

EFFICACY OF TAMSULOSIN AND ALFUZOSIN IN MANAGEMENT OF DISTAL URETERAL STONES

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**ABSTRACT**

Introduction: Urinary tract calculi are the most frequent condition in urology clinics worldwide. The overall prevalence is about 5 % and lower urinary tract stones account for 70% among them. Medical expulsive therapy has been used to treat distal ureteric stone as it reduces symptoms and facilitates stone expulsion. The aim of this study is to evaluate and compare the efficacy of tamsulosin and alfuzosin as medical therapy in ureteric stones.

Materials and Methods: A total of 87 patients with distal ureteral stones of size ≤ 10 mm were randomly divided into 3 groups. Group A patients (n-30) received 0.4 mg of tamsulosin daily, group B patients (n-29) received 10 mg of alfuzosin daily and group C patients (n-28) received 75 mg of diclofenac sodium. Patients in all groups received diclofenac sodium for one week and then as required. Follow-up was done on a weekly basis for 4 weeks. The stone expulsion rate, time for stone expulsion, and side-effects were recorded in each group.

Results: The mean stone size (5.66, 5.79, 5.67) mm and age (29.1, 30.31, 29.4) were comparable in each group. The stone expulsion rate was 83.3%, 79.3%, and 50% in groups A, B, and C respectively. It showed that both the study groups (Group A and Group B) were effective than the control group (p-value 0.006 and 0.02 respectively) but there was no difference between tamsulosin and alfuzosin (p-value 0.69). The duration of stone expulsion was 11.5 days, 11.8 days, and 17.3 days for Group A, B, and C respectively. The drugs related side effects reported by patients were mild and transient.

Conclusion: The use of tamsulosin and alfuzosin for the medical treatment of ureteric stones proved to be safe and effective and neither did have any significant benefits over the other.

Keywords: alfuzosin; ureteral stones; tamsulosin

INTRODUCTION

Urinary tract calculi are the most frequent condition in urology clinics worldwide. The overall prevalence is about 7-13% in North America, 5-9% in Europe and 1-5% in Asia and the incidence of the disease seems to be increasing.¹ For small stone, observation and medical therapy is also one of the treatment options for management whereas, failure of the medical therapy and for larger stones requires either minimal invasive approach or open surgery.² The 2016 Guideline for Surgical Management of stones of The American Urological Association (AUA) recommend observation with medical therapy (alpha blockers) for distal ureteric stone size < 10 mm in diameter and symptoms that are well controlled.³

Medical expulsive therapy (MET) has been used as an adjunct to watchful waiting which is often unpredictable. Pharmacological measures are directed to reduce the edema of the ureter and ureteric spasm.⁴ Blocking of these receptors ($\alpha 1$ -blockers) which are dispersed along

the entire course of the ureter with the highest density in the distal ureter, causes relaxation of the ureteric musculature, decreases the basal tone, and inhibits the rate of peristalsis and colic, thus facilitating the passage of stones.^{4,5}

The main objective of this study was to analyze the effectiveness of tamsulosin and alfuzosin in the conservative management of uncomplicated, symptomatic distal ureteric stones.

MATERIALS AND METHODS

This prospective observational study was conducted between October 2016 to October 2017 at Chitwan Medical College, Bharatpur, Chitwan. The study protocol was approved by the institutional review board of the hospital. Symptomatic patients with distal ureteric calculi with a size of less than 10 mm in maximum diameter

were included in the study. Patients with urinary tract infection, single kidney, deranged kidney function tests at presentation, severe hydronephrosis, bilateral ureteric calculi, lactation or pregnancy, current use of α -blockers, calcium channel blockers or steroids, age less than 18 years, and any allergic reaction to the drugs were excluded from the study.

At the initial visit, a detailed history was taken, physical examination was done and urinalysis and serum creatinine levels were sent. All patients were evaluated with an ultrasound of the abdomen and pelvis and x-ray KUB and the size of the stone was calculated based on ultrasound abdomen and pelvis. CT abdomen was done in case of failure of medical therapy and if the pain did not resolve with the usual dose of medication or development of any complications.

Patients were divided into three groups. All the patients in three groups received diclofenac sodium (50 mg, tablet) two times a day for 7 days and then injection diclofenac sodium 50 mg as needed up to twice daily. Patients in Group A received 0.4 mg of Tamsulosin per day, patients in Group B received 10 mg of Alfuzosin per day and patients in Group C received 75 mg of Diclofenac sodium daily for 28 days or clinical and radiological evidence of spontaneous stone expulsion whichever is shorter. Failure of the spontaneous expulsion of the stone by the end of 28 days was regarded as treatment failure and patients were advised for surgical intervention.

All patients were followed on days 7, 14, 21, and 28. During each follow-up visit, patients were evaluated with serum creatinine level, urine analysis, a plain x-ray KUB and ultrasonography of the abdomen. Time to the spontaneous passage of stones and any side effects of the drugs were also noted.

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) for Windows version 19. ANOVA was used for continuous variables and the chi-square test was used for categorical variables. p -value <0.05 was considered clinically significant.

RESULTS

The study consisted of 87 patients. No significant differences were found in baseline characteristics of the 3 groups (Table 1).

The rate of spontaneous stone expulsion was highest in group A (83.3%) and lowest in group C (50%). Group A and group B had a statistically significant stone expulsion rate as compared to the control group (group C), p -value 0.006 and 0.02 respectively and there was no significant difference between Group A and Group B ($p=0.69$) in terms of rate of stone expulsion.

Table 1: Baseline patients' characteristics

Variables	Group A(n=30)	Group B(n=29)	Group C(n=28)
	Tamsulosin group	Alfuzosin group	Diclofenac sodium group
Mean age (years)	29.1 \pm 6.30	30.31 \pm 7.22	29.4 \pm 7.63
Sex (male:female)	1.3:1	1.6:1	1.5:1
Stone size (mm)	5.66 \pm 1.58	5.79 \pm 1.84	5.67 \pm 1.64

Similarly, a significant statistical difference was observed in terms of stone expulsion time between Group A and B as compared to Group C ($p=0.01$) (Table 2)

Table 2: Duration of spontaneous stone expulsion

	Group A	Group B	Group C
Mean stone expulsion time (days)	11.5 \pm 2.93	11.8 \pm 3.08	17.3 \pm 3.5
Weeks to stone passage			
1 st	11(36.6%)	9(31%)	2(7.1%)
2 nd	6(20%)	6(20.6%)	4(14.2%)
3 rd	5(16.6%)	6(20.6%)	6(21.3%)
4 th	3(10%)	2(6.8%)	2(7.1%)

Four patients in group A and two patients in group B developed retrograde ejaculation while postural hypotension was seen in two and one patients in Group A and Group B respectively. Two patients in group B also had nasal congestion as side effects, during the study period.

DISCUSSION

There are different methods for the treatment of the ureteral stones including ureterorenoscopy, percutaneous approaches, extracorporeal shockwave lithotripsy and open ureterolithotomy. Some believe that uncomplicated ureteral stones with maximum diameter less than 10 mm should be observed if they pass without treatment.

Size of the stone is directly proportional to the rate of spontaneous expulsion. Coll DM et al reported that the spontaneous stone expulsion rate was 87% for stones 1 mm in diameter, whereas it was 25% for stones more than 9mm.⁶ Ahmed et al in their study found that spontaneous stone passage rate was 88.6% for stones less than 5 mm and 67.9% for stones 5-10 mm. They also noticed that stone passage rate was 33.3%, 81.6% and 91.6% for stones located at upper, middle and lower ureter respectively and concluded that the stone passage rate is highly variable and depends on the size, site of the stone.⁷ On our study, the rate of spontaneous stone expulsion for distal ureteric stone with only observation

was 50% over a period of 4 weeks.

Tamsulosin and alfuzosin are the most commonly used for MET with majority of the studies showing statistically significant differences between the patients who use the drugs when compared to control group.

In a study by Sun, Yi et al, tamsulosin significantly increased the passage of distal ureteral stones and the stone passage rate was greater in those with stones greater than 6 mm in diameter.⁸ Similarly, Nuraj et al in their study found a significant difference between stone expulsion rate for patients using tamsulosin and placebo which were 90.4% and 71.2% respectively in distal ureteric calculi.⁹ Singal et al in their study observed stone expulsion rate of 72% in patients using tamsulosin, 68% with alfuzosin.¹⁰ These results were comparable to present study which showed the stone passage rate of 83.3% and 79.3% with tamsulosin and alfuzosin respectively compared to analgesic only which had stone passage rate of 50% only.

In contrast to above study, study done by Hermanns et al, the stone expulsion rate was about 86.7% and 88.9% for the patient receiving 0.4 mg tamsulosin and control group respectively.¹¹ Similarly, Pedro et al also demonstrated that there was no statistical difference in stone passage rate between alfuzosin and control group (73.5% and 77.1%), however, alfuzosin led to reduced patient discomfort during stone passage as well as reduced the time of lower ureteric stone expulsion.¹²

While comparing the mean time of stone expulsion in our study, we found duration of stone passage is 11.5 and 11.8 days in tamsulosin and alfuzosin group respectively which is shorter than 17.3 days in group receiving analgesic only. In a study done by Cha et al, the mean duration of stone expulsion was 7.83±5.08 days with 0.4 mg tamsulosin, 8.22±5.96 days with 10 mg alfuzosin compared to 13.56±6.49 days with tiroprium chloride¹³ which is similar to a study by Ahmed et al where the duration of stone passage is 7.52 days, 8.26 days and 13.9 days in patients receiving tamsulosin, alfuzosin and placebo respectively.¹⁴ In a study by Singal et al the mean stone passage time was 7.1 days, 6.8 days in patients receiving 0.4 mg tamsulosin, 10 mg alfuzosin respectively.¹⁰

In this study, 13% of patients in tamsulosin group and 17% of patients in alfuzosin group had mild adverse effects related to the medical therapy. The adverse events were mild and transient and required no withdrawal from the therapy. Pedro et al reported that alfuzosin was associated with adverse events in 12% of the patients while there were no side effects in control group¹² whereas Yilmaz et al and Arda et al reported no serious side effects with

alpha adrenergic blockers.^{15,16} Study by Ibrahim et al reported side effects in 13% of patients using tamsulosin and 15% of patients using alfuzosin with ureteric stones.¹⁷

CONCLUSION

Tamsulosin and alfuzosin are safe and equally effective options for medical expulsive therapy of ureteric stone in distal part of the ureter because both increase the stone passage rate, taking less time to stone expulsion.

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