

# Comparison of Tamsulosin versus Tadalafil as an Effective Expulsive Treatment for Distal Ureteral Stones – A Prospective Comparative Study

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## Abstract

**Introduction:** The increasing prevalence of ureteric stone is a matter of concern in this era and it may be linked to improved quality of life. Medical expulsive therapy, including alpha-blockers, steroids, and calcium channel blockers, has been extensively studied for improving the rate of stone passage in patients who do not require immediate urologic intervention.

**Aim:** The aim of this study is to compare the efficacy of tamsulosin and tadalafil in expulsive treatment for distal ureteral stones.

**Materials and Methods:** This was a prospective comparative study included 120 adult patients (>18 years of age) presenting with distal ureteric stones were randomized into 60 patients with tamsulosin 0.4 mg once daily (Group A) or 60 patients with tadalafil 10 mg once daily (Group B) treatment. Therapy was given for a maximum of 4 weeks.

**Results:** About 85% of study patients had a size between 5 mm and 7 mm and 18 patients had size between 8 mm and 10 mm. There was no statistical difference noted in the pain duration and analgesic usage of both groups. In Group A, 67% of patients had expulsion of stones; in Group B, 63% of patients had expulsion of stones. About 90% of patients in 40 cases of expelled stones are in <5 days in Group A and 89% of patients 38 cases of expelled stones are in <5 days in Group B. There was no statistical difference noted between both groups.

**Conclusion:** Tamsulosin and tadalafil have shown similar expulsion rate. Both of them simultaneously provides better pain control and significantly lower the needs for analgesia.

**Key words:** Medical expulsive therapy, Tadalafil, Tamsulosin

## INTRODUCTION

Urolithiasis is a major health problem worldwide with increasing incidence and prevalence.<sup>[1]</sup> When ureteral stones are diagnosed, the management may consist of observation, shockwave lithotripsy, or ureteroscopy, depending on the clinical situation. The probability of spontaneous stone passage decreases with increasing stone size and location above the distal ureter.<sup>[2,3]</sup>

Determining the proper treatment approach involves the size, localization, and composition of the stone, severity of obstruction, symptoms, and anatomy of the urinary system. Medical expulsive therapy (MET) has now become an established modality of treatment and it involves the use of various drugs acting on ureter by different mechanisms. MET has a proven role to promote stone passage and reduce the need for minimally invasive surgery.

MET, including alpha-blockers, steroids, and calcium channel blockers, has been extensively studied for improving the rate of stone passage in patients who do not require immediate urologic intervention.<sup>[4-6]</sup>

Tamsulosin, a selective alpha-blocker with equal affinity for both  $\alpha$ -1A and  $\alpha$ -1D receptors, has a proven role in MET in increasing the stone expulsion rate and decreasing

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expulsion time. Tadalafil has emerged, which acts on nitric oxide/cyclic guanosine monophosphate (cGMP) signaling pathway of smooth muscles, resulting in increased levels of cGMP, and causing ureteric relaxation. Due to its smooth muscle relaxation property, tadalafil received the Food and Drug Administration (FDA) approval for use in lower urinary tract symptoms with benign prostatic hyperplasia and erectile dysfunction. It also received the FDA approval for use in pulmonary arterial hypertension for both men and women.<sup>[7,8]</sup>

### Aim

The aim of this study is to compare the efficacy of tamsulosin and tadalafil in expulsive treatment for distal ureteral stones.

## MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Urology at Tirunelveli Medical College Hospital for 1 year from 2017 to 2018. After taking written informed consent, patients aged 18 years with a ureteral stone of 5–10 mm in size in the greatest dimension situated below the common iliac vessels as diagnosed by non-contrast computed tomography (CT) or ultrasonography kidney, ureter, and bladder (KUB) were included in this study. Patients with fever, hydronephrosis, acute or chronic renal insufficiency, multiple ureteral stones, open surgery or endoscopic interventions, diabetes, peptic ulcer, or concomitant treatment with b-blockers, calcium antagonists, or nitrates; pregnant or lactating mothers; or who demand immediate intervention were excluded from the study. A total of 120 patients were enrolled in the study. They were divided into 2 groups randomly into Group A and Group B. Group A were given tamsulosin 0.4 mg once daily and Group B was given tadalafil 10 mg once daily, continued until stone expulsion or maximum of 4 weeks. Each enrolled patient was assessed by physical examination, serum creatinine level, urine culture, ultrasonography, and non-contrast CT of the KUB region as needed. The primary endpoint studied was the stone expulsion rate.

## RESULTS

In this study, 120 patients were divided into two groups, Group A tamsulosin 0.4 mg once daily and Group B was given tadalafil 10 mg once daily. The mean age of the study patients was  $36.42 \pm 9.68$  years, 56 male patients and 64 female patients were included in the study. No statistical difference was observed in patients demographic characters. There was no significant difference observed in the uric acid level in both groups. No statistical difference noted in the site of the stones, 68 patients had it in lower

ureteral (UR) and followed by 42 patients in vesicoureteric junction [Tables 1 and 2].

About 85% of study patients had a size between 5 and 7 and 18 patients had size between 8 and 10. There was no statistical difference observed between groups [Table 3].

About 52% of patients had the stone in the right side, there was no statistical difference noted between groups [Table 4].

There was no statistical difference noted in the pain duration and analgesic usage of both groups [Table 5].

In Group A, 67% of patients had expulsion of stones; in Group B, 63% of patients had expulsion of stones. About 90% of patients in 40 cases of expelled stones are in <5 days in Group A and 89% of patients 38 cases of expelled stones are in <5 days in Group B. There was no statistical difference noted between both groups [Table 6]. In Group A, 2 patients had body ache, 2 patients had headache, and 3 patients had giddiness. In Group B,

**Table 1: Crosstabulation of uric acid level**

Group	Uric acid		Total	P value
	Normal	Elevated		
Tamsulosin	42	18	60	0.559
Tadalafil	46	14	60	
Total	88	32	120	

**Table 2: Crosstabulation of site**

Group	Site			Total	P value
	Lower UR	Vesicoureteric junction	Middle UR		
Tamsulosin	36	20	4	60	0.999
Tadalafil	32	22	6	60	
Total	68	42	10	120	

**Table 3: Crosstabulation of size**

Group	Size		Total	P value
	5–7 mm	8–10 mm		
Tamsulosin	50	10	60	0.718
Tadalafil	52	8	60	
Total	102	18	120	

**Table 4: Crosstabulation of side**

Group	Side		Total	P value
	Right	Left		
Tamsulosin	32	28	60	0.796
Tadalafil	30	30	60	
Total	62	58	120	

**Table 5: Crosstabulation of pain**

Group	Pain		Total	P value
	<1 week	>1 week		
Tamsulosin	26	34	60	0.795
Tadalafil	28	32	60	
Total	54	66	120	

**Table 6: Crosstabulation of expulsion days**

Group	Days		Total	P value
	<5 days	>5 days		
Tamsulosin	36	4	40	0.957
Tadalafil	34	4	38	
Total	70	8	78	

4 patients had headache, 2 patients had weakness, and 1 painful erection. There was no statistical difference noted between groups.

## DISCUSSION

The natural course of ureteral stones without treatment must be balanced against the relatively limited risks of treatment that is now possible with nonsurgical techniques. Management of ureteral stones depends on the type, size, location, number and structure of the stone, and presence of symptoms. The presence of ureteral spasm, mucosal edema or inflammation, and ureteral anatomy also influence stone expulsion.<sup>[9,10]</sup>

The management of patients with ureteral calculi has changed dramatically in the current era with a conservative approach being the primary focus, which brings the patient minimum morbidity. Conservative nonsurgical approaches are usually instituted in the treatment plan of distal ureteral stone of size 5–10 mm as they are less likely to pass spontaneously.<sup>[10]</sup>

According to earlier studies, the expulsion rate of distal ureteric stone by watchful waiting is 25–54% with mean expulsion time >10 days and associated with high analgesic requirement even for stones <5 mm. To improve the expulsion rate and reduce analgesic requirements, medical therapy is considered for distal ureteral stones.<sup>[11,12]</sup>

The first high-quality trial was reported by Hermanns *et al.*<sup>[13]</sup> in 2009. They evaluated the expulsion rate of single distal ureteral stones 7 mm confirmed by CT. Ninety participants were randomized between tamsulosin and placebo groups. The mean stone the size was 4.1 and 3.8 mm, respectively. The stone expulsion rate did not differ between the tamsulosin (86.7%) and placebo (88.9%)

groups. The only reported advantage of tamsulosin was the decreased analgesic requirement until stone expulsion.

Phosphodiesterase inhibitors (PDEi) are a class of drugs that inhibit the breakdown of cyclic adenosine monophosphate and cGMP, enhancing smooth muscle relaxation. Therefore, PDEi may be able to decrease ureteral spasm and facilitate stone passage. Tadalafil is a selective phosphodiesterase 5-inhibitor (PDE5i) and due to its smooth muscle relaxation property, tadalafil.<sup>[14,15]</sup>

A ureteral stone usually causes severe colicky pain as a result of an increase in intraurethral pressure above the site of ureteral obstruction. At present, nonsteroidal anti-inflammatory drugs and antispasmodic drugs are generally used for relieving the pain caused by acute ureteral obstruction. Tamsulosin and tadalafil might reduce the colicky episodes, hence analgesic requirement and hospital visits by relaxing the ureteral smooth muscles and early stone expulsion.<sup>[15,2]</sup>

## CONCLUSION

Tamsulosin and tadalafil have shown similar expulsion rates. Both of them simultaneously provide better pain control and significantly lower the needs for analgesia. As  $\alpha 1$  adrenoreceptor antagonist (tamsulosin) and PDE5i (tadalafil) act through different pathways, combined therapy can further aid in distinctiveness, uniformity, and stability expulsion.

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