

EFFICACY OF TAMSULOSIN VERSUS SILODOSIN IN UREETRIC STONE EXPULSION

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ABSTRACT:

Objective:

To assess the efficacy of Tamsulosin versus Silodosin in Medical Expulsion Therapy for Distal Ureteric Stones.

Materials and Method:

70 patients were enrolled in this prospective study. Patients presenting with ureteric colic, diagnosed with unilateral distal ureteric stone less than or equal to 7 mm were included in the study from an age range of 18 to 60 years. Patients with multiple comorbid, complicated stones and associated UTIs were excluded from the study. Patients were sorted into two groups of 35 patients, and were advised a combination of NSAID, an alpha blocker (either Tamsulosin or Silodosin) and an anti-inflammatory in form of serratiopeptidase. All patients were followed at 1 weekly by ultrasound and clinical assessment.

Results:

In the Tamsulosin Group, 28 (80%) were male while 7 (20%) were females. 22 patients took the medicine for less than a week and then either passed the stone or were surgically intervened. Total 19 (54.2%) patients passed the stone with the earliest on 3rd day of medication. 23 patients had complete resolution of hydronephrosis. 16 (45.7%) Patients were surgically intervened with URS. Ureteral access was achieved in 10 patients, while 6 only underwent DJ stenting. 7 Patients achieved complete stone clearance while 1 could get partial clearance, 3 patients were pre stented. In Silodosin Group, 22 (62.8%) were males while 13 (37.1%) patients were females. 26 patients took the medicine for less than or till 7 days and then either passed the stone or were surgically intervened. Total 23 patients passed the stone, with the earliest on 3rd day of medication. 12 (34.2%) Patients were surgically intervened with URS.

Conclusion:

Both drugs were comparable in terms of stone expulsion but Silodosin proved superior in relevance of earlier stone expulsion (p-value - 0.09)

Key words: Tamsolusin, Silodosin, Lower urinary Tract symptoms, Ureteric stone, METs

INTRODUCTION:

Urological emergencies are dominated by patients with ureteric colic. The incidence of urolithiasis in Asia ranges from 1 to 19.1%, while in Pakistan it has reached up to 16%.^{1,2} The increasing incidence of urolithiasis worldwide is continuously on increasing trend and extensive research is being carried out in terms of management of renal and ureteric stones.³ Ureteric stones, especially the distal ones may be managed conservatively with surgical options reserved for larger stones, complicated stones, or failure of conservative management.⁴ Our point of focus will be ureteric stones, specifically distal ureteric stones as they can be managed conservatively to some extent. Smaller stones in the distal ureter have a tendency to get expelled, especially under the influence of alpha blockers, owing to the alpha receptors present on the distal ureters⁵. Different combinations and drugs have been used and evaluated to provide maximal efficacy with minimal side effects to promote timely stone expulsion. Guidelines recommend giving medical expulsion therapy for stones less than or equal to 8 mm and stones tend to pass within 40 days⁶. Cautious follow up is advised to confirm stone expulsion as patients tend to get lost to follow up after resolution if symptoms, only to present later in life with loss of renal reserves or complications pertaining to it.⁷ Combination of drugs is given as Medical Expulsion Therapy, this combination as advised by the guidelines can be comprised of an alpha blocker, NSAIDs, Calcium channel blockers or Phosphodiesterase Inhibitors. Beta agonist and serotonergic drugs are also being introduced and tried in this regard.⁸

Alpha blockers are widely used for medical expulsion therapy. Tamsulosin has conventionally been used and now newer agents are being introduced to promote selectivity and minimize adverse effects.⁹ Tamsulosin is associated with postural hypotension, headache, and dizziness and Floppy Iris syndrome due to its generalized action on alpha-1 receptors, present on blood vessels, non-prostatic smooth muscles and Central nervous system. Silodosin, a newer alpha blocker has better selectivity and fewer side effects with more potency.^{10,11,12} Alpha blocker render the ureteric wall aperistaltic and relaxed to promote stone expulsion

along with anti-inflammatory agents that target in resolving ureteric wall edema and alleviating pain.¹³

This study aims to assess the effect of Silodosin and Tamsulosin as Medical expulsive therapy for ureteric stones in adult population of Pakistan.

METHODOLOGY

70 patients were enrolled in this prospective study at Tabba Kidney Institute, Urology Department and approved by institutes's Ethical review committee. Patients presenting to ER with ureteric colic diagnosed with unilateral distal ureteric stone less than or equal to 7 mm were included in the study from an age range of 18 years to 60 years. Patients with multiple comorbidities, complicated stones including multiple stones and stones that were surgically intervened and associated UTIs were excluded from the study. Patients were diagnosed as having distal ureteric stone less than or equal to 7 mm and confirmed on CT KUB. Diagnosed cases were randomly sorted into two groups and were advised a combination of NSAID, an alpha blocker (either Tamsulosin or Silodosin) and an anti-inflammatory in form of serratiopeptidase. 35 patients were placed in each group. All patients were followed at 1 weekly intervals on the basis of ultrasound and clinical assessment and were advised to follow in between if they passed the stone or with worsening pain or fever. Stone expulsion if noted, was documented by ultrasound and clinical assessment and if collected, the stone was sent for analysis. Data and demographics were entered and analyzed on Statistical package for social sciences (SPSS) v23.0 Continuous variables were analyzed as mean and standard deviation while categorical variables were analyzed as frequency and percentages, comparison between two groups was performed with the help of cross-tabulation test. Pearson chi-square test was used to assess mean difference between two mean values, and p-value <0.1 was taken as significant.

RESULTS

Total 70 patients were enrolled in the study, with an age range of 18 till 50 years (Mean 36.4 ± 7.49). 35 patients were placed in each group and followed weekly. In the Tamsulosin Group, 28 (80%) were male while 7 (20%) were

females. Majority of the patients presented with Nausea (43%), followed by Strangury (40%), Anorexia (37.1%), Vomiting (20%) and Hematuria (11.4%). 14 (40%) patients had previous positive history of renal stones and 12 (17%) patients had history of stone passage. 16 (45.7%) patients presented with mild hydronephrosis and hydroureter, while 15 (42.8%) patients presented with moderate hydronephroureter and 4 presented with severe hydronephrosis and hydroureter. 21 (60%) patients had significant perinephric stranding on CT scan. (Table 01)

Table I: Categorical comparison and evaluation of demographic details, medical history and stone characteristics in study population.

Comparative analysis of demographic details				
Variable	Tamsulosin	Silodosin	P-Value	
Gender	Male	28	22	0.003
	Female	7	13	
Family Hx	Positive	27	25	0.182
	Negative	8	10	
Presenting complain	Nausea	15	21	0.031
	Vomiting	7	8	
	Anorexia	13	15	
	Hematuria	4	4	
	Strangury	14	9	
Previous Hx Renal stone	Positive	14	18	0.314
	Negative	21	17	
HDN	Mild	16	19	0.034
	Moderate	15	15	
	Severe	4	1	
HDU	Mild	16	19	0.029
	Moderate	15	15	
	Severe	4	1	
Stone Location	Mid Ureter	2	1	0.0001
	Distal Ureter	33	34	
Perinephric Stranding	Yes	21	20	0.05
	No	14	15	

After prescribing the drug, 22 (62.8%) patients took the medicine for one week, and then either passed the stone or were surgically intervened, while rest of the patients

continued the medication for more days (mean 9 days \pm 3.2). Total 19 (54.2%) patients passed the stone with the earliest on 3rd day of medication (n=4, 11.4%). 1 (2.8%) patient passed the stone on 4th day and 3 (8.5%) patients passed it on 5th day. 13 (37.1%) patients followed the prescription till 2 weeks with 6 (17.1%) patients passing the stone on 9th day, 2 (5.7%) on day 13 and 1 (2.8%) on day 14. (Mean 9.1 \pm 3.2 days) 23 (65.7%) patients had complete resolution of hydronephrosis. 16 (45.7%) Patients were surgically intervened with URS. Ureteral access was achieved in 10 (28.5%) patients, while 6 (17.1%) only allowed DJ stenting due to narrow ureters or pinpoint orifices or due to purulent urine on guide wire insertion. 7 (43%) out of the 16 intervened patients of the group achieved complete stone clearance while 1 (6.2%) could get partial clearance, 3 (18.7%) patients were pre stented even after achieving ureteral access because of narrow segment or kinking. In Silodosin Group, 22 (62.8%) were males while 13 (37.1%) patients were females. Majority of the patients presented with Nausea (60%), followed by Anorexia (42.8%), strangury (25.7%), Vomiting (22.8%) and Hematuria (11.4%). 18 (51.4%) patients had previously positive history of renal or ureteric stones. 19 (54.2%) patients presented with mild hydronephrosis and hydroureter while 15 (42.8%) patients presented with moderate hydronephroureter and 1 (2.8%) presented with severe hydronephrosis and hydroureter. 20 (37.1%) patients had significant perinephric stranding on CT scan. After prescription, 26 (74.2%) patients took the medicine for less than or till 7 days and then either passed the stone or were surgically intervened, while rest of the patients continued the medication for upcoming days. Total 23 (65.7%) patients passed the stone, with the earliest of 9 patients on 3rd day of medication. 2(5.7%) patients passed the stone on 4th day and 7 (20%) patients passed it on 5th day, 4 (11.4%) on 6th day and 1 (2.8%) on 7th day. (table 1) 8 (22.8%) patients followed the prescription till 2 weeks with 1 (2.8%) patient passing the stone on 9th day, 3 (8.5%) on day 10 and 2(5.7%) on day 11. (mean 5.6 \pm 3.5 days) 12 (34.2%) Patients were surgically intervened with URS. Ureteral access was achieved in 9 (35%) patients, while 3 (8.5%) only allowed DJ stenting due to aforementioned reasons. 5(14.2%) Patients achieved complete stone clearance while 4 (11.4%) got partial clearance. (Table 02)

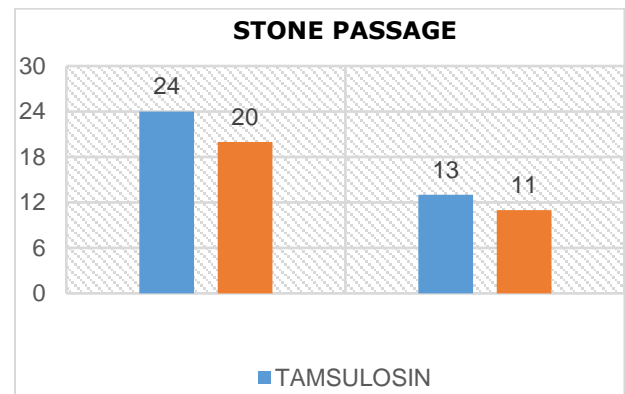
Table II: Comparative analysis of METs between both groups (Sildosin vs tamsulosin) in study population.

Comparative analysis of METs details				
Variable		Tamsulosin	Silodosin	P-Value
Drug Duration	< 1 week	22	26	0.284
	> 1 week	13	8	
Drug prescription day	1st Day	5	7	0.0005
	2nd Day	1	3	
	3rd Day	10	7	
	4th Day	10	9	
	5th Day	5	4	
	6th Day	1	2	
	8th Day	1	2	
Stone passed	Yes	19	23	0.128
	No	16	12	
Stone passage day	3rd Day	4	14	0.041
	4th Day	1	2	
	5th Day	3	7	
	6th Day	0	4	
	7th Day	0	1	
	9th Day	6	1	
	10th Day	0	3	
	12th Day	2	2	
HDN relieved	Yes	23	20	0.03
	No	12	15	
Surgical intervention	Yes	14	12	0.089
	No	21	23	
Ureter access	Yes	10	9	0.249
	No	25	26	
Only Stenting	Yes	14	11	0.437
	No	21	24	
Clearance	Complete	7	4	0.05
	Partial	1	4	
	Not cleared	6	3	

While comparing both groups, Silodosin group was found to have an earlier stone passage than Tamsulosin (mean 5.6± 3.5 vs 9.1± 3.2 days) with a p-value of 0.09., Tamsulosin group had 11 patients with stone size of 1-2 mm, 11 with 3-4 mm, 8 with 5-6 mm and 5 in 7-8 mm (mean 5 ± 0.19 mm). Silodosin group had 9 patients with 1-2 mm stone size, 11 with 3-4 mm, 9 with 5-6 mm and 6 with 7-8 mm. (mean 4.8 ± 1.2 mm) , (p- value, 1.204).

The stone passage was found to be relevant to size in the Tamsulosin Group, none of the stone passed with size of 7-8 mm, 50 % (4 out of 8) stones passed with size of 5-6 mm. 9 out of 11 stones passed in the size group of 1-2 mm. 6 out of 11 stones passed in the size group of 5-6 mm. In the Silodosin Group, 8 out of 9 stones with the size of 1-2 mm, 5 out of 11 passed in the size group of 3-4 mm, 7 out of 9 passed in the size group of 5-6 mm, and 3 out of 6 passed in the size group of 7-8 mm. The fact can be compared that stones smaller in size were prevalent in our study and hence passed and responded earlier. (Fig 01)

Fig I: Comparison between silodosin and tamsulosin group with stone passage frequency.



In terms of tolerance, both drugs were well tolerated with minimal side effects. Tamsulosin group showed one patient with Orthostatic hypotension (3%).

DISCUSSION

Small <6mm distal ureteric stones have traditionally been managed with Medical Expulsive Therapy. Many studies show different combinations of medical expulsive therapy being used to successfully promote stone expulsion.¹⁴ These combinations include alpha blockers in adjunct with

either NSAIDs, calcium channel blockers, steroids or PDE5 inhibitors. These work by reducing the ureteric wall inflammation and edema, and combined with good oral hydration and physical exertion is said to reduce friction between stone and ureteric wall to facilitate stone expulsion.^{15, 16, and 17} The role of alpha blockers has well been established, hence we have compared two alpha blockers in our study. A Cochrane systematic review by Campshroer T et al included 67 studies and 10,509 patients. The extensive study concluded the efficacious nature of alpha blockers in medical expulsive therapy, with increased efficacy in smaller stones < 5mm.¹⁸

Another large scale review included 6642 patients and ureteric stones in all proximal, mid and distal ureteric sites. This review was done by Yallapa S. et al and included 70 studies. They revealed many important insights into spontaneous stone expulsion and clinical outcomes associated with ureteric stones given alpha blockers. Median age of the patient was 46 years with a range of 17 to 84 years. Spontaneous stone passage was reported as 46% overall with further categorization into 49% of proximal ureteric stones, 58% mid ureteric and 68% distal ureteric. Stone size also influenced expulsion rates with 75% of stones < 5 mm and 62% of >5mm. Average time taken for SSP was 17 days (ours was mean 5.6 ± 3.5 vs 9.1 ± 3.2 days for Tamsulosin and Silodosin respectively), ranging from 6 to 29 days. Adverse outcomes were less reported with 5% necessitating hospitalization. These complete findings offer valuable understanding into the natural history and management of ureteral stones, providing clinicians with evidence-based data to update patient care and treatment decisions.¹⁹

Nuraj P et al reported the efficacy of Tamsulosin in stone expulsion in their study, although the sample size was 104.²⁰ Moon YJ et al reported in a study titled "**Distribution of ureteral stones and factors affecting their location and expulsion in patients with renal colic**", published in Korean Journal of Urology, that ureteric stone impaction site and size also play an important role in stone expulsion but with all these unmodifiable factors, role of alpha blocker (Tamsulosin 0.2 mg in this case) has been well established in potentiating and facilitating stone expulsion.²¹

The efficacy and safety of alpha-adrenergic blockers for medical expulsion therapy in patients with ureteral calculi is a meta-analysis involving multiple studies comparing their patients with alpha blockers versus placebo in stone expulsion. Majority of the studies focused on Tamsulosin, while Silodosin, Alfuzosin, Doxazosin and Terazosin were also evaluated. Retrograde ejaculation and dizziness were most commonly reported side effects. Tamsulosin also showed benefit of decreased analgesic requirement, although this was not a comparative observation. Efficacy of alpha blockers was proved superior to placebo in stone expulsion, none of these studies compared any two alpha blockers amongst each other.²² Huang W et al conducted another meta-analysis scrutinizing many studies which compared Silodosin with either placebos or Tamsulosin. Silodosin proved superior to either in all studies, in terms of stone expulsion rate, expulsion time and pain episodes. The adverse effects were equivocal and comparable in both alpha blockers but Silodosin showed more tendency of abnormal ejaculation. This meta-analysis comprised 1048 patients.²³ Bayar G et al reported comparison of stone passage with of Mirabegron versus Silodosin. With Silodosin Monotherapy, mean stone passage of was 7.1 ± 4.5 days, for distal ureteric stones, with an even shorter interval of 5.8 ± 4 for stones less than 6 mm, which is in support of our data also depicting early stone passage with Silodosin Therapy. Stone sizes included was between 4 mm to 10 mm.²⁴

A meta-analysis by G Sharma compared studies detailing alpha blockers for medical expulsive therapy and compared with control, tamsulosin and alfuzosin, silodosin was favored in terms of shortest interval of stone expulsion²⁵. Contradicting to the above and our study results, a prospective comparison of 1136 patients was done. Patients were sorted into 3 groups and efficacy of Tamsulosin, Nifedipine and placebo was compared. None was found superior and both groups of drugs were rendered as ineffective in alleviating ureteric colic and facilitating stone expulsion. This is in contrast with our studies, although our results were not compared with a placebo.²⁶ and another comparison between Tamsulosin and Silodosin rendered Silodosin as inferior in terms of Medical Expulsion.²⁷

CONCLUSION:

Both Tamsulosin and Silodosin were comparable in terms of stone expulsion, while Silodosin showed superior results in early passage of stone.

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