

## To Evaluate the Efficacy of Tamsulosin in the Expulsion Rate and Expulsion Time of Lower Ureteral Calculi

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### Abstract

**Background:** There has been a paradigm shift in the management of ureteral calculi in the last decade with the introduction of new less invasive methods, such as ureterorenoscopy and extracorporeal shock wave lithotripsy. Recent studies have reported excellent results with medical expulsive therapy (MET) for distal ureteral calculi, both in terms of stone expulsion and control of ureteral colic pain. **Aims:** To evaluate the efficacy of tamsulosin in the expulsion rate and expulsion time of lower ureteral calculi and to note the effect of tamsulosin administration on frequency of analgesic use for relief of ureteral colic due to lower ureteral calculi. **Materials and methods:** This comparative study in 100 patients attending urology out patient with symptoms suggestive of ureteral calculi for a period of 2 years. All patients were received and evaluated on outpatient basis and underwent a standard evaluation of transabdominal renal ultrasonography. **Results:** Majority of patients in our study were in the age group between 30-40 years. There was no statistical significant difference in age and calculus size distribution in the two groups. The expulsion rate was significantly higher in the tamsulosin group. The expulsion time was significantly less in the tamsulosin group. The analgesic dose used by patient in the tamsulosin group was significantly lower. **Conclusion:** Tamsulosin proved to be safe and effective as demonstrated by the low incidence of side effects and the increased stone expulsion rate and reduced expulsion time.

**Keywords:** Urolithiasis, Tamsulosin, Expulsion time.

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### Introduction

Urolithiasis (urinary stones) is an ailment affecting 12% of the world population[1]. Symptomatic urolithiasis represents the most common condition observed by surgeons and urologists in an emergency setting. 70% of urolithiasis are located in the lower third of the ureter. The transport of stones from the kidney into the bladder and their movement through the ureter is accompanied by three basic factors as spasm of smooth muscles, submucosal oedema and pain. Determining factors for spontaneous passage of stones are their size, their configuration, and the smooth muscle activity of the ureters. In the transport of stones, the greatest obstacle is usually the terminal part of the ureters, mainly in the intramural 'detrusor tunnel'[2]. Most stones are 4 mm or smaller and pass spontaneously, although this is not without discomfort and expense to the patient. Ureteral calculi of any size are often associated with renal obstruction, and care must be taken to prevent irreversible damage to the kidney whether choosing expectant or active management. In the last 20 years, the introduction of new, minimally invasive procedures like percutaneous nephrolithotripsy (PCNL), flexible ureteroscopy, extracorporeal shock wave lithotripsy (ESWL), ureterorenoscopy (URS) and laser for ureteral stones have considerably changed the historical therapy for this disease with a substantial increment in treatment costs.

Pharmacologically it is possible to treat the possible causes of stone retention such as oedema, ureteral spasm and infection, trying to

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favour its expulsion by using drugs such as steroids, calcium antagonists and glyceryl trinitrate. Currently alpha 1-adrenergic receptor antagonists represent the treatment of choice for lower urinary tract symptoms as shown in many randomized controlled clinical trials as well as in several case studies[2]. Further studies have also revealed alpha 1-adrenergic receptors in ureteral smooth muscle cells was significantly higher than other adrenergic receptors. Furthermore, alpha 1-adrenergic antagonists have proved to inhibit basal tone, peristaltic frequency and ureteral contractions even in the intramural tract. The study is taken up to assess the possible role of the combined alpha 1a and alpha 1d selective antagonist tamsulosin for facilitating the spontaneous expulsion of lower ureteral stones.

### Materials and Methods

This study included consecutive one hundred patients attending urology out patient department in Osmania general hospital with symptoms suggestive of Ureteral Calculi between July 2019 to June 2021. All patients were received and evaluated on outpatient basis and underwent a standard evaluation of transabdominal renal ultrasonography. The patient would be considered for study only if the stone would be located in the distal ureter.

### Inclusion criteria

All patients evaluated in Osmania General Hospital with colic due to radiologically proven distal ureteral stones less than or equal to 10 mm and who are managed conservatively.

### Exclusion criteria

Stone larger than 10 mm, Clinical and laboratory signs of urinary tract infections (UTIs), Severe hydronephrosis on ultrasound

examination ( gross pelvicalyceal dilatation with parenchymal thinning), Co-morbid conditions such as diabetes, alteration in renal parameters (serum creatinine and blood urea), Previous history or ureteral manipulation and/or surgery, Multiple ureteral stones, Known sensitivity to alpha blockers AND Pregnancy.

**Experimental prospective study**

The study included 100 patients who were selected using purposive sampling technique. The patients were divided into two groups.

- A. Patients with ureteral colic would receive diclofenac ( 50/75 mg) orally/ parenterally as needed for pain.
- B. Same therapy plus tamsulosin(0.4 mg/daily) orally.

The duration of trial was until expulsion of the stone, but no longer than 2 weeks.

**Outcome measures**

1. Expulsion rate: Stone expelled or not.
2. Expulsion time: If expelled, time to expulsion from the commencement of therapy.
3. Number of times/ cumulative dose of diclofenac administered.

Objective documentation of stone expulsion was done based on follow-up renal ultrasonography. Patients who did not pass the stone spontaneously were referred for intervention (URS, ureteric stent insertion, ESWL). Collected data was analyzed with Student’s t test and Chi-square test.

**Results**

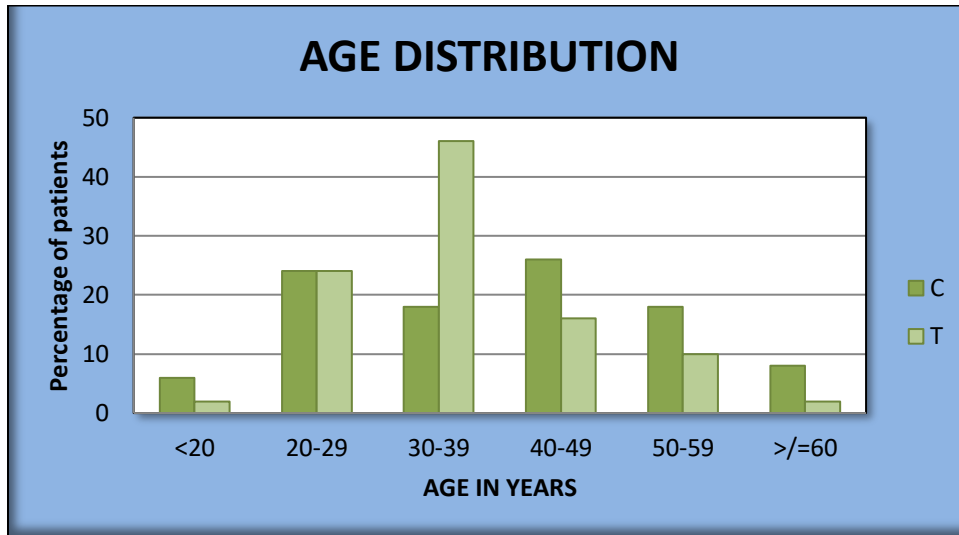


Fig. 1: Age distribution in present study

The mean age in control arm [C] was 38.72 years while the mean age in tamsulosin arm [T] was 35.48 years with standard deviation

of 13.735 and 9.840. The p value was 0.178 and therefore, no significant difference in age groups was present.

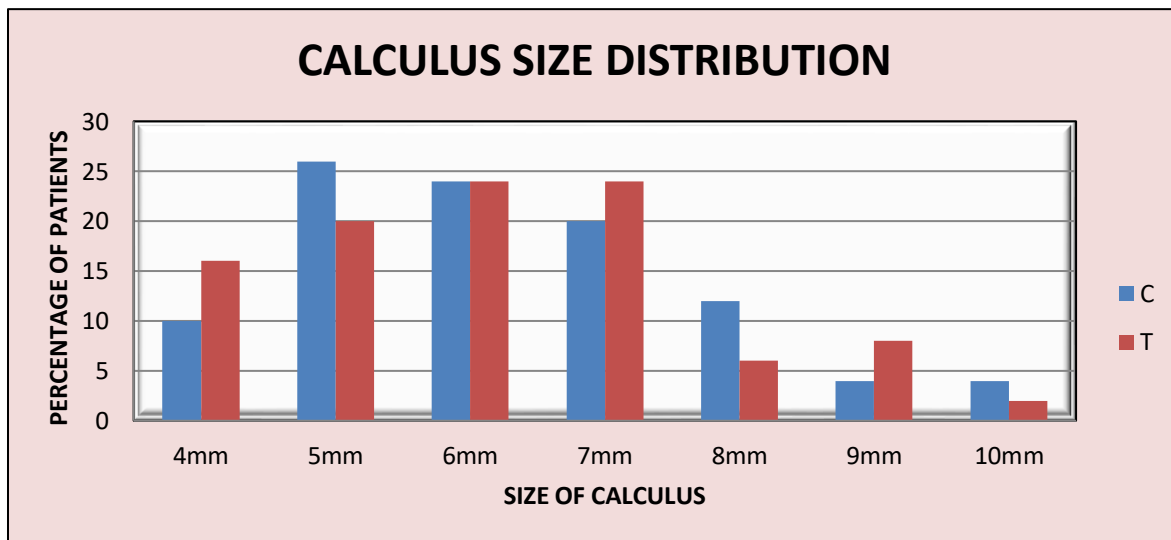


Fig. 2: Calculus size distribution

The mean calculus size in the control arm [C] was 6.26 mm and that in the tamsulosin arm [T] was 6.16 mm with standard deviation of

1.53 and 1.543 respectively. The p value was 0.745 and hence not significant

**Table 1: Calculus side distribution**

		Group		Total
		C	T	
Side	Left	24 48.0%	29 58.0%	53 53.0%
	Right	26 52.0%	21 42.0%	47 47.0%
Total		50 100.0%	50 100.0%	100 100.0%

$\chi^2 = 1.004, p=0.316, NS$

In the control arm [C], 48% of the calculi were located on the left side while 52% were on the right side. In the tamsulosin arm [T], 58% of the calculi were located on the left side while 42% were on the right side. In total, 53% of the calculi were on the left side and

47% were on the right. The p value was 0.316 and hence not significant.

**Table 2: Expulsion Rate**

		Group		Total
		C	T	
EXPL	No	31 62.0%	7 14.0%	38 38.0%
	Yes	19 38.0%	43 86.0%	62 62.0%
Total		50 100.0%	50 100.0%	100 100.0%

$\chi^2 = 24.448, p=0.000, HS$

In our study, 19 out of 50 patients in the control arm expelled the lower ureteral calculus within 2 weeks from the time of diagnosis, whereas 31 patients did not, with expulsion rate of 38%. In stark

contrast, 43 out of 50 patients in the tamsulosin arm spontaneously expelled the calculus with expulsion rate of 86%. The p value of this parameter was (<0.001) which was highly significant.

**Table 3: Time to expulsion in days**

Group	N	Mean	Std. Deviation	Median	
C	19	6.68	2.335	7.00	$t = 4.673, p=0.00$ HS
T	43	3.95	2.023	4.00	
Total	62	4.79	2.457	4.00	

The mean time taken for stone expulsion (in those who expelled) in the control arm was 6.68 days, whereas it was 3.95 days in the

tamsulosin arm. The p value was 0.000 (<0.001) which is highly significant.

**Table 4: Analgesic dose**

Group	N	Mean	Std. Deviation	Median	
C	50	903.00	289.336	1000.00	$t = 11.67, p=0.000,$ HS
T	50	285.00	237.386	200.00	
Total	100	594.00	407.151	600.00	

The mean analgesic dose consumed by a patient in the control arm was 903 mg, while it was 285 mg by a patient in the tamsulosin arm. The p value was 0.000 (<0.001) which is highly significant.

symptoms and/ or stones are small. Recently, use of the watchful waiting approach has been extended by using pharmacological therapy, which can reduce symptoms and facilitate stone expulsion. The likelihood of ureteral stone spontaneous passage essentially depends on stone size and site, the internal anatomical structure of the ureter and a history of spontaneous expulsion, which are unmodifiable factors. The possible causes of stone retention are spasm, edema and ureteral infection, which are modifiable factors. The goals of medical conservative therapy are to prevent modifiable factors and expulsion rate and time to expulsion and control painful symptoms until stone expulsion. In this study, we used the selective alpha-1a blocker, tamsulosin to evaluate the efficacy of medical expulsive therapy in lower ureteral calculi less than or equal to 10 mm.

**Discussion**

Urinary stone disease is a common condition affecting up to 12% of the population. Furthermore its incidence is growing. Ureteral stones occupy an important place in daily urological practice, and clinicians are frequently asked to choose adequate treatment. The efficacy of mini-invasive therapies, such as extracorporeal shock wave lithotripsy and ureteroscopy, has been proven by several studies. Nevertheless these techniques are not risk-free, are problematic and are quite expensive. On the other hand, a watchful waiting approach can be used in a large number of cases, as demonstrated by several studies that revealed spontaneous passage rates of up to 98% for small distal ureteral stones. Moreover, even the simple watchful waiting approach can result in complications, such as infection of the urinary tract, hydronephrosis and renal function effects. Therefore, it is difficult to choose between mini-invasive therapies and a watchful-waiting approach, especially when patients report few

There was no statistical significant difference in the age distribution or the size of the calculus in the two groups. Mean stone size was 6.21 mm which was in the similar range found in most studies.

The expulsion rate in the tamsulosin group in the present study was 86% which was in concurrence with other studies<sup>3,4,5,6</sup>. The mean

time to expulsion in the tamsulosin group in the present study was 3.95 days which was in comparable with and shorter than in Dellabella study[4] (4.4 days) and Autorino study[5] (4.8 days). The frequency of analgesic use was significantly reduced in the tamsulosin group in the present study (285 v 903 mg) which was in concurrence with other studies. However, there is considerable

variation in the absolute value of the analgesic dose which maybe due to various factors like difference in the standard dose available and patient's threshold for pain. There were no significant side effects in either group which confirmed the clinical profile of tamsulosin and diclofenac as considerably safe and convenient.

**Table 5: Comparison of outcome parameters**

Study	Expulsion Rate	Expulsion Time	Analgesic Dose
Cervenakov[3]	80.1%	—	—
Dellabella[4]	90%	4.4 days	P=0.003
Autorino[5]	88%	4.8 days	P=0.003
Porpiglia[6]	60%	7.7 days	27.3 mg
Our study	86%	3.95 days	285 mg P< 0.001

Therefore, it is possible to suggest that the effect of tamsulosin on the obstructed ureter is to induce an increase in the intraureteral pressure gradient around the stone, that is an increase in the urine bolus above the stone ( and consequently an increase in intraureteral pressure above the stone) as well as decreased peristalsis below the ureter (and consequently a decrease in intraureteral pressure below the stone) in association with the decrease in basal and micturition pressures even at the bladder neck. For these reasons there would be a stronger urge to expel the stone. Furthermore, the decreased frequency of phasic peristaltic contractions in the obstructed ureteral tract induced by tamsulosin might determine a decrease in or the absence of the algogenic stimulus, as in our study.

Corticosteroid drug in association with tamsulosin seemed to induce more rapid stone expulsion. In addition, tamsulosin alone as MET (medical expulsive therapy) for distal ureteral calculi had excellent expulsive effectiveness[7,8,9].

Alfa1-blockers decreased the number of ureteral colic episodes and the intensity of pain during spontaneous passage at the lower ureteral calculi. Also, it was beneficial to patients' quality of life[10,11].

#### Conclusion

The results of this study have shown a potentially important role of tamsulosin for conservative expulsive therapy of lower ureteral stones, broadening pharmacological indications rather than endoscopic treatments for the resolution of this disease. Obviously further studies with larger number of cases are necessary to validate these promising and statistically significant results. The comparison with minimally invasive procedures in terms of cost and efficacy was useful, highlighting a predominant role of first line pharmacological treatment, which can be easily be provided in an outpatient setting and not only at large, technologically advanced, special centers. The drug, tamsulosin proved to be safe and effective as demonstrated by the low incidence of side effects and the increased stone expulsion rate and reduced expulsion time. Moreover, medical expulsive therapy with tamsulosin considerably decreased the analgesic use thereby reducing additional need for pain relief and served as an effective bridge between watch-and-wait management and surgical intervention.

**Conflict of Interest: Nil**

**Source of support: Nil**

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