Original Research Article

Management of lower ureteral stones using Tamsulosin - A prospective study

Sasi Kumar Jonalagadda, Subith Kumar Kilari*, Srilakshmi, Ramakrishna Reddy YV

Mamata General and Mamata Super specialty Hospital, Khammam, Telangana, India
*Corresponding author email: **rahultej.pappala@gmail.com**

International Archives of Integrated Medicine, Vol. 6, Issue 1, January, 2019.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 01-01-2019 **Accepted on:** 05-01-2019
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Sasi Kumar Jonalagadda, Subith Kumar Kilari, Srilakshmi, Ramakrishna Reddy YV. Management of lower ureteral stones using Tamsulosin - A prospective study. IAIM, 2019; 6(1): 96-102.

Abstract

Introduction: It has been scientifically established that α1-adrenergic antagonists cause inhibition of the basal tone, peristaltic frequency, and contractions in the lower ureter. Earlier studies have shown promising results with Tamsulosin (α1-adrenergic antagonist) helping in spontaneous passage of Ureteral stones. Hence this prospective randomized double-blind placebo-controlled study is taken up to establish the real impact of Tamsulosin a specific alpha blocker (α1-adrenergic receptors) in expelling distal ureteral stones. This study aimed to include 80 patients with ureteral stones of less than 5 mm and more than 5 mm in size located in the distal ureter.

Materials and methods: In the Present study, informed consent was obtained from all 80 patients and the study was conducted after institutional ethical committee approval. Patients are randomized to two groups to receive Tamsulosin and placebo along with analgesics whenever required. Patients were followed up for a period of one month to study the stone expulsion rate, drug side effects and pain episodes.

Results: All 80 patients complied with prescribed treatment schedules except 4 patients in placebo group and 2 in study group who were lost to follow up. At the end of 4 weeks, stone expulsion was seen in 30 out of 38 (79% patients in study group and 20 patients out of 36 (56%) in placebo group. The stone expulsion time was shorter in the study group (6.2±3.2 days) and in 9.67±5.4 days for placebo group. No significant impact on the expulsion rate was seen in relation with age, gender and ureteric stones present either in right side or left side. The frequency of pain episodes was almost same and mild in both groups.

Conclusion: Tamsulosin is safe and effective drug to enhance spontaneous passage of smaller stones present in distal ureter.

Key words

Tamsulosin, Ureteric Stones, α1-adrenergic antagonist.

Introduction

Urolithiasis affects approximately 12% of the populace worldwide [1], affecting 1–5% of the inhabitants in Asia, 5–9% in Europe, 13% in North America, and 20% in Saudi Arabia [2]. Ureteric stones indicate around 20% of urolithiasis cases, from which roughly 70% are located in the lower third of the ureter and termed 'distal ureteric stones' (DUS) [1]. Urolithiasis is alone of the most common diseases of the urinary tract. The lifetime incidence of urinary stones 15%, and the pinnacle age of occurrence is at 30 years. Men are affected 2 to 3 times more seldom than women. Ureteral stones report for 20% of the calculi in urolithiasis and about 70% of ureteral stones are present in the distal third of the time of presentation. Ureteral stones provoke ureteral spasms that obstruct with stone expulsion [3].

Over the previous two decades, the management of ureteric stones had altered to a great extent, particularly after the introduction of shockwave lithotripsy (SWL) and ureteroscopy, as minimally invasive treatments. However, these treatments are costly and are not risk free [1].

Most of the studies were randomised and revealed that tamsulosin treatment significantly improvesthe expulsion rate of medium-sized (3–10 mm) distal ureteral stones [4]. Scientific studies have shown that an increased density of α-adrenergic receptors in the distal ureter and α1-adrenergic antagonists cause inhibition of the basal tone, peristaltic frequency, and contractions in the lower ureter [5, 6]. Several studies using specific α1-adrenergic antagonist for the treatment of lower ureteral stones have demonstrated good results [7-11]. Thus, tamsulosin represents a non-invasive and cost-effective alternative to interventional approaches [12, 13]. None of the studies, however, was performed in a double-blind, placebo-controlled fashion. The main objective of this trial was to evaluate the efficacy of medical expulsion therapy (MET) with tamsulosin for ureteral stones of < 5mm to >5mm in a randomised study.

Materials and methods

All the 80 patients in the present study gave an informed consent and the institutional ethical committee approved the study. Eighty (80) patients with normal renal function and non–contrast computed tomography (NCCT) showing single, radio-opaque, unilateral and less than 10 mm diameter stones located in the distal ureter were included in the study. Flank pain was the presenting symptom in all patients. Exclusion criteria included patients below 20 years of age, radiolucent-stones, Multiple stones, Hydronephrosis, Pregnancy, hypotension, UTI, earlier ureteral surgery or shock wave lithotripsy (SWL) and other major ailments. Patients taking calcium antagonist medications were also excluded. The sample size in each arm was calculated, based on earlier studies. Forty patients per group were finally randomized between study and placebo groups. Randomization data was made confidential and all the parameters were made to look alike. All patients were evaluated using X-rays of the kidney, ureter, and bladder (KUB), ultrasonography of urinary system in addition to biochemical, hematological and urine analysis. Weekly once all patients were evaluated using KUB films, ultrasonography of urinary system and NCCT, until passage of the stone or for a maximum duration of one month. Study Group (40 patients) received 0.4 mg Tamusulosin once daily and Control group received Placebo (40 patients). All the patients were advised to drink a minimum of two litres water daily and to get symptomatic therapy with pain killers whenever required for pain relief. Possible side effects of the medications were noted. Patients were asked to collect and to filter their urine for detecting calculus passage. Once the stone was detected in

urine (expelled out) medication was stopped and patient was advised to report back to the investigator. The number of pain episodes and the need for pain killers and time for spontaneous passage of the stone confirmed by the absence of radio-opaque calculi shadow on KUB was recorded. If stone was not expelled out within a month or appearance of uncontrolled pain, fever, increase in serum creatinine (>2 mg/dL) or severe hydronephrosis, the patient was relieved from study for getting appropriate treatment (**Figure - 1**).

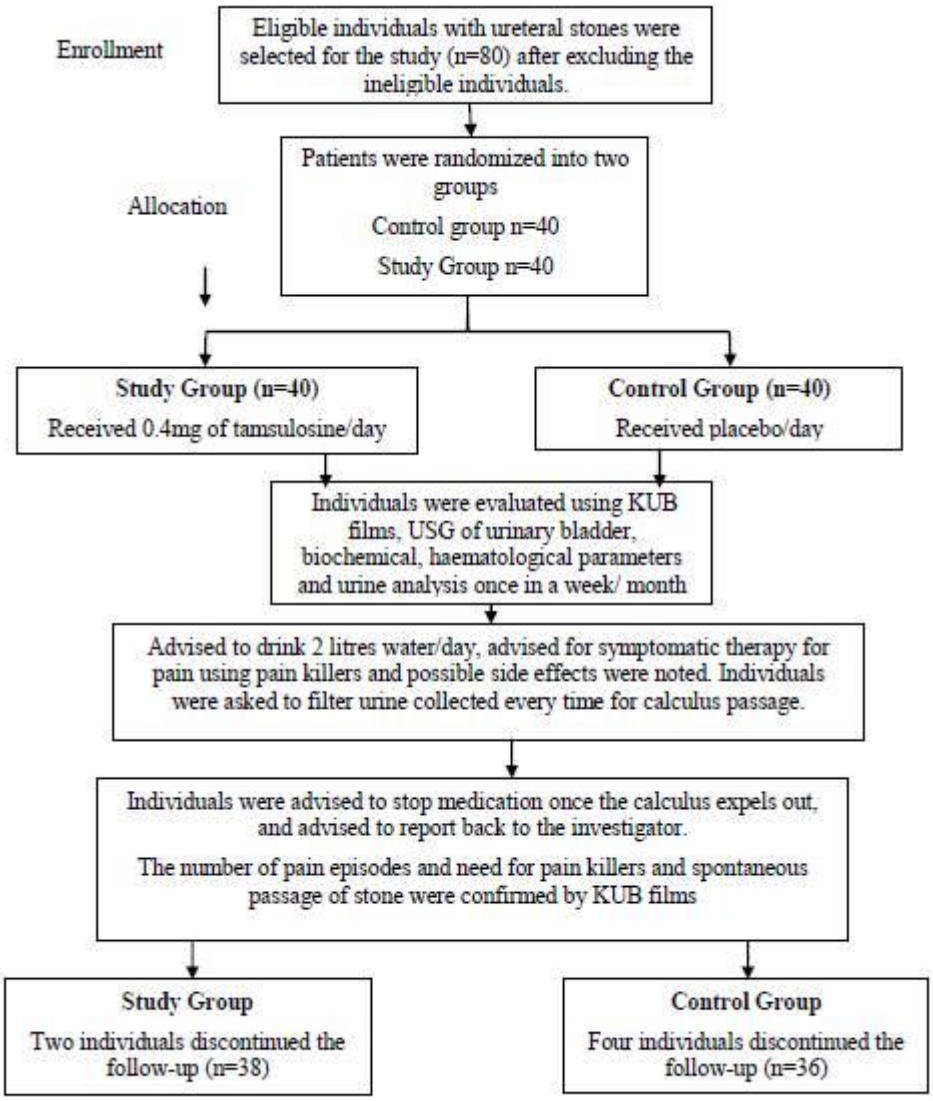

Figure1: Diagrammatic representation of the work done

Results

Out of 80 patients included in the study, 54 male and 26 were female. Two patients in study group and 4 in the placebo group discontinued treatment and lost to follow-up. The remaining patients completed their treatment and continued with the follow-up schedule. The distribution of 80 patients as per age, gender, location of calculi and stone size in both groups are shown. The distribution of the renal calculi in different age groups was as shown in the (**Table - 1**). Renal calculi distribution in age groups of <40 was Male 8 (62%) Female 5 (38%) in the study group, whereas, and >40 years Male 18 (67%) Female 9 (33%), Placebo Group has showed Male 8 (73%) Female 3 (37%) in < 40 years, whereas, > 40 years showed Male 20 (69%) and female 9 (31%), the renal calculi formation was

more in the age group >40 years. The formation of calculi was right in 24 and 21 cases were dominant compared to left in both the groups. The size of the renal calculi with <5 mm, and >5 mm were also studied (**Table - 2**).

Side effects: in the Study group, we have observed dizziness and headache-1, fatigue -1, postural hypotension-1 case and in placebo group 2 cases with fatigue were noted. The variability (characters) was 38/40 study group and 36/40 Placebo cases.

Table - 1: Distribution of patients according to Gender and age.

Age (Years)	Study Group			Placebo Group		
	Total	Gender		Total	Gender	
	40	Male (26)	Female (14)	40	Male (28)	Female (12)
21-30	5	4	1	4	3	1
31-40	8	4	4	7	5	2
41-50	13	8	5	12	8	4
51-60	10	7	3	11	8	3
>60	4	3	1	6	4	2

Table - 2: Distribution of patients according to Stone size.

Groups	Study Group			Placebo Group		
	Total	Gender		Total	Gender	
Stone Size	40	Male (26)	Female (14)	40	Male (28)	Female (12)
<5mm	25	17	8	22	13	9
>5mm	15	9	6	18	15	3

Table - 3: Distribution of patients according to Stone Location and rate of expulsion based on size of stone.

Stone locations/ Stone size	Study Group	Percentile	Placebo Group	Percentile
Right	18/24	75%	14/24	58%
Left	12/14	85%	6/12	50%
<5mm	20/25	80%	12/22	54.5%
>5mm	10/15	66.6%	8/18	44.4%

In the follow-up study, the study group showed spontaneous expulsion of stones in 30 out of 38 (79%) patients, whereas in placebo group it was in 20 patients out of 36 (56%). The stone expulsion time was 6.2±3.2 days in the Tamsulosin administered in study group compared to 9.67± 5.4 days for placebo groups (P=0.001). The difference in expulsion rate were also observed based on the size of the renal calculi, in study group and placebo group with size of <5mm expelled in 5±1.2 and 11±2.1days respectively were significant, and renal calculi with size of >5mm expelled are, 8±2.3 and 18±3.1 days respectively were significant. The frequency of pain episodes were comparable and mild in study group (32%), placebo groups (58%) without analgesics. Remaining study group (58%), placebo groups (62%) were on analgesics for painful episodes. Analysis of the impact factors like stone localization on the rate of spontaneous passage of the stones in both groups showed no significant difference. Out of 25 Study group patients with smaller stones (≤5mm) 20 patients (80%) showed spontaneous passage of the stones compared to 10 out of 15 (66.6%) patients with larger stones (>5 mm) (**Table - 3**).

Discussion

There were 54 men and 26 women with a mean age of 38.3±7.15 years. All patients had acute flank pain as the main complaint and single radio-opaque, unilateral stones with normal renal function without urinary tract infection (UTI). No patient received SWL before presentation. Since, the probability of spontaneous passage was 71%-98% with distal ureteral stones of less than 5 mm in diameter compared to 25%-51% with stones of more than 5mm size, patients were kept under observations pr the studies of Segura, et al., 1997 [14]. In view of the foreseen probable complications like UTI, hydronephrosis, and impairment of renal function 4 weeks waiting period was suggested for the spontaneous passage of the stone [15].

In a meta-analysis of 11 randomized clinical trials using α-blockers and conservative therapy for the treatment of ureteral stones, Parsons, et al. reported 44% more likely to spontaneously expel the stones, compared to patients receiving conservative therapy [16]. In this present study also patients receiving Tamsulosin had a significantly higher stone expulsion rate (80%) compared with the placebo group (54.5%) with stone size of <5mm and the expulsion rate (66.6%) in tamsulosin group compared to placebo (44.4%) for >5 mm stone size. However some studies have shown no significant advantage of using tamsulosin over conservative therapy alone in terms of stone expulsion rate at 6 weeks [17]. Probably varying stone characteristics must have influenced this difference in results. Several studies have shown that, compared to conservative therapy, tamsulosin reduces stone expulsion time [15, 18, 19]. The present study results using tamsulosin also showed decrease in the stone expulsion time 6.2±3.2 days compared to placebo group patients 9.67±5.4 days. Tamsulosin therapy has drastically reduced the frequency of episodes of renal colic requiring higher doses of pain killers, probably by decreasing the frequency of phasic peristaltic contractions in the ureter [15, 17, 18, 20, 21]. In this study also pain episodes were seen only in 32% of cases in study group compared to 58% of cases in placebo group of patients. The age, mean stone size, the number of stones and stone localization (left vs. right) were comparable in both groups. Out of all the variables analyzed in this study, the impact of stone size was seen clearly from the expulsion rates of spontaneous passage from distal ureteral stones and few studies have confirmed the same [16, 19]. Though Tekin, et al. emphasized that the ratio of spontaneous passage of the stones decreases in patients older than 50 years of age, other studies have shown no affect of age, gender, and stone laterality on the spontaneous passage of the stones [22].

During the course of the study period none of them developed fever, hydronephrosis, increase in serum creatinine (2 mg/dl) and intractable pain. In the Tamsulosin group, one patient had dizziness and headache, one patient experienced fatigue and one had mild postural hypotension. In the Placebo group two patients had fatigue. Side effects seen in this study were of mild nature and no patient required cessation of therapy. The frequency of side effects seen in the present series is similar and comparable to the published data [19, 20]. Studies of porpiglia F, et al., 2006 on randomized trials using alpha blockers for spontaneous passage of distal ureter stones, showed no difference, probably due to smaller stone size (<4 mm), non-availability of exact time of stone passage, incomplete randomization and higher exclusion rate after randomization [17, 23]. The difference of high statistical significance in favor of the tamsulosin group (P 0.001) in the present study may be due to the uniform distribution of stone size in both groups, available stone expulsion time in all 50 out of 74 patients with zero exclusion rate after randomization.

Conclusions

This randomized double-blind placebo-controlled study results have shown that tamsulosim is safe and effective to enhance spontaneous passage of distal ureteral stones with <5 mm or >5 mm. The stone expulsion rate was high and expulsion time and drug toxicity was low.

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