



EFFECTIVENESS OF SILODOSIN AND TAMSULOSIN FOR MEDICAL EXPULSION THERAPY OF DISTAL URETERIC CALCULI(5MM-9MM)- A PROSPECTIVE RANDOMIZED CLINICAL STUDY.

Urology

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ABSTRACT

Introduction and Objectives : Urolithiasis is most common causes of urinary tract symptoms with an estimated life time prevalence of 1-15%. Ureter is affected in 20% of cases of which 68% are seen in distal ureter. MET is the one of the nonsurgical management of distal ureteric calculi with good response rate, cost effectiveness and with less complication risk. hence we have aimed at comparing effectiveness of silodosin and tamsulosin for MET of distal ureteric calculi of 5-9mm calculi. **Material and Method:** This was a prospective randomized clinical study with 178 patient conducted in the department of urology, vijayanagar institute of medical science ballari from january 2021 to december 2021. As per exclusion criteria 28 patients were excluded from the study. All patient with nonobstructive distal ureteric calculi of 5-9mm were included in the study. Patient were randomized into group A with silodosin 8mg and Group B with Tamsulosin 0.4mg using computer generated random sequence allocation. The effectiveness of spontaneous expulsion of stone studied using both drugs in term of stone expulsion rate and time of stone expulsion. **Result:** A total of 150 patient with non-obstructive distal ureteric calculi of 5-9mm divided into Group A(75 patient) and Group B(75 patient) and taken silodosin 8mg and tamsulosin 0.4mg respectively for 2 weeks in the age group of 18-60years. Male affected more than the female in both group. There was a significant difference noted in terms of stone expulsion rate of 78.2 percent in group A compared to 56.8 percent in group B. The stone expulsion time was 8.4+/- 2.6 days in group A compared to 10.8+/- 3.1 days in group B. There were fewer episodes of ureteric colic and less analgesic use in silodosin group. Retrograde ejaculation was more common in silodosin group as compared to tamsulosin group. **Conclusion:** Silodosin 8mg is found to be more effective in terms of stone expulsion rate and mean stone expulsion time with fewer ureteric colic episode and less use of analgesic as compared to tamsulosin 0.4mg. hence silodosin 8mg is safe and effective for distal ureteric calculi of 5-9mm for medical expulsion therapy.

KEYWORDS

Silodosin, Tamsulosin, Medical expulsion therapy(MET), Stone expulsion rate, Stone expulsion time.

INTRODUCTION

Urolithiasis is one of the most common causes of urinary tract symptoms with a prevalence of 1-15%. 20% of stone are located in the ureter of which 68% are seen in the distal ureter(1). Male are affected 2-3 times more than women. however recent data suggest incidence is narrowing.

According to a meta-analysis, the rate of spontaneous expulsion of the stones smaller than 5mm is approximately 70% while it is 47% for the stones between 5 and 10 mm [2]. When we consider the anatomic location of the stone, we find that 71% of the distal ureteral calculi and 22% of the proximal ureteral calculi expelled spontaneously[3].

Itoh et al. reported that $\alpha 1D$ -adrenoceptor mRNA is more expressed in each region of the ureter than $\alpha 1A$ receptor mRNA and the highest amount of $\alpha 1D$ receptors are expressed in the distal ureter. Also, the distribution of alpha receptors in the ureter was $\alpha 1D$ (54%) $\geq$ $\alpha 1A$ (38%) $\geq$ $\alpha 1B$ (8%). [4]

It has also been shown that the highest density of $\alpha 1$ receptors is in the distal ureter in comparison to medial and proximal ureters. [5]

Sasaki et al conducted an in-vitro study on ureteral specimens obtained from patients undergoing nephrectomy. The results suggested that the $\alpha 1A$ subtype plays the predominant role in contraction in the human ureter than the $\alpha 1D$ receptor. [6]

The mechanism of action of MET can be explained by the presence of α -receptors in the distal third of ureteric musculature, mostly $\alpha 1$ -adrenoreceptors [7]. Blocking of these receptors results in inhibition of hyperperistaltic uncoordinated frequency, while maintaining tonic propulsive contractions, and therefore causes ureteric lumen dilatation with subsequent facilitation of stone expulsion [8].

Medical expulsive therapy (MET) aiming for spontaneous passage of ureteric stones is accepted worldwide as initial management of small distal ureteric stone [9]. Spontaneous passage of stone prevents potential pain, related complications, and costs of a surgical intervention [10].

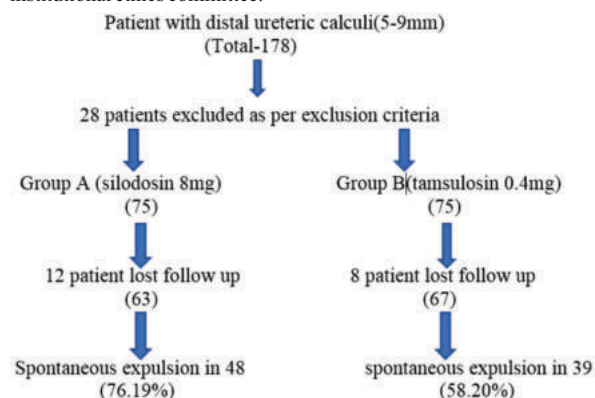
Silodosin is considered as an $\alpha 1A$ -adrenoreceptor antagonist which is more selective than tamsulosin [11].

EAU recommends α -blockers for management of distal ureteric stone [12]. It has been shown that use of α -blockers is associated with a higher stone-free rate and less time interval for spontaneous stone expulsion in contrast to placebo [13]. Hence we are comparing different alpha blocker for expulsion of distal ureteric calculi of 5-9mm in our study.

MATERIAL AND METHOD

This was a prospective randomized clinical study conducted in the department of urology, Vijayanagar institute of medical science, Ballari from January 2021 to December 2021. All patient with inclusion criteria were divided into - Group A has received tab silodosin 8mg and Group B received tab Tamsulosin 0.4mg daily for a period of 2 weeks and compared for the spontaneous expulsion of stone rate and expulsion time and number of episodes of ureteric colic and need for analgesia during treatment and complication like retrograde ejaculation in both groups.

An informed and written consent was taken from each patient before enrolment into the study. Ethical clearance was taken from the institutional ethics committee.



During follow up each patient assessed for lithuria, any persistent of symptoms, number of ureteric colic episode, use of analgesia and complication like retrograde ejaculation. if patient is symptomatically free stone expulsion is confirmed with either USG KUB or NCCT KUB. if stone is expelled, treatment discontinued.

Inclusion Criteria

- All patient with nonobstructive distal ureteric calculi of size 5-9mm in the age group of 18-60years

Exclusion Criteria

- Patients with solitary kidney,
- History of previous surgery on same ureter or double J stent,
- Deteriorating renal function
- Fever
- Acute or chronic renal failure,
- Multiple ureteral stones,
- Pregnant or lactating mothers,
- Patients who demanded urgent stone removal.

The primary end point of the study was spontaneous expulsion of stone. And secondary end point was stone expulsion time. Patient who has not passed stone in both group underwent URSL using semirigid ureteroscope and complete clearance of stone done.

Satistical Analysis

Method of Randomization: Randomization of patients to 2 intervention groups was performed using Computer generated random sequence allocation.

Sample Size Estimation

$$n = \frac{Z_{1-\alpha/2}^2 [P_1(1-P_1) + P_2(1-P_2)]}{d^2}$$

Where,

P_1 : Proportion in the first group

P_2 : Proportion in the second group

d^2 : Population risk difference

$1-\alpha$: Desired confidence level

Proportion in group I = 0.82

Proportion in group II = 0.62

Risk difference = 0.2

Population risk difference = 0.10

Desired confidence level (%) = 95

Side = 2

Required Sample size = 147, which was rounded off to 150 patients.

Each group will consist of 75 patients. [75 patients x 2 groups = 150 patients].

(Note: The rate of stone expulsion for Silodosin was 82% & Tamsulosin was 62% as per the reference from Gharib et al, 2018)

RESULTS

A total of 150 Patient with distal ureteric calculi of 5-9mm are included in the study. Patient are divided into Group A (63) who has taken tab silodosin 8mg and Group B (67) who has taken tab tamsulosin 0.4mg daily for a period of 2 weeks.

In both group male dominance is noted. But there is no statistically difference noted in terms of age, and Mean stone size.

	GROUP A (Silodosin 8mg)	GROUP B (Tamsulosin 0.4mg)
Mean age	41.9+/-7.21	39.3+/-9.81
Sex (Male/Female)	42/21	44/23
Mean stone size	7.38+/-1.02	6.95+/-1.42

It was noted that the spontaneous stone expulsion in Group A was 48 out of 63 with a stone expulsion rate of 76.19%. But in group B spontaneous stone expulsion noted in 39 out of 67 patient with a stone expulsion rate of 58.20%. Hence Group A with silodosin 8mg has better stone expulsion rate compared to Group B with tamsulosin 0.4mg.

Mean duration of stone expulsion in Group A with silodosin 8mg was 8.4+/- 2.6 days and in Group B with tamsulosin 0.4 mg was 10.8+/-3.1 days. Hence Group A with silodosin 8mg has lesser mean duration of stone expulsion compared to Group B with tamsulosin 0.4mg.

It was noted that number of patients requiring analgesic during the study in Group A was lesser when compared to Group B. Complication like Retrograde ejaculation is noted in 16 patients in silodosin Group compared to tamsulosin group of 7.

In Silodosin group ureteric orifice dilatation was noted in 78.57% compared to tamsulosin group of 46.42%. hence silodosin has better effect on ureteric dilatation and surgical intervention was easier.

Stone size	Group A-Silodosin 8mg (Stone expulsion)	Group B-Tamsulosin 0.4mg (Stone expulsion)	P value
5-7mm	44(39) 88.63%	51(34) 62.74%	0.023
7.1-9mm	19(9) 47.36%	17(7) 29.41%	0.7817
Total	63	67	

	Group A (Silodosin 8mg)	Group B (Tamsulosin 0.4mg)
Stone expulsion rate	48(76.19%)	39(58.20%)
Mean time of expulsion	8.4+/- 2.6 (days)	10.8+/-3.1(days)
Retrograde ejaculation	16	7
Ureteric dilatation	11(78.57%)	13(46.42%)

DISCUSSION

Urolithiasis is one of the most common causes of urinary tract symptoms. Distal ureter is effected in 68% out of 20% incidence in ureter (1). MET has studied in various study using different group of drugs like alpha blocker, calcium channel blocker, corticosteroids, phosphodiesterase inhibitors by causing relaxation of smooth muscle of ureter. as alpha receptors are located more in the distal ureter as compared to the mid and proximal ureter. Alpha blockers are used more frequently for the MET of distal ureteric calculi <10mm and found to have good result in response to spontaneous stone expulsion rate and mean expulsion time with minimal side effect, reduces the cost of treatment, hospital stay and surgical complication. Hence it is recently used by most of the urologist for the management of distal ureteric calculi of size <10mm.

Alpha blockers are currently recommended for use as MET by the EAU [14]. In vitro, the affinity of Silodosin for $\alpha 1A$ -adrenoceptors was approximately 580-fold greater than for $\alpha 1B$ -adrenoceptors and approximately 55-fold greater than for $\alpha 1D$ -adrenoceptors. By contrast, Tamsulosin had 15-fold greater affinity for $\alpha 1A$ -versus $\alpha 1B$ -adrenoceptors and 3- fold greater affinity for $\alpha 1A$ versus $\alpha 1D$ -adrenoceptors. [15]

In our study we are used alpha blockers like silodosin and tamsulosin and compared both drug safety and effectiveness in the management of distal ureteric calculi of 5-9mm. Silodosin is considered as an $\alpha 1A$ -adrenergic receptor antagonist which is more selective than tamsulosin [11]. Our study also showed silodosin is more effective than tamsulosin for MET.

Due to the risk of renal damage, most authors recommend that stone passage should not exceed 4 - 6 weeks [16]. but in our study we have used alpha blocker for 2 weeks.

Meltzer et al. [17] in their randomized study including 512 patients with ureteral stones between 1 and 8 mm, didn't find a difference in stone passage rates between patients treated with tamsulosin compared with placebo (52% versus 49%).

Recently, large prospective randomized trial [18] had compared tamsulosin with placebo for 4 to 7 mm distal ureteral stones in greater in a population of 3200 patients. The results were similar to those of the Meltzer and al trial: there is no difference for stones 5 mm or less and an increase in stone passage in the group with 5.1- to 7-mm stones (87% versus 75%), with a small overall benefit when all sizes were

considered (4 to 7 mm; 86% versus 79%).

Dell'Atti L. compared the effectiveness of Silodosin and Tamsulosin in the expulsion of distal ureteral stones measuring 4 to 10 mm. A significant increase in the expulsion rate was found in patients treated with Silodosin (80.3%) in comparison to Tamsulosin (61.2%); Silodosin showed a statistically relevant advantage in terms of stone expulsion rate ($p:0.003$) as well as in terms of expulsion time (weeks) ($p:0.002$). No severe complications were recorded. [19]

Elgalaly et al, compare the silodosin 8mg and tamsulosin 0.4mg for distal ureteric calculi <10mm for 4weeks and found stone expulsion rate for silodosin is 83% and 57% for tamsulosin. [20]

Gharib et al, ompare the silodosin 8mg and tamsulosin 0.4mg for distal ureteric calculi <10mm for 4weeks and found stone expulsion rate for silodosin is 82.4% and tamsulosin is 61.5%. Stone Expulsion time for Silodosin is 9.4 ± 3.8 days and for Tamsulosin is 12.7 ± 5.1 days [21]

CONCLUSION

Silodosin 8mg is found to be more effective interms of stone expulsion rate and mean stone expulsion time with fewer ureteric colic episode and less use of analgesic compared to tamsulosin 0.4mg. hence silodosin 8mg is safe and effective for distal ureteric calculi of 5-9mm for medical expulsion therapy.

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