the kidneys, ureters and bladder before further shocks. Factors analyzed were stone clearance, stone-free status, clearance time, steinstrasse formation and outcome, and the dose of analgesic required. For the purpose of analysis when parenteral analgesia was used each dose was given a value twice that of the oral analgesic in the case of parenteral diclofenac and 3 times if pethidine was used. Successful clearance was defined as stone-free status or presence of clinically insignificant asymptomatic residual fragments of less than 3 mm at 1 month or earlier. If a column of fragments obstructed the ureter it was considered steinstrasse. Intervention was performed if there was fever or severe pain. Those who did not complete 1-month followup without clearance were excluded from final analysis. Statistical analysis was performed using Stata® 8.0 software. Continuous variables were expressed as mean and SD or median and range between the treatment groups. Categorical variables were expressed as percentages. The Student t test or Mann-Whitney U test was used to compare the continuous variables between tamsulosin and the placebo group, and the chi-square test was used for categorical variables. All p values less than 0.05 were considered to indicate significance.

RESULTS

Of the 60 patients who were randomized 58 completed the study, and 1 from each group discontinued medication and was excluded from analysis. The 2 groups were comparable in their baseline demographic and clinical characteristics (table 1). Stone size was relatively larger in group 2 but without statistical significance. The overall stone clearance rate was 79.3% in group 1 and 96.6% in group 2, and the difference was statistically significant (p = 0.04, table 2). In those with a stone diameter of 6 to 10 mm, the difference (5.9%) was not statistically significant (p = 0.35, table 3). With a larger stone diameter 11 to 24 mm, the clearance was 58.3% (7 of 12) in group 1 and 93.3% (14 of 15) in group 2, and the difference (35%) was statistically significant (p = 0.03, table 3). Residual fragments were seen in the ureter in 5 patients in the control group and none in the study group. Residual fragments were seen in the kidney in 1 patient each in both groups. Steinstrasse was observed in 8 patients in the placebo group and 10 patients in the tamsulosin group. Those in the latter group cleared spontaneously whereas 2 in the placebo group required intervention with percutaneous nephrostomy in 1 and ureteroscopy and placement of Double-J® stent in the other. The mean clearance time for steinstrasse was higher in group 2 at 16.2 + 9.8 vs 13.44 + 8.4 days.

The average dose of analgesic used in group 1 was higher (median 2) than in group 2 (median 1), but was not statistically significant (p = 0.4). Five patients in group 1 needed admission for pain relief, 2 in the emergency setting and 3 in the ward. They received injectable diclofenac or pethidine. There were no adverse effects of shock wave lithotripsy and it was tolerated well with patients under sedation. Apart from 1 patient who had dizziness, there was no other complication that could be attributed to tamsulosin.

TABLE 1. *Baseline demographic and clinical characteristics of trial groups*

	Placebo Group	Tamsulosin Group
Mean pt age ± SD	42.3 ± 12.3	35.9 ± 7.8
No. sex (%):		
Male	24 (82.8)	22 (75.9)
Female	5 (17.2)	7 (24.1)
No. mm stone size (%):		
6–10	17 (58.6)	14 (48.3)
11–24	12 (41.4)	15 (51.7)
No. stone location (%):		
Calix	12 (41.4)	14 (48.2)
Pelvis	9 (31.0)	6 (20.7)
Upper ureter	6 (20.7)	5 (17.2)
Lower ureter	2 (6.9)	4 (13.8)

TABLE 2. *Effect of tamsulosin on stone clearance and analgesic dose*

	Primary Outcome: No. Stone Clearance (%)	Secondary Outcome: Median Analgesic Dose (range)
Tamsulosin group	28 (96.6)	1 (0–10)
Placebo group	23 (79.3)	2 (0–32)
Difference (95% CI)	17.3 (1.1–33.5)	0 (0–2)
p Value	0.04	0.3

DISCUSSION

Following the initial phase of stone disintegration in SWL, the final clearance of the fragments from the ureter is akin to the spontaneous passage of ureteral calculi. The expulsion rate for stones less than 5 mm is up to 98% and up to 53% for size 5 to 10 mm.[1] Therefore, fragment size is an important factor that determines the passage of stone through the ureterovesical junction, the narrowest part of the ureter. Spasm, edema or infection may hinder stone passage.[2,3] Ureteral colic, associated with stone, is the manifestation of the visceral pain that is referred to the somatic region corresponding to the spinal segments of the sympathetic supply of the ureter.[3] Increased intraluminal pressure due to calculus obstruction and the increased lactic acid production

TABLE 3. *Stone clearance stratified by size*

	No. Tamsulosin Group (%)	No. Placebo Group (%)	p Value for Treatment
Large stones (11–24 mm):			
Clearance	14 (93.3)	7 (58.3)	0.03
No clearance	1 (6.7)	5 (41.7)	
Small stones (6–10 mm):			
Clearance	14 (100.0)	16 (94.1)	0.35
No clearance	0	1 (5.9)	