



## **Alfuzosin versus Tamsulozin in the Treatment of Patients with Distal Ureteral Calculus - Prospective, Randomised, Comparative Study**

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### **Abstract**

**Introduction:** *Ureteral calculus 4mm or smaller will usually pass spontaneously. Conservative medical treatment to be applied first. The simple waiting approach may result in complication. So, the simple watchful waiting approach is extended by pharmacotherapy. The drugs used as medical expulsive therapy are calcium channel blockers, alpha blockers, corticosteroids.*

**Aim:** *We evaluated and compared the efficacy of Tamsulozin and Alfuzosin in the medical treatment of symptomatic uncomplicated distal ureteric calculus.*

**Materials and Methods:** *A total of 150 patients with distal ureteric calculus of  $\leq 10\text{mm}$  were randomly divided into 3 groups. Group A patients ( $n=50$ ) received placebo ,Group B patients ( $n=50$ )received Tamsulozin 0.4mg/day, Group C patients ( $n=50$ ) received Alfuzosin 10mg/day. All patients received Diclofenac sodium 50 mg on demand. Follow up was done on weekly basis for 30 days.*

**Results:** *The mean calculus size was comparable in the 3 groups ( $6.98 \pm 1.6\text{mm}$ ,  $6.34 \pm 1.7\text{mm}$ ,  $6.7 \pm 1.5\text{mm}$ , respectively). The calculus expulsion rate was 32%, 72%, 74%. A statistically significant difference was noted between group A and B( $p=0.00006$ ) and between A and C ( $p=0.00003$ ), whereas no significant difference between B and C. The mean calculus expulsion time was ( $8.63 \pm 3.24$ ,  $7.75 \pm 3.14$ ,  $8.57 \pm 4.52$  days respectively). There was no statistical difference was observed between the groups(  $p=0.5961$ ).The analgesic requirement was  $6.60 \pm 1.82$  doses in group A,  $3.86 \pm 2.51$  doses in group B, and  $4.18 \pm 3.02$  in group C. Analgesic requirement was more in group A than in group B and C. No severe complications which require suspension of therapy due to drugs were found (2 patients retrograde ejaculation in group B , few days of dizziness 1 patient in group C).*

**Conclusion:** *The use of Tamsulozin or Alfuzosin as medical expulsive therapy for lower ureteric calculus proved to be safe and effective. Moreover, alfuzosin did not have any significant benefit over tamsulozin.*

**Keywords:** *Ureteric calculi;Tamsulozin; Alfuzosin.*

### **Introduction**

Most of the renal calculus become symptomatic when they fall into the ureter.The goal of the management is to achieve complete stone clearance with minimal morbidity. Treatments for

distal ureteral calculus include Watchful waiting, ESWL, Ureteroscopy, and open Ureterolithotomy. Ureteral calculus 4mm or smaller will usually pass spontaneously. It is generally believed that conservative medical treatment should be applied

first. If conservative treatment unsuccessful other treatments can be utilised<sup>1</sup>. The simple watchful waiting approach may result in complication such as infection of the urinary tract, renal function effects<sup>2</sup>. Therefore the watchful waiting approach is extended by using pharmacologic therapy, which can reduce symptoms and facilitate stone expulsion. Most of the studies evaluated the efficacy of Tamsulozin. Only very few studies described the use of Alfuzosin. So the present study was carried out to evaluate the efficacy of Alfuzosin and to compare the efficacy of Alfuzosin with Tamsulozin in the management of distal ureteric calculus.

### Aim and Objective

To evaluate and compare the efficacy of Alfuzosin with Tamsulozin in the management of distal ureteric calculus.

### Materials and Methods

Patients presented with history of ureteric colic to the urology department in the period between Jan 2015 to September 2016 were evaluated in the study. Informed consent were obtained from all the patients .Patients≥18 years of age with a single, unilateraluretral calculus of ≤ 10mmwere included in the study. The following patients were excluded from the study :(1) Age less than 18 years,(2)Pregnant and lactating women,(3) Stone more than 10mm,(4) Multiplestones,(5) Bilateral ureteral stones, (6) Solitary kidney,(7) severehydronephrosis,(8) Urinary tract infection,(9) History of previous surgery in the ipsilateral ureter,(10) Patients taking alpha blockers, calcium channel blocker, nitrates, (11)known allergy to tamsulozin or alfuzosin,(12) Renal insufficiency. Patients were segregated into 3 groups. Group A patients received placebo. Group B patients received Tamsulozin 0.4 mg/day. Group C Patients received Alfuzosin 10 mg/day. Diclofenac sodium 50 mg were given on demand. All the patients were evaluated with history, physical examination, urinalysis, urine culture sensitivity, complete blood count, serum urea,

creatinine measurements, X –ray KUB, abdominal ultrasonography, and CT KUB whenever necessary. Follow up visits were performed on a weekly basis .Patients received medications for 30 days.The study medications were discontinued after stone expulsion, intervention, or at the end of the 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. Factors age, sex, (Calculus passage rate-stone size), (calculus passage time- stone size), patients requiring intervention, and analgesic requirements were analysed.

### Statistical Analysis

Statistical analysis were done using SPSS, chi-square test, Multi range test-Turkey-HSD test, Levene“s test for equality of variance.

### Results

Total of 153 patients were enrolled in the study, and 150 patients completed the study (1 patient from each group dropped out).Group A (50 patients) consist of 31 male and 19 female (mean age 27±7.3), Group B (50 patients) consist of 30 male and 20 female (mean age 26.7±7.4), Group C (50 patients) 31 male and 19 female( mean age 25.4±5.2). Mean calculus size in Group A was 6.98±1.6mm, for Group B 34±1.7mm, for Group C 6.7±1.5mm. There were no statistically significant difference between the 3 groups in terms of sex, age, and in stone size.The base line characteristics are summarised in Table1

The results of the data analysis showed that 16 of 50 cases in Group A (32%), 36 of 50 cases in Group B (72%), and 37 of 50 cases in Group C (74%) expelled the stones by the end of the study. A significant statistical difference was noted between groups A and group B( $p=0.00006$ ) and between group A and C ( $p=0.00003$ ), whereas no significant difference between group B and group C. For stones ≤ 6mm,the expulsion rate was 84.6% in group A, 84% in group B,90% in group C. No statistically significant difference were observed between the 3 groups. For stones >6mm

the expulsion rate was 13.5 % in group A ,60% in group B and 63.3 % in group C. A significant statistical difference was noted between group A and group B and between group A and group C whereas no significant difference between group B and group C. There was a significant statistical difference was noted in each group in expulsion of  $\leq 6$  mm and  $> 6$ mm calculus (Group A= 0.000001, Group B= 0.00016 , Group C =0.0013). Only 8/58 (13.7 %) cases had failure in  $\leq 6$ mm groups, compared with 53/92 cases (57.6%) cases in  $> 6$ mm groups. This difference had high statistical significance in all the groups

**Table 1** Baseline characteristics

Variables	Group A Placebo group	Tamsulosin group	Group B Alfuzosin group	GroupC	p-value
No of patients	50	50	50		
Mean age	27 $\pm$ 7.3		26.7 $\pm$ 7.4	25.4 $\pm$ 5.2	ns
Sex (Male: Female)	1.6:1		1.5:1	1.6:1	ns
Stone size (mm)	6.98 $\pm$ 1.6		6.34 $\pm$ 1.7	6.7 $\pm$ 1.5	ns
Stone side (R:L)	1.08:1	1.08:1	1.6:1		ns

ns- non -significant

The mean calculus expulsion time was 8.63 $\pm$ 3.24 days in group A , 7.75 $\pm$ 3.14 days in group B , and 8.57  $\pm$ 4.52 days in group C. There was no statistical difference was observed between the groups (p=0.5961). The mean expulsion time of calculus size  $\leq 6$ mm was 7.34  $\pm$ 2.91 days in group A, 6.50 $\pm$  2.50 days in group B and 5.53  $\pm$  1.23 days in group C. There was no statistical difference was observed between the groups (p = 0.1155). The mean expulsion time of calculus size  $> 6$ mm was 11.40  $\pm$  2.07 days in group A, 10.25 $\pm$ 2.83 days in group B and 11.15 $\pm$  4.70 days in group C .There was no statistical difference was observed between the groups (p = 0.7844).

Patients who did not expel the stones were undergone ureteroscopy. Intervention requirement in group A, group B, and group C were 68%,28%, 26% respectively. Statistically significant difference was found (p =0.00001). Intervention requirement of  $\leq 6$ mm calculus in group A, group B ,and group C were 15.4 %, 16 %,10 % respectively. Intervention requirement of  $> 6$ mm calculus in group A, group B, and group C were 86.5%, 40 %, 37.7 %respectively. There was a high statistical significance was noted in the

intervention requirement between  $\leq 6$  mm and $> 6$  mm calculus in each group( p value group A =0.00001, group B= 0.00016, and group C =0.0134).

The analgesic requirement was 6.60  $\pm$  1.82 doses in group A, 3.86  $\pm$  2.51 doses in group B, and 4.18  $\pm$ 3.02 in group C. Analgesic requirement was more in group A than group B and group C. (Table 2)

No severe complications were found in the 3 groups. 2 patients in group B recorded retrograde ejaculation and 1 patient's complained few days of dizziness in group C, which did not require suspension of therapy

**Table 2** Expulsion rate, Intervention, Analgesic requirements

Variables	Group A	Group B	Group C	p-value
Expulsion rate(%)	32	72	74	0.00001
Expulsion rate (%)				
= 6mm		84.6	84	90
> 6 mm		13.5	60	63.3
Expulsion time (days)	8.63 $\pm$ 3.24	7.75 $\pm$ 3.14	8.57 $\pm$ 4.52	0.5691
Analgesics (doses)	6.60 $\pm$ 1.82	3.86 $\pm$ 2.51	4.18 $\pm$ 3.02	0.03
Intervention(%)	68	28	26	

## Discussion

Recently a great enthusiasm for adjuvant pharmacologic intervention to increase the expulsion rate and to reduce the pain attacks during conservative treatment. Normal ureteral peristalsis does not require outside autonomic input but, originate and propagate from pacemaker located in the minor calyces of renal collecting system.

Autonomic nervous system may exert some modulating effect on this process, but exact role is unclear. Parasympathetic system through muscarinic cholinergic receptor increase the frequency and force of contraction<sup>3</sup>. Atropine is a competitive antagonist of Acetylcholine. Atropine inhibit ureteral activity, but its effects are minimal and inconsistent<sup>4</sup>, thus providing little rational for its use in the treatment of ureteral calculus. The sympathetic system modulate ureteral activity through adrenergic receptors<sup>5</sup>. Alpha adrenergic receptor stimulate ureteral and renal pelvic

activity, Beta adrenergic receptor inhibit ureteral and renal pelvic activity<sup>6</sup>. The human ureter contain Alpha adrenergic receptor along its entire length, with highest concentration in distal ureter<sup>7,8</sup>. Alpha1d receptors are greater amounts than Alpha1a or Alpha1b in both proximal and distal ureter. In the absence of external ureteral compression or internal narrowing the width of the stone is the most significant factor affecting the likelihood of stone passage.

Medical expulsive therapy has been aimed at modifiable factors that can affect stone passage such as mucosal oedema, inflammation, ureteral spasm<sup>9</sup>. The drugs generally used in medical expulsive therapy are Calcium channel blockers, Alpha blockers, and corticosteroids<sup>10-14</sup>. Tamsulosin is adrenergic alpha receptor antagonist. It inhibits alpha 1A and alpha 1D subtype receptors<sup>15</sup>. Alfuzosin is another adrenergic alpha receptor antagonist, but no receptor selectivity. It has been widely used in the management of BPH. Most studies demonstrated favourable results to Tamsulosin in the distal ureteral calculus management. Only limited studies are available for Alfuzosin. The present study was designed to compare and the effectiveness of Tamsulosin and Alfuzosin in the management of distal ureteral calculus management.

Our results confirmed the efficacy of Tamsulosin and Alfuzosin for distal ureteric calculus. A total of 72% of patients taking Tamsulosin and 74% of taking Alfuzosin were found to expel their stones at the end of the study, but only 32% of patients taking placebo.

Tamsulozin and Alfuzosin also decrease the frequency of pain attacks with stone passage. Regarding the expulsion rate we found that Tamsulozin and Alfuzosin are of more value in the treatment of distal ureteric calculus of size > 6 mm than in the treatment of ≤ 6 mm size. We believe that the further studies using larger group are needed to confirm this findings. Alfusozin did not have any significant benefit over Tamsulozin. Only 1 out of 50 in the tamsulozin group

complained retrograde ejaculation, which may be due to shorter duration of treatment or possible decrease or absence of coitus due to ureteric colic. In medical management of BPH alfuzosin scores over tamsulozin in view of retrograde ejaculation. In this study we found that the efficacy of alfuzosin and tamsulozin is same, and alfuzosin has no advantage over tamsulozin in the management of distal ureteric calculus.

Many studies showed evidence that patients taking alfuzosin and tamsulozin expelled their stones in significantly fewer days than the placebo. But in this study we found that there is no statistically significant difference in expulsion time between the groups. Intervention requirements and analgesic requirements was more in the placebo group than the tamsulozin and alfuzosin group.

## Conclusion

The use of tamsulosin and alfuzosin as a medical expulsive therapy for distal ureteric calculus proved to be safe and effective. Moreover patients taking alfuzosin did not have any significant benefit over patients taking tamsulozin. So, it is better to choose cost effective alpha blockers between the two. These drugs can be safely used for the management of uncomplicated distal ureteric calculus before undertaking any intervention

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