

A COMPARATIVE STUDY OF EFFICACY OF TAMSULOSIN PLUS NIFEDIPINE VERSUS TAMSULOSIN PLUS TADALAFIL AS MEDICAL EXPULSIVE THERAPY OF DISTAL URETERIC STONES

Urology

Dr M Abrar Ahmed*

Senior Resident, Department of General Surgery, Shri Atal Bihari Vajpayee Medical College and Research Institution, Bangalore, Karnataka, India. *Corresponding Author

Dr Vijay Anand

Assistant Professor, Department of General Surgery, SMSR, Sharda University, Greater Noida, Uttar Pradesh, India.

Dr Ravi Kale

Professor, Department of General Surgery, SMSR, Sharda University, Greater Noida, Uttar Pradesh, India.

ABSTRACT

Background and Aims: Urolithiasis is one of the common disorder with which about 1/5th is found in the ureter, of which 2/3rd is seen in the lower ureter. Medical expulsive therapy is one of the routine modalities of treatment which uses various drugs acting on the ureter smooth muscle by different mechanism. Many studies had compared efficacy of combination drugs versus single drug. This study will compare the efficacy of the combination of tamsulosin and tadalafil against a standard drug combination of tamsulosin and nifedipine as medical expulsive therapy of distal ureteric stones. **Materials and Methods:** This Randomized Control Study was performed from December 2020 to July 2022. A total of 120 adult patients presenting with distal ureteric stones (5-10mm) were randomized to treatment with Tamsulosin 0.4mg+Nifedipine 30mg once daily (Group A) and Tamsulosin 0.4mg+Tadalafil 10mg once daily (Group B). Therapy was given for a maximum of 4 weeks. The stone expulsion rate was the primary endpoint. Time to stone expulsion, frequency of analgesic use, number of hospital visits for pain and adverse effects of the drugs were noted. **Results:** 60 patients were included in group A and group B respectively. No statistically significant differences were observed regarding patients' age, sex, and stone size distribution between both groups. There was a statistically significant reduction in time to stone expulsion in group B (9.69 ± 4.37) as compared to group A (12.88 ± 5.13), $p = 0.043$. No statistical difference was found for adverse drug effects. Statistically significant reduction in analgesic use was noted in the group B compared to group A. ($p=0.02$) **Conclusion:** According to the findings of this study, Tamsulosin plus tadalafil is more effective than tamsulosin plus nifedipine as a medical expulsive therapy for distal ureteric stones.

KEYWORDS

Medical expulsive therapy(MET), distal ureteric stones, Tamsulosin, Tadalafil, Nifedipine.

INTRODUCTION

The total prevalence of urinary stones is around 1% to 15%, and the average peak age of incidence is 30 years. Men are affected 2 to 3 times more than women [1]. Ureteric stones amount to 20% of urolithiasis and among that 70% of ureteric stones are present in the distal one-third of the ureter [2].

The overall likelihood of forming stones varies in different parts of the world and is estimated to be 1–5 % in Asia, 13 % in North America and 5–9 % in Europe. Prevalence of urolithiasis in India ranges from 4-20% [3].

Medical expulsive therapy (MET) has now become a well-recognized treatment modality. This involves various drugs acting on the ureter by different mechanisms including corticosteroid, calcium-channel blocker, α -adrenergic blockers and phosphodiesterase-5 (PDE5) inhibitors have been studied.[4]

Drugs that expel stones might act by relaxing ureteral smooth muscle through inhibition of calcium channel pumps or α -1 receptor blockade. Tamsulosin, α -1 adrenergic antagonists are the most commonly used agents for medical expulsive therapy (MET) [5].

A PDE5 inhibitor - Tadalafil, specific for cyclic guanosine monophosphate (cGMP) signaling pathway of smooth muscles, inhibits the degradation of cGMP, resulting in high levels of cGMP. This causes relaxation of ureteric muscles [6]. This study will compare the efficacy of the combination of tamsulosin and tadalafil against a standard drug combination of tamsulosin and nifedipine as medical expulsive therapy of lower ureteric stones.

MATERIAL AND METHODS

This Randomized Control Study has been undertaken after obtaining approval from the institutional ethics committee in department of General Surgery, School of Medical Sciences & Research, Greater Noida, UP from December 2020 to July 2022. 120 patients ≥ 18 years of age who are diagnosed with Lower Ureteric Stones of 5-10 mm diameter by ultrasound abdomen pelvis or NCCT KUB were included in study.

Patients with solitary kidney, history of previous surgery on same ureter, UTI, deteriorating renal function, fever, hydronephrosis, acute

or chronic renal failure, multiple ureteral stones, a history of open surgery or endoscopic procedures in the urinary tract, allergy to tamsulosin or tadalafil, concomitant treatment with α -blockers, calcium antagonists, or nitrates, pregnant or lactating mothers, patients who demanded urgent stone removal were excluded from the study.

The patients were randomly allocated to one of the two groups by using closed envelope method. The patients in group A received tamsulosin 0.4mg + nifedipine 30mg orally at bedtime. The patients in group B received tamsulosin 0.4 mg+ tadalafil 10mg orally at bedtime for a duration of 4 weeks. The patients were advised use a sieve while voiding the urine to highlight the stone expulsion. If the patient gives history of expulsion of the stone in less than 4 weeks, Medical Expulsion Therapy was stopped. Confirmation of expulsion of stone was done by NCCT KUB at the end of 4th week. Stone expulsion rate, time to stone expulsion, Frequency of Analgesic use, Number of hospital visits for pain and adverse drug effects were analyzed. Statistical analysis was done using Fisher's exact test and Chi-square test.

RESULTS

All the patients attending surgery OPD with distal ureteric calculi from December 2020 to July 2022 were screened. Based on inclusion and exclusion criteria, 120 patients were enrolled for the study. They were randomly assigned through closed envelope method into group A (Tamsulosin + Nifedipine) or group B (Tamsulosin + Tadalafil). No statistically significant differences were observed regarding patients' age, sex, and stone size distribution between both groups (Table 1).

Table-1

Parameter	Mean+SD		P value
	Group A	Group B	
Age	37.6 $\pm$ 14.3	34.6 $\pm$ 10.8	0.634
Gender	32 28	30 30	0.7957
Male			
Female			
Stone size(mm)	7.54+ 1.11	7.60+ 0.91	0.74
Analgesic use*	11.82+ 3.34	9.15+ 3.80	0.02
Number of hospital visits	0.51+ 0.22	0.39+ 0.26	0.15
Expulsion time (days)	12.88 $\pm$ 5.13	9.69 $\pm$ 4.37	0.043
*Number of tablets of NSAIDs used during study period			

As far as primary objectives of the study are concerned, the rate of stone expulsion of group A was 53.3% and that of group B was 70%. Although this was on the higher side in Group B, but the difference was not significant ($p=0.18$). There was a statistically significant reduction in time to stone expulsion in group B (9.69 ± 4.37) as compared to group A (12.88 ± 5.13), $p=0.043$.

Statistically significant reduction in analgesic use was noted in the group B compared to group A. ($p=0.02$)

Adverse effects such as headache, dizziness, orthostatic hypotension, nausea and painful erection occurred more often in group B (43.33%) than group A (26.66%) these were not significant enough to exclude the patients from the study. (Figure-1)

There was no significant statistical difference in the number of hospital visits for episodes of ureteric colic ($p=0.15$).

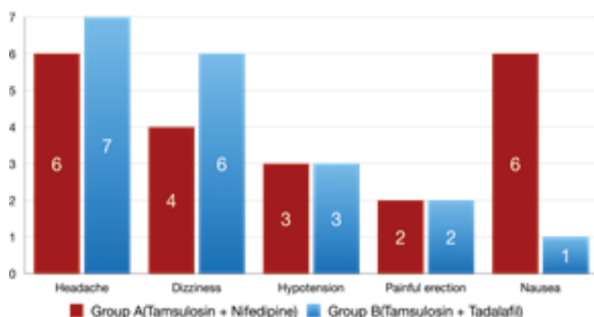


Figure-1

DISCUSSION

Urolithiasis affects 8-15% of the world population. Geographical area, racial distribution and socioeconomic status influence incidence of urolithiasis. Urolithiasis has a higher recurrence risk of 50% at 5 years and 70% at 9 years after initial episode [7]. Prevalence of urolithiasis in India ranges from 4-20% with a male: female ratio of 2:1. Ureteric stones account for approximately 20% of urolithiasis cases, out of which 70% are located in the lower one third of the ureter [1,2]. The likelihood and time to spontaneous expulsion of stones mainly depend on size of the stone and its location in the ureter. Stones up to 6mm might require 42 days for spontaneous expulsion [8]. They can be managed conservatively using pharmacological intervention to control pain, ureteric spasm, edema and infection thus facilitating stone expulsion. Medical expulsion therapy (MET) with active monitoring is a valid option for stones up to 10 mm especially for distal ureteric calculus [9]. This approach can be a cost effective strategy before opting for active stone removal. The EUA/AUA guidelines suggest tamsulosin and nifedipine for MET especially in distal ureteric stones and in patients with no role for immediate surgical removal [10,11].

In a randomized trial of combination therapy including tadalafil with tamsulosin compared with tamsulosin, Diwas et al. found an increased expulsion rate and more rapid stone expulsion time with combination therapy as compared to mono therapy with tamsulosin. In the present study, stone expulsion rate in patients treated with tamsulosin plus tadalafil was 70% and expulsion time was 9.69 ± 4.37 days which is comparable with the earlier studies. [12]

A ureteral stone usually causes severe colicky pain as a result of an increase in intraureteral pressure above the site of ureteral obstruction. At present, NSAIDs and anti-spasmodic drugs are generally used for relieving the pain caused by acute ureteral obstruction. Tamsulosin and tadalafil might reduce the colicky episodes, hence analgesics requirement and hospital visits by relaxing the ureteral smooth muscles and early stone expulsion. [13,14] In our study, analgesics requirement and number of hospital visits were lower in group B than in group A (11.82 ± 3.34 & 0.51 ± 0.22 respectively, for group A vs. 9.15 ± 3.80 & 0.39 ± 0.26 for group B).

Many studies have compared the efficacy and safety of tamsulosin and nifedipine, but those comparing combination of the two with tamsulosin and tadalafil are very few. Hence in this study we used a combination of tamsulosin and tadalafil to compare the standard drug combination of tamsulosin and nifedipine with regard to rate of stone

expulsion, time to expulsion, decrease in the frequency of analgesic requirement and safety.

CONCLUSION

According to the findings of our study, tamsulosin combined with tadalafil has a higher rate of stone expulsion than tamsulosin combined with nifedipine. Tamsulosin and tadalafil together can reduce the need for analgesics and significantly promote early stone expulsion. Both drug combinations are well tolerated, safe, and have just modest adverse effects. Tamsulosin plus tadalafil is therefore more effective than tamsulosin plus nifedipine as medical expulsive therapy for distal ureteric stones.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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