



EFFECTIVENESS OF TAMSULOSIN AND ALFUZOSIN IN EXPULSION OF DISTAL URETERIC CALCULUS- A DOUBLE BLINDED RANDOMIZED CONTROL TRIAL

Nephrology

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ABSTRACT

Background: Medical therapy in concurrence with conservative approach is the current advance in treatment of ureteric stones which negates the adverse effect of invasive approaches. Tamsulosin and Alfuzosin are two important modalities used in medical expulsive therapy (MET).

Methodology: 100 patients were categorized into 2 groups in a 1:1 ratio where Group A Patients were given Alfuzosin 10 mg/day and Group B Patients were given Tamsulosin 0.4 mg/day. Analgesics 100 mg SR tablets were given on demand.

Results: Mean age group of the patient were in Group A was 25.4 years (range between 18-41 years) and in Group B was 26.8 years (range between 18- 45 years). Male:female ratio in Group A and Group B was found to be 1.6:1 and 1.5:1 respectively. Right side:Left side ratio in Alfuzosin (Group A) and Tamsulosin (Group B) was found to be 1.6:1 and 1.08:1 respectively. Mean calculus size was 6.7± 1.5 mm in Alfuzosin group and 6.34± 1.7mm in Tamsulosin. Patients had a mean colicky pain for about 1.7 days before presentation, duration ranged in between (1-5 days). In Alfuzosin (Group A) patients 37/50 (74%) of patient's calculi found to be expelled and 13/50 (26%) patients required interventions. In Tamsulosin (Group B) Patients 36/50 (72%) of calculus found to be expelled and 14/50 (28%) patients required interventions. No significant difference between groups with regards to expulsion of stones.

Conclusion: The use of Tamsulosin or Alfuzosin as medical expulsive therapy for ureteric stones in distal ureter was effective, as shown by the increased overall stone expulsion rate, reduced stone expulsion time and fewer pain episodes.

KEYWORDS

Alfuzosin, Tamsulosin, distal ureter, expulsion, calculus.

INTRODUCTION

Urinary tract stones are one of the most common urological conditions worldwide. The prevalence is estimated to be 1-5% in Asia, 5-9% in Europe and 13% in the USA.

Nephrolithiasis refers to the clinical picture due to formation of stones or calculi and passage in the urinary tract.(1) The recent advances in the management for distal ureteric calculi include watchful waiting, ESWL (Extracorporeal Shock Wave Lithotripsy), ureteroscopy, percutaneous approach and open ureterolithotomy etc. Although many of these procedures are minimally invasive, with increased expulsion and success rates and decreased pain and morbidity, conservative medical treatment is still the most preferable option for patients. (2,3) Watch and wait approach can be problematic which will not always result in stone passage and recurrent renal colic and is unpredictable leading to ureteric oedema and spasm.(4,5)

Most urinary stone related visits to the hospital are ureteral stones less than 5mm in diameter, majority of which expulse spontaneously.(6) For stones between 5 mm to 10 mm, medical expulsive therapy (MET) has been recommended to facilitate stone passage according to the 2016 European Association of Urology guidelines. In addition to the expulsive therapy, the stone size and location also affect the probability of spontaneous passage and the expulsion time of the ureteral stones.(3,7) The primary agents that have been evaluated for MET are calcium-channel blockers, steroids, NSAIDs and α 1-adrenergic receptor antagonists.(2)

Alpha(α)adrenergic receptors are present along the entire length of ureter but more concentrated in the lower intramural portion of the ureter (distal ureter) where it passes through the detrusor muscle.(8) The α 1-adrenoreceptor antagonists (α 1-blockers) inhibit contractions of the ureteric musculature, reduce the basal tone, and decrease the peristaltic frequency and colic pain, facilitating the expulsion of ureteric stones.(9)

Many studies have shown that Tamsulosin drug which acts as an antagonist more selectively at α 1A and α 1D adrenergic receptors have been used for effective expulsion of ureteric stones.(10,11) Alfuzosin drug, a non-selective α adrenergic receptor blocker and highly uroselective with a low incidence of adverse side effects and blood

pressure changes is recently introduced for expulsion of ureteric stones.(7) So this study was intended to compare the efficacy of Alpha blockers (Tamsulosin and Alfuzosin) for treatment of distal ureteral calculus and its spontaneous expulsion.

METHODOLOGY

We designed an open label double blinded Randomized Control Trial with 1:1 allocation among 100 the patients who presented to the Urological Department in Chettinad Medical College Chennai with a history suggestive of ureteric colic. The study was conducted for one and a half year from October 2017. Informed consent was obtained from the patient. Patients with renal colic- radiologically proven distal ureteric calculus of <10 mm were included in the study. Patients with urosepsis, presence of multiple calculi, severe hydronephrosis, known sensitivity to α blockers, concomitant treatment with α blockers, β blockers, calcium channel blockers, nitrates for any co-morbidities, pregnancy, previous surgery or endoscopic procedures in the urinary tract, known ureteral stricture, severe back pressure changes with perinephric collection, known history of alternative medicine intake are excluded from the study.

All the patients who presented with history suggestive of ureteric colic were evaluated with history & physical examination, urinalysis & urine culture sensitivity, complete blood count, renal function test, ultra sonogram KUB, X-ray KUB. Calculus size was measured based on X-ray KUB. X ray KUB was taken initially and after 28 days or after the calculus was using lot technique. The box for this technique contained 100 numbers (50 odd numbers and 50 even numbers). Every patient included in the study was allowed to pick a lot with numbers. Odd numbers were allotted in group A and even numbers in group B. Double blinding was done during the randomization and the treatment part. The investigator and the patient were not aware of the group or the drug they were receiving. A person other than the investigator who was not a part of research was assigned for allocation of patients to groups and distribution of drugs. Group A patients were given Alfuzosin 10 mg/day and Group B Patients were given Tamsulosin 0.4 mg/day till the expulsion of stone but not for more than 4 weeks (28 days). Analgesics were given on demand. The calculus passage time and rate was observed. Details regarding complications and reasons for interventions were noted.

All the data were entered in Microsoft excel and analysed using SPSS

version 16. Descriptive statistics of socio demographic and morbidity characteristics of the study sample was represented using frequencies & percentages for categorical data and mean & standard deviation for continuous data. Independent t test, Chi-square test and Fisher's exact test were used to test whether the characteristics of the study subjects in both groups were similar post randomization. Normality of the continuous variables was checked using Shapiro Wilk's test. A p value of < 0.05 was taken as significant for all analyses. Intention to treat method was used for analysis.

RESULTS

The mean age of the patients in the group A was 25.4 years with 66% of

the subjects in the age group of 21 – 30 years. The mean age of the patients in the group B was 26.8 years with 54% of the subjects in the age group of 21 – 30 years. There were almost 60% males and 40% females in both groups. The distribution of kidney stones was more on left side (57%) compared to right side (43%).The mean duration of colicky pain in Group A subjects was 1.78 days whereas in Group B was 1.66 days. The mean calculus size in Group A subjects was 6.78 mm whereas in Group B was 6.34 mm. There was no statistical significant difference between group A and group B with regards to age, gender distribution, distribution of stones in kidney, mean duration of colicky pain and mean calculus size. (Table 1)

Table 1: Baseline characteristics of Group A and Group B

		Group		Total	p value
		A (Alfuzosin)	B (Tamsulosin)		
Age Group	< 20 years	8(16%)	7(14%)	15(15%)	0.287*
	21-30 years	33(66%)	27(54%)	60(60%)	
	31-40 years	8(16%)	11(22%)	19(19%)	
	> 40 years	1(2%)	5(10%)	6(6%)	
Age	Mean ± S.D	25.42 ± 5.29	26.76 ± 7.43	26.09 ± 6.45	0.302#
Sex	Male	31 (62%)	30 (60%)	61 (61%)	0.837*
	Female	19 (38%)	20 (40%)	39 (39%)	
Ureteric Stone Side	Right	19 (38%)	24 (48%)	43 (43%)	0.312*
	Left	31 (62%)	26 (52%)	57 (57%)	
Duration of colicky pain	Mean±SD	1.78 ± 0.89	1.66 ± 0.82	1.72 ± 0.85	0.485#
Calculus size	Mean±SD	6.78 ± 1.58	6.34 ± 1.73	6.56 ± 1.65	0.188#

*Chi-square / Fischer's test; # Independent t test

Table 2: Comparison of outcome variables among Group A and Group B of study population

Group	OUTCOME		Chi sq test p value
	Expelled	Failure	
A	37 (74%)	13 (26%)	0.821
B	36 (72%)	14 (28%)	
Total	73 (73%)	27 (27%)	

37(74%) of the subjects in Group A, who had been on treatment with Alfuzosin and 36(72%) of the subjects in Group B who had been on treatment with Tamsulosin had a spontaneous expulsion of renal calculi. There was no statistical difference between the two groups regarding the expulsion of renal calculi.(Table 2)

Those who had failure in treatment with alpha blockers (26% in group A and 28% in group B) were given intervention with Ureterscopy.

Table 3: Comparison regarding treatment variables

	GROUP	MEAN	S.D.	't' test p value
Duration of treatment	A	10.54	5.73	0.651
	B	11.12	6.98	
Analgesic doses	A	4.18	3.02	0.56
	B	3.86	2.51	

The minimum duration of treatment in Group A and Group B was 3 days and maximum were 25 and 28 days respectively. The maximum dose required in Group A and Group B were 15 and 11 respectively. There was no statistical significance between two groups regarding mean duration of treatment and number of analgesic doses.(Table 3)

Among the 37 patients in group A and 36 in Group B, who had spontaneous expulsion of calculus with medical treatment, the mean days of expulsion of calculus in was 8.57 days and 7.75 days respectively There was no statistical difference between the two groups regarding the days required for expulsion of calculus.

Table 4: Distribution of the outcome of the subjects based on calculi size within the groups

Group	Calculus	Outcome		Chi sq test p value
		Expelled	Failure	
A	≤6 mm	17 (94.4%)	1 (5.6%)	< 0.001
	> 6 mm	20 (62.5%)	12 (37.5%)	
B	≤6 mm	24 (96%)	1 (4%)	< 0.001
	> 6 mm	12 (48%)	13 (52%)	

In group A 17(94.4%) of patients with calculus size ≤ 6mm had a treatment success. And in group B 24(96%) of patients with calculus size ≤6 mm had success. Within groups, the subjects who had calculus

size ≤ 6 mm had a significant spontaneous expulsion on treatment with alpha blockers.

DISCUSSION

100 patients were included in the study to compare the efficacy of Alpha blockers (Tamsulosin and Alfuzosin) for treatment of distal ureteral calculus and its spontaneous expulsion. Group A Patients were given Alfuzosin 10 mg/day and Group B Patients were given Tamsulosin 0.4 mg/day. Analgesics 100 mg SR tablets were given on demand. Among the study population, 37(74%) of the subjects in Group A who had been on treatment with Alfuzosin and 36(72%) of the subjects in Group B who had been on treatment with Tamsulosin had a spontaneous expulsion of renal calculi. This was similar to a randomized trial to compare the efficacy of alfuzosin with Tamsulosin in the treatment of lower ureteral stones.(12) Stone expulsion rate was 82% in Tamsulosin group, 70% in Alfuzosin group. The mean time for expulsion was 12.3 days for Tamsulosin group of patients and 14.5 days for Alfuzosin group of patients. The present study showed same pattern of expulsion of 8.5 days for Alfuzosin and 7.75 days for Tamsulosin. The study also showed no statistical difference between Tamsulosin and Alfuzosin which is evident by the current study also.

Many other studies–(7,11,1316) also showed similar results reinforcing the effect of alpha blockers in expulsion of stones<10 mm. A blockade of α1-receptors inhibits basal tone, reduces peristaltic amplitude and frequency there by reducing colic pain and induce an increase in the intra-ureteral pressure gradient around the stones that helps in stone expulsion.(9,13)

Patients taking Tamsulosin and Alfuzosin expelled the stones in significantly fewer days and needed less analgesic doses and there is no significant benefit of using one drug over the other. We believe that further studies using larger groups are needed to confirm these findings and to evaluate the effect of different variables such as age, sex, body mass index, location of the stone, and size of the stone, type of the stone and duration of pain on the stone expulsion rate. Need of other intervention or failure of Medical expulsive therapy should be evaluated in detail. Side effects regarding the usage of drugs were not studied in detail which is an important entity in success of medical therapy.

CONCLUSION

The use of Tamsulosin and Alfuzosin as a medical expulsive therapy for distal ureteric stones proved to be safe and effective as demonstrated by the increased stone expulsion rate, decreased expulsion time, and reduced pain attacks and decreased need for analgesics.

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