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Research Article

Efficacy of Tamsulosin in Expulsion of Lower Ureteric Stone upto 10mm

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Abstract

Background: Amongst numerous treatment modalities available for the lower ureteric calculi, medical expulsion therapy (MET) is the cost effective and popular amongst patient as it avoids invasive surgery. Although the efficacy of Tamsulosin as MET has been well studied in the other countries, in our population it remains unanswered.

Methods: This randomized control trial was done in 70 patients of lower ureteric calculi less than 10 mm in size who presented to the surgical outpatient department or the emergency department of the Tribhuvan University Teaching Hospital, Kathmandu, Nepal over a period of 10 months (From February 2016 to November 2016). Patients were randomized to two groups (Tamsulosin vs. control) using computer generated random number generator. Patients were followed up at one week and three weeks of initial visit to determine the expulsion rate of stone and dose of analgesic use.

Result: Among 70 patients who consented for the trial, 5 were lost to follow up (2 in Tamsulosin and 3 in control group). Among remaining 65, 46 were males and 19 were females. Average stone size was 6.17 mm in Tamsulosin group and 6.03 mm in control group (p=0.724). The expulsion rate was 54.54 % in the Tamsulosin group and 43.75% in the control group (p=0.384). Mean amount of analgesic (Tab. Diclofenac) use was 563.32 mg in the Tamsulosin group and 637.5mg in the control group (p=0.121).

Conclusion: This study shows that medical expulsive therapy using tamsulosin for the lower ureteric stones is not efficacious as thought before.

INTRODUCTION

Urolithiasis is one of the common urological problems in Nepal. The prevalence of this disease varies according to the geography, race/ethnicity, climate, gender, age and occupation [1]. Although the prevalence in our country is yet to be determined, life time prevalence is estimated at 10% to 15% [2], afflicting 13% of men and 7% of women [3]. Symptomatic ureterolithiasis is one of the important issues that the urologists face in emergency clinical settings. Of all urinary tract stones, 20% are ureteral stones, and 70% of these ureteral stones are located in the distal portion of the ureters [4].

Among the various treatment modalities available, the efficacy of mini-invasive therapies, such as extracorporeal shock wave lithotripsy (ESWL) and ureteroscopic lithotripsy has been proven by several studies [5,6]. Nevertheless these techniques are not risk-free, are problematic and are expensive [7]. A watchful waiting approach can be used in a large number of cases, as demonstrated by several studies that revealed high spontaneous passage rates of small distal ureteral stones [1,8]. Even the simple watchful waiting approach can result in complications, such as infection of the urinary tract, hydronephrosis and impaired renal function [9].

These days, use of the watchful waiting approach has been extended by using pharmacological therapy, which can reduce symptoms and facilitate stone expulsion [10,11].

The therapeutic potential of α-blockers for ureteral stone disease has been recognized after the detection of Alpha receptors in ureteral smooth muscle cells [12]. A1-alpha receptors are known to densely populate in the smooth muscle cells of the distal ureter, bladder and prostatic urethra [13]. Successful medical expulsive therapy (MET) for patients with distal ureteral stones using the nonselective alpha-blocker doxazosine was first reported in the late 1990's [11]. Since then, numerous clinical trials have been performed to investigate the efficacy of MET using the selective alpha-blocker tamsulosin alone and in combination with other drugs like corticosteroids and antibiotics [14-17].

The joint EAU/AUA Nephrolithiasis Guideline panel have shown efficacy of tamsulosin as a drug for MET for ureteric stone 10mm or less in size [18]. However, the results of various studies done in the different part of the world to evaluate the efficacy of tamsulosin (MET) have been conflicting and there has not been enough studies in Nepal to judge the efficacy of MET using selective a-blocker like tamsulosin. Hence this study aims

to evaluate the efficacy of tamsulosin in explusion of the lower ureteric stone less than 10 mm.

MATERIALS AND METHODS

This was a randomized control trial conducted in the department of urology and kidney transplant surgery, TUTH, over a period of 10 months (From February 2016 to November 2016) after taking the clearance from the institutional review board. All patients presenting with lower ureteric stone up to 10mm in size, diagnosed by USG abdomen/pelvis or X-ray KUB, were included in the study. Exclusion criteria were: presence of multiple ureteric stones, radiolucent stones, urinary tract infection, pregnancy, pediatric population, patients with a history of ureteral surgery or previous endoscopic procedures and patient requiring emergency intervention.

Informed consent was taken from the patients and randomly allotted to either an intervention group who received the drug Tamsulosin 0.4mg along with an analgesic (Diclofenac 50mg TDS for three days then as per need basis), antispasmodic (Hyoscine butylbromide 10mg along with diclofenac) and proton pump inhibitor (Pantoprazole 40mg once daily), or a control group who received similar medications except for Tamsulosin (Table 1).

The sample size was determined with the formula:

$$N = K \times \frac{p_1(1-p_1)+p_2(1-p_2)}{(p_1-p_2)^2}$$

Where

N= sample size

P_1= successful passage in conservative group

P_2=successful passage in tamsulosin group

K= constant which depended on value of α and β as given below:

	Power				
		50%	80%	90%	95%
		β= 0.5	β= 0.2	β= 0.1	β= 0.05
α	0.10	2.7	6.2	8.6	10.8
	0.05	3.8	7.9	10.5	13.0
	0.02	5.4	10.0	13.0	15.8
	0.01	6.6	11.7	14.9	17.8

Guideline for the management of ureteral calculi by EAU/AUA Nephrolithiasis Guideline panel was taken as a reference for P_1 and P_2 values; power of 80% and level of significance of 95% was used for the test. Computer generated random number were divided in control and study groups. Detailed history and clinical examination followed by routine urine examination and/or urine culture, serum creatinine, X-ray KUB and/or USG abdomen and pelvis were done in all patients. Stone size was determined using greatest dimension in the X-ray KUB or the USG abdomen and pelvis. Patients were followed up on 1st and 3rd week after the initial presentation and distal migration or expulsion of the ureteric calculi was determined with X-ray KUB and/or USG abdomen and pelvis and total dose of analgesic used was recorded.

Chi-square test was used for analysis of qualitative data like patient sex, location of stone (right vs left), expulsion of stone, Fisher's exact test was used for analysis of stone expulsion in subgroup with less than 5mm or more than 5mm and t-test was used for continuous variables. *P* value of <0.05 was considered statistically significant.

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 17.0.

RESULTS

Among 70 patients who consented for the trial, 5 were lost to follow up (2 in Tamsulosin and 3 in control group). Among remaining 65 (33 in Tamsulosin group and 32 in control group), 46 were males and 19 were females, with M: F ratio of 2.4:1. Average stone size was 6.17 mm in Tamsulosin group and 6.03 mm in control group (p=0.724). The expulsion rate was 54.54 % in the Tamsulosin group and 43.75% in the control group (p=0.384). Mean amount of analgesic (Tab. Diclofenac) use was 563.32 mg in the Tamsulosin group and 637.5mg in the control group (p=0.121) (Table 2).

As per the analysis, use of tamsulosin was not significantly associated with higher expulsion rate (p=0.384) or significantly less dose of analgesic use (p=0.121).

Only five patients complained of side effects of tamsulosin, among which one male patient complained of abnormal ejaculation and two patients complained of headache and two other patients complained of dizziness. None of them required stoppage of the drug and symptoms of dizziness improved on its own where as abnormal ejaculation resolved after the course of tamsulosin.

DISCUSSION

Recent advances in the urological procedures and fine instruments have largely diverted the management of ureteral stones to either minimal invasive methods like ESWL and ureteroscopy or to watchful waiting [19]. The minimally invasive therapies for distal ureteral stone are now recommended by recent EAU guidelines, with URS being first choice for stone larger than 10mm and both URS and ESWL for stone smaller than 10mm [20]. Nevertheless, these techniques are not risk free, are quite expensive and are concentrated at tertiary care centers [21]. Moreover, the simple watchful waiting approach, although shown to be effective in some studies, can result in complications, such as infection of the urinary tract, hydronephrosis and impaired renal function [9]. In complete obstruction, the signs of kidney injury appear in 3 to 4 weeks. For this reason the spontaneous passage of the stones can be waited on for 4 weeks [22].

Since 1990s, numerous clinical trials have been performed to investigate the efficacy of MET using the selective alpha-blocker tamsulosin alone and in combination with other drugs like corticosteroids and antibiotics [14-18].

This study investigates the efficacy of the drug Tamsulosin in expulsion of stones in our population. Although the number of stone passers were relatively higher in tamsulosin group as compared to the control group but statistically it was not significant (p=0.384). Similarly, the amount of analgesic use was

Table 1: Demographic data of two groups.			
	Tamsulosin	Control	p-value
Mean Stone size in mm ± SD	6.17 ± 1.8	6.03 ± 1.3	0.724
Sex ratio (M/F)	24/9	22/10	0.789
Mean Age in yrs	29.12 ± 9.91	30.13 ± 8.81	0.668
Stone location (Rt/Lt)	23/11	20/12	0.797

Table 2: Comparison of results in two groups.			
	Tamsulosin	Control	p-value
Expulsion rate	54.54% (18/33)	43.75% (14/32)	0.384
Expulsion rate in <5mm stones	66.66% (8/12)	61.53% (8/13)	0.790
Expulsion rate in >5mm stones	47.61% (10/21)	31.57%(6/19)	0.301
Mean analgesic use	563.3 ± 213mg	637.5 ± 166mg	0.121

statistically not significantly different the two groups. In the sub-group analysis, difference in the stone expulsion was greater in those with stone >5mm (i.e. 16.04% more expulsion was seen in tamsulosin group) as compared to those with stone <5mm (only 5.13% more expulsion in tamsulosin group), however, it was not statistically significant (p= 0.477).

Similar to our study, the study done in Switzerland in 2009 [23] has concluded that Tamsulosin treatment does not improve the stone expulsion rate in patients with distal ureteral stones 7 mm. however, patients in their study benefited from a supportive analgesic effect of tamsulosin.

A recent study done in Australia in 2015 [24] found no benefit overall of tamsulosin in distal ureteric calculi less than or equal to 10mm in terms of spontaneous passage, time to stone passage, pain, or analgesia requirements. However, in the subgroup with large stones (5 to 10mm), tamsulosin did increased passage.

Contrary to our study, study done in Turkey [25] concluded that the addition of tamsulosin to conventional treatment seemed beneficial in terms of stone clearance of lower ureteral stones. Another study done in Italy [10] concluded that tamsulosin used as a spasmolytic drug during renal colic due to juxtavesical calculi increased the stone expulsion rate and decreased expulsion time, the need for hospitalization and endoscopic procedures, and provided particularly good control of colic pain. In the recent systemic review and meta-analysis by John M Hollingsworth et al., they concluded that alpha blockers seem efficacious in the treatment of patients with ureteric stones who are amenable to conservative management and, the greatest benefit might be among those with stone 5-10mm [26]. However, recent high quality trial with large sample size from Pickard et al., demonstrated that tamsulosin and nifedipine are not effective in routine expectant management of ureteal stone causing ureteric colic [27].

The disparity in the results of different studies might be due to the fact that patients in different setting might have presented in different period of time after impaction of the stone in the lower ureter. Although, like most of the studies, we have taken the incidence of first pain attack to mark the start of treatment, the account given by patient of first pain might in fact be in much later date than the actual first pain they might have experienced due to which significant impaction of stone might have caused less stone expulsion rate. Also, the number of patients with stones more than 5mm were greater in our study as compared to those with stones less than 5mm, this might have also contributed to the fact that over all less stone expulsion was seen.

CONCLUSION

Although the use of Tamsulosin for MET seem to cause more number of stone expulsion, this study could not find the statistical benefit of Tamsulosin in spontaneous passage of lower ureteric stones less than 10 mm in size. More randomized control studies with higher sample size are required to establish Tamsulosion as standard therapy for small distal ureteric stones.

LIMITATION OF THE STUDY

The main limitation of our study was the fact that it was carried out in outpatient basis, hence, we could not follow up the patient for longer period of time. Although, many similar studies have followed up patient for four to six weeks to see the expulsion rate in both the tamsulosin and control group, we could not do so mainly because there would have been higher dropout rate if the study was carried out for longer duration. Also, the fact that patients in our setting already present late for treatment meant that we had to intervene earlier in other to persevere the renal function.

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