ORIGINAL ARTICLE

Is Medical Expulsive Therapy an Option for Ureteral Calculi ?

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ABSTRACT

Objective — *To compare tamsulosin with simple observation in terms of lower ureteral stone expulsion.*

Study design — *Randomized controlled trial.*

Place & Duration of study — *Surgical C unit, Department of surgery, Khyber Teaching Hospital Peshawar, from February 2008 to January 2009.*

Methodology — *The patients were divided into two groups. Group A patients were offered medical expulsive therapy (tamsulosin) while group B patients treated with observation receiving analgesics only. Data regarding age, gender, stone expulsion rate and time, and analgesic requirement were collected and analyzed. Frequency and percentages were calculated for categorical variables while mean ± SD was used to express continuous variables. Chi square test and Student t test were used to compare categorical and numerical variables respectively.*

Results — *After randomization, 56 patients in group A and 55 patients in group B were analyzed. The mean age of patients in group A and B was 37.37 ± 7.51 years and 37.90 ± 10.34 years, respectively (p 0.756). The mean stone size was 6.39 ± 1.78 mm in group A compared to 6.47 ± 1.71 mm in group B (p 0.81). In tamsulosin group, for stone size of 5mm, 48 (86%) patients expelled the stone, while for the same stone size, expulsion noted in 30 (56%) patients in the observation group (p 0.001). The expulsion rate in group A and B, for stone size of more than 5 mm, was 91% and 38%, respectively (p < 0.001). The mean time taken for stone expulsion was 8.32 ± 2.73 days in group A and 12.23 ± 2.12 days in group B (p < 0.001). Patients taking tamsulosin experienced significantly less pain attacks compared to patients on observation therapy (p 0.017).*

Conclusion — *Alpha blocker (tamsulosin) is a safe and effective treatment modality for distal ureteral stones of appropriate size.*

Key words — *Ureteral stone, Tamsulosin, Ureter, Urinary tract infection.*

INTRODUCTION:

Ureteral stone has emerged as a global health issue. Almost 20% of urinary tract stones are found in the ureters with majority (70%) being located in the lower third of the ureter.[1] The life time risk of developing urinary calculi is between 5 and 12%, affecting more men compared to women.[2]

Various management options including, minimally invasive therapies (extracorporeal shock wave ithotripsy [ESWL], ureteroscopy) and watchful waiting lsupplemented by medical expulsive therapy (MET) exist for ureteric calculi. The choice of most appropriate modality of treatment depends on many factors such as location and size of the stone, patient's preference, and the expertise available.[3] The inherent complications of minimally invasive therapies are balanced by complications of failed expected treatment such as hydronephrosis, urinary tract infection and renal function derangement.[4]

The disease spectrum and its outcome is different in our part of the world due to various reasons such as the lack of advanced minimally invasive therapies, delay in diagnosis due to delay in investigation and less awareness. This in addition to the sparse local studies further compounds the problem.[5] Keeping these issues in mind and also the socioeconomic

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conditions of the majority of our patients this study was carried out. This study on one hand would provide local perspective of the issue, and on the other hand offer an additional treatment modality for a suitable group of patients having distal ureteral stones.

METHODOLOGY:

This study was conducted at surgical 'C' Unit, Department of Surgery, Khyber Teaching Hospital, Peshawar, from February 2008 to January 2009. This was a randomized controlled trial. The objective of the study was to compare the efficacy of tamsulosin with observation using only analgesics, in lower ureteral calculi in terms of stone passage. Approval for the study was obtained from the Ethics Committee of the hospital.

In this study, one hundred and sixty patients, presenting to outpatients department with clinical diagnosis (history and clinical examination) of ureteric colic due to ureteral calculi were included. Patients with age 18 years or older with a single unilateral stone in the lower segment of the ureter measuring less than 10 mm in the greatest dimension were included in the study. Patients with pregnancy or lactation, history of previous surgery on the ipsilateral ureter, solitary kidney, urinary tract infection, moderate or severe hydronephrosis, currently on alpha-blocker therapy, known allergy to tamsulosin, contraindications for non-steroidal anti-inflammatory agents (e.g., gastritis) or renal insufficiency, were excluded.

The diagnosis was confirmed with x-ray kidney-ureter-bladder (KUB), abdominal ultrasonography, intravenous urography (IVU), and computerized tomography scan (CT scan) where necessary. In addition investigations such as urine R/E, serum urea and creatinine were also carried out. Patients were selected through consecutive non-probability sampling and were divided into two groups A and B using lottery method. Patients in group A received diclofenac sodium and tamsulosin while patients in group B received diclofenac sodium only.

All patients in both the groups received a first treatment of diclofenac 75 mg by intramuscular injection, with a second dose after 30 minutes if necessary. If diclofenac gave inadequate pain relief, tramadol hydrochloride 100 mg by intravenous injection was given. If the pain resolved, the patient was enrolled in the study. Patients were explained the risks and benefits of the modality of treatment and an informed written consent was obtained.

All patients in the 2 groups received diclofenac sodium (50 mg, tablet) every 12 hours for 1 week and then diclofenac sodium injection (75 mg) as needed, up to a maximum of 2 times per day. Patients in group A (n=60) received a daily oral dose of tamsulosin (0.4 mg), while patients in group B (n=(60) received oral diclofenac sodium (50 mg) only. The study medications were discontinued after spontaneous stone expulsion, intervention, or at the end of the study period. Absences of stone expulsion at the end of the study or intervention before the end of the study due to uncontrollable pain or adverse events were considered failed therapy.

Follow-up visits were performed on a weekly basis. At the follow-up visit, every patient underwent urine analysis, serum creatinine measurement, a plain x-ray KUB, and abdominal ultrasonography. Also patients were asked if they had seen any stone passage during urination. Abdominal CT was performed for patients with radiolucent stones if the stone was not expulshed by the end of study. For patients with a stone-free ureter on the last imaging study but unnoticed stone expulsion, the date of last positive stone status was recorded. Patients who failed to spontaneously expel the stone during the study period or developed complication were offered alternative therapies in the form of ESWL, or ureteroscopy.

The efficacy of treatment was evaluated in terms of rate and time of stone passage, and frequency of pain attacks. Distal ureteral segment was defined as the part of ureter below the lower border of sacroiliac joint up to the uretero-vesical junction. Tamsulosin, an alpha receptor blocker, specifically active against á1-a and á1-d, found abundantly in the distal ureter was used as a relaxant of the ureteral smooth muscle.

The data were analyzed using SPSS version 15 for windows. Continuous variables such as age were presented with mean ± SD while categorical variables such as gender were expressed with frequency and percentages using 95% confidence interval. Student *t* test was used to compare the means of continuous variables while categorical variables were compared using Chi square or Fisher exact test, as appropriate. Probability equal to or less than 0.05 was considered statistically significant.

RESULTS:

A total of 120 patients were enrolled in the study. Due to failure to abide by the follow up protocol 4 The mean stone size was 6.39 ± 1.78 mm in group A compared to 6.47 ± 1.71 mm in group B, which was statistically insignificant (p 0.81). Data analysis

patients from group A and 5 patients from group B were dropped out. Therefore, a total of 56 patients in group A and 55 patients in group B were statistically analyzed.

The mean age of the patients in group A was 37.37 ± 7.51 years compared to 37.90 ± 10.34 years in group B. There were 30 (53.6%) males and 26 (46.4%) females in group A (male to female ratio 1.1:1) compared to 30 (54.5%) males and 25 (45.5%) females in group B (male to female ratio 1.2:1), as shown in Table I.

Table I: Baseline Patient Characteristics (n=111)

	Group A (n 56)	Group B (n 55)	p. value
Age (years)			**0.756**
Mean	37.37	7.90	
SD	7.51	10.34	
Gender			**0.652**
Male	30	30	
Female	26	25	
BMI (kg/m^2)			**0.475**
Mean	25.02	24.68	
SD	3.12	2.64	
Stone Size (mm)			**0.811**
Mean	6.39	6.47	
SD	1.78	1.71	
Stone laterality			**0.578**
Left	25	27	
Right	31	28	

BMI = Body mass index

regarding stone laterality showed that there were 31 (55%) patients with right sided stones and 25 (45%) patients with left sided stone in group A. In contrast 28 (51%) patients in group B had right while 27 (49%) had left sided ureteral stones.

In tamsulosin group, 48 (86%) patients expelled stones which were less than 5 mm, while for the same stone size expulsion noted in 30 (56%) patients in the observation group, which proved to be statistically significant (Table II). The expulsion rate in group A and B, for stone size of more than 5 mm, was 91% and 38%, respectively, again proving to be significant on statistical analysis.

The mean time taken for stone expulsion was 8.32 ± 2.73 days in group A and 12.23 ± 2.12 days in group B. The statistical difference was significant between the two groups (p < 0.001). Patients taking tamsulosin experienced less pain attacks compared to patients on observation therapy. The mean number of pain attacks in tamsulosin and observation groups was 1.32 ± 0.69 and 1.70 ± 0.97, respectively, proving to be statistically significant (p 0.01).

Table II: Comparison of Primary Outcome Measures

Outcome Measures	Group A (n 56)	Group B (n 55)	p value
Stone Expulsion Rate (= 5mm)			**0.001**
n (%)	48 (86)	30 (56)	
Stone Expulsion Rate (> 5 mm)			**< 0.001**
n (%)	51 (91)	21 (38)	
Stone Expulsion Time (Days)			**< 0.001**
Mean	8.32	12.23	
SD	2.73	2.12	
Number of Pain Attacks			**0.017**
Mean	1.32	1.70	
SD	0.69	0.97	

DISCUSSION:

The management of patients having ureteral caluculi has changed dramatically in this current era with minimal invasiveness being the primary focus of concern, so far selection of any treatment modality is concerned.[2] A variety of treatment options available for ureteral stones include, open ureterolithotomy, ureteroscopic extraction, extracorporeal shock wave lithotripsy and conservative management in the form of watchful waiting with or without adjuvant medical expulsive therapy.[6]

Conservative watchful waiting using simple analgesics is currently practiced, routinely supplemented with MET which has beneficial effects in the form of reduced analgesics requirement, decreasing colic attacks and increasing stone expulsion rate. The different drugs used in MET include á-blockers, calcium channel blockers and corticosteroids.[7-10] A recent study by Sigala and colleagues, studying the á-adrenoceptors in the ureter, demonstrated that á-1a adrenoceptor was the most common (and is expressed in all portions of the ureter), and that á-1d adrenoceptor was found in greater abundance in the distal ureter.[11] Alpha 1 antagonist (tamsulosin) decreases the frequency of peristaltic contractions by decreasing the resting tone and interference with ureteric contractions. This effect culminates in early stone passage, decreased colics, and therefore, decreased analgesic requirements.[12]

In this study statistically significant proportion of patients expelled ureteral stones in the tamsulosin group. This was the finding in patients with stone size less or more than 5 mm. This observation is corroborated by others.[13-15] In a comparative randomized controlled trial, however, alpha blockers were found to be more effective in stone expulsion for stone size of more than 5 mm but not for stone size less than 5mm, which contradicts our results.[1] Tamsulosin, in addition to abating lower urinary tract symptoms, also accelerates the expulsion of ureteral calculi.[16] The present study confirms that patients taking tamsulosin expelled the stones in significantly less time compared to patients taking analgesics only. There are others who affirm our results.[1,17] Alpha blockers cause a change in the pressure gradient above, around and below the obstructing stone, thereby facilitating and expediting its passage.[5]

It would be befitting to consider the shortcoming of the present study. The patients were not blinded which could have caused bias in the study results. The follow up period was short. The pain assessment and dose of analgesics was subjective, totally dependent on the patients' compliance.

CONCLUSIONS:

Tamsulosin is an effective and safe treatment modality for distal ureteral stones of less than 10 mm and may prove to be a useful adjunct to watchful waiting approach in these patients. It is therefore, recommended as a first line therapy in patients with suitable stone size and uncomplicated stone disease. This fact is even more applicable in our setting where cost and available facilities ultimately alter the treatment modality.

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