VOLUME - 9, ISSUE - 11, November - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Urology

COMPARATIVE STUDY OF EFFICACY OF SILODOSIN AND TAMSULOSIN IN PATIENTS OF LOWER THIRD URETERIC CALCULUS

Dr Rushabh Daga* Dept of Urology ,MMCHRI ,Kanchipuram*Corresponding Author

Dr Saurabh Nikumbh ACPM Dhule

Dr V.Selvaraj Dept of Urology ,MMCHRI ,Kanchipuram

ABSTRACT

OBJECTIVES: Present study was conducted to compare the efficacy of Silodosin and Tamsulosin in terms of Stone expulsion rate,time to stone expulsion and adverse reactions **PATIENTS AND METHODS:** A prospective randomised study was conducted on 100 patients, aged 20–60 years, who had unilateral lower third ureteric calculus of less than 10 mm. Patients were divided into two groups. Group A received Tablet silodosin (8 mg) and Group B received Tablet tamsulosin (0.4 mg) daily for 4 weeks .The patients were followed-up by ultrasonography, plain abdominal radiograph of the kidneys, ureters and urinary bladder. **RESULTS:** There was a significantly higher stone clearance rate in Group A (82 %) vs Group B (66%) (P = 0.109). Group A also showed a significant advantage for stone expulsion time and analgesic use($p<0.05$).Adverse effects were significantly higher for Group B than Group A. **CONCLUSION:**Silodosin also provides early stone expulsion due to its specific action,early onset of action, a greater decrease in colicky pain episodes, and a greater decrease in analgesic requirement

KEYWORDS :

INTRODUCTION

Stone formation is one of the painful urologic disorders that occur in approximately 12% of the global population and its re-occurrence rate in males is 70-81% and 47-60% in female. It is assessed that at least 10% of the population in industrialised part of the world are suffering with the problem of urinary stone formation.[1]Ureteric calculi or stones are those lying within the ureter, at any point from the ureteropelvic junction (UPJ) to the ureterovesical junction (UVJ). They are the classic cause of renal colic-type abdominal pain.

Usually, stones smaller than 5 mm are expected to pass spontaneously, whereas only 20% of stones larger than 8 mm will pass. The best treatment modality depends upon various factors such as size, localization and composition of the stone, severity of obstruction, symptoms, and anatomy of the urinary system. The watchful waiting approach can result in complications, such as infection of the urinary tract, hydronephrosis, and deranged renal function. Ureteric stones have been treated traditionally with interventional techniques like ureteroscopy or open surgery.

Improvements in minimally invasive procedures in the last few decades have considerably changed the treatment of ureteral stones, but such procedures are not free of risks and are costly as well. A conservative approach through medical expulsive therapy (MET) as a supplement to conservative treatment has now become an established treatment modality that employs various drugs acting on the ureter by different mechanisms.[2]

The ureter is lined by smooth muscle cells with alpha-1 adrenergic receptors, especially in the distal third. Receptor blockade inhibits both basal smooth muscle tone and hyper peristaltic uncoordinated frequency in order to maintain tonic propulsive contractions. Ureteric calculi can induce ureteric spasms that interfere with expulsion; thus, muscle relaxation while maintaining normal peristaltic activity may facilitate passage. Ureteric stones at the impaction site produce noticeable pathological changes; that is, an intense inflammatory reaction with mucosal oedema that could further worsen the ureteric obstruction, increasing the risk of impaction and retention.Therefore, alpha-1 adrenergic receptor antagonists work by creating an increased pressure gradient around the stone, which propels distal ureteral stones out of the ureter.[3]

The most frequently recommended agents are -blockers, specifically tamsulosin. Commonly used for benign prostatic hypertrophy, tamsulosin acts at the -1D adrenergic receptors present in the distal ureter.[4] Tamsulosin, a selective alpha-blocker with equal affinity for both -1A and -1D receptors, has a proven role in MET in increasing the stone expulsion rate and decreasing expulsion time.[5,6] 1D receptors are found in abundance in the detrusor and the intramural part of the ureter. 1A and 1D adrenergic receptors are present more densely in the distal 1/3 of ureter (including intramural part) than other adrenergic receptors. When stimulated, they inhibit the basal tone, peristaltic wave frequency and the ureteral contractions even in the intramural part of lower ureter. 1 antagonists have a crucial impact in spontaneous painless elimination of the stones smaller than 8 mm locate in the uretero-bladder junction.[7]

Silodosin, which has greater specificity to alpha 1-A than other alpha blockers is the latest alpha blocker approved for use. Few recent RCT studies [8-10]demonstrated that Silodosin, a highly selective alpha 1A-adrenoceptor antagonist, could improve the stone expulsion rate (SER) in patients with ureteral stones and may be superior to the current α-blockers, and patients may benefit from Silodosin treatment. Silodosin has been also proposed for MET instead of tamsulosin but studies comparing these substances for MET are still scarce.

On the other hand, tamsulosin has been widely used for ureteral stones in our practice and has been found to be efficacious. This study aimed to analyze the safety and efficacy of Silodosin in distal ureteral stones and also to compare the efficacy of Silodosin with that of tamsulosin.

Thus, by comparing these two drugs, we aim to discover whether we can achieve better ureteric relaxation and reduction in intramural pressure in order to facilitate stone passage. Thus our main aim of comparing Silodosin and tamsulosin is to determine single best montherapy for medical expulsive therapy of distal ureteric stones.

MATERIALS AND METHODS

The Prospective, randomized and an open label study

waconducted during October 2019 to March 2020.The patients attending the Department of Urology formed the material of study. Patients between 20 and 60 years having ureteral calculi of 10 mm or less located in lower ureter on Xray KUB and/or Ultrasonographyand willing to have expectant treatment were included in the study.Pregnant women or nursing mothers, patients with febrile UTI or severe hydronephrosis, hypotension or patients with severe hepatic dysfunction,patients on -blockers or / blockers or CCB or steroid, patients with anatomically deformed or stenosed anamolies,patients who underwent invasive operation on their ureter before,Patients whose blood creatinine levels are 2mg/dl and over,patients who take part in clinical trials other than the present study,patients hypersensitive to Silodosin or comorbidies were excluded from the study.

One hundred patients were selected in the present study.These patients were divided randomly into two groups each of 50 patients. One group was given Tab. Tamsulosin (0.4mg/d) and another group, Tab.Silodosin (8mg/d). The patients were given treatment for a maximum period of 4 weeks and observed for stone expulsion. Patients were further categorized into those having <5mm,5-7 mm and 8-10 mm subgroups for analysis Follow up was done in weekly intervals and data was recorded in a specially designed proforma. It was then transformed to a master chart and then subjected to statistical analysis.

RESULTS

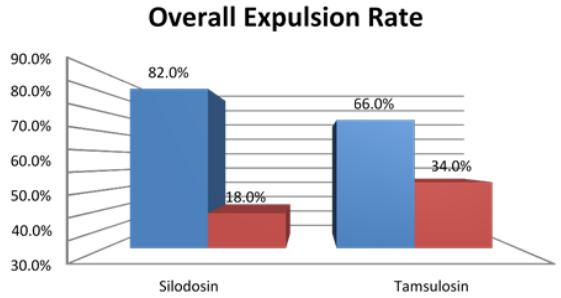
Over half of the cases in present study were between 31-40 years of age with 8% and 2% cases between 51-60 years and above 60 years of age. Mean age of the study subjects was 37.1 +/- 10.97 years.
Male predominance was seen in present study with 66% males to 34% females.

Most common presenting complaints were pain in lower abdomen (91%) followed by burning micturition (68%), nausea/ vomiting (23%) and hematuria (14%).
Most of the stone were between 5-7 mm in size (59%) while 14% and 27% stone were below 5 mm and between 8-10 mm in size.

Mean stone size in cases of Silodosin and tamsulosin group was 7.21 mm and 7.28 mm respectively. Thus no significant difference was observed between the study groups with respect to mean stone size (p-0.54).
No difference was seen between the study groups as per size of ureteric stone (p- 1.0).

Higher expulsion rate was observed in cases of silodosin across all stone sizes, however the difference was statistically significant for smaller stones. Poor stone expulsion arte was seen in both groups for stone size over 8 mm.

Complete expulsion was seen in 82% cases on silodosin as compared to 66% cases on tamsulosin (p-0.109).Mean expulsion of calculi was significantly earlier in patients managed by Silodosin as compared to tamsulosin (13.1 vs 16.92 days; p<0.05 by Chi Square test).
Mean analgesic use (269.4 vs 181.0 mg; p<0.05 by Chi Square test) was significantly higher in patients managed by tamsulosin.



The number of hospital visits required during treatment were more with tamsulosin, but the difference did not reach significance levels (2.56 vs 2.02 days; p-0.06 by Chi Square test).

Mean episodes of colicky pain (1.41 vs 0.43; p<0.05 by Chi Square test) were significantly higher in patients managed by tamsulosin.

The various side effects noted during the study period in patients on Silodosin and tamsulosin group were headache (8% vs 6%), dizziness (8% vs 6%), backache (6% vs 8%), hypotensive episodes (4% vs 6%) and abnormal ejaculation (0% vs 4%). No difference was seen in the adverse effect profile of both drugs.

DISCUSSION

The advances in minimally invasive techniques like shock wave lithotripsy and ureteroscopic lithotripsy have led to a decrease in the treatment related morbidity associated with management of ureteric calculi. These advances. Although, they are expensive and have inherent risks. Hence, observation has been advised for small ureteral stones, which have a high probability to pass spontaneously. The use of the expectant approach for distal ureteric stones can be extended with the use of adjuvant medical expulsive therapy (MET), which is able to reduce symptoms and facilitate stone expulsion.

The factors influencing expulsion of calculi include stone size, shape, and location, ureteric edema, and ureteric convolutions. Of these, the location of the calculus and its size are the most important factors.The management of patients with ureteral calculi has changed dramatically in the current era, with the conservative approach being the primary focus, its main benefit being minimum patient morbidity. Conservative nonsurgical approaches are usually implemented in the treatment plan of distal ureteral stones of size 5–10 mm as these are less likely to pass spontaneously 13,14.

According to earlier studies, the expulsion rate of distal ureteric stone by watchful waiting is 25–54% with mean expulsion time >10 days and is associated with high analgesic requirement even for stones <5 mm. To improve the expulsion rate and reduce analgesic requirement, medical therapy is considered for distal ureteral stones 15,16.

Complete Expulsion	Group		Total	p- value
	Silodosin	Tamsulosin		
< 5 mm	6/7	5/7	12/14	1.0
	86%	71%	86%	
5-7 mm	27/29	22/30	49/59	<0.05
	93%	73%	83%	
8-10 mm	8/14	6/13	14/27	0.7
	57%	46%	52%	

The present study was thus conducted to determine single best monotherapy for medical expulsive therapy of distal ureteric stones by comparing Silodosin and Tamsulosin.

PRESENTING SYMPTOMS

Most common presenting complaints were pain in lower abdomen (88.3%) followed by burning micturition (65%), nausea/ vomiting (18.3%) and hematuria (11.7%).Various studies have shown that colicky pain in the flank and ipsilateral lower abdomen with radiation to the testicles or the vulvar area is a characteristic feature of ureteric calculus. In most of the cases pain in lower abdomen is the only presenting complaint 11,22.

Table 16: Presenting complaints in various studies

Complaints	Present Study	Kumar S et al. 11	Jayant K et al. 22
Pain in Lower Abdomen	88.3%	93.0%	100.0%
Burning Micturition	65.0%	56.0%	51.0%
Hematuria	11.7%	3.0%	-
Nausea/ Vomiting	18.3%	11.0%	17%

Stone Size

According to the European Association of Urology Guidelines (2015) on Urolithiasis, there exists a high likelihood of spontaneous passage of stones up to ~5 mm, hence MET is less likely to increase the stone-free rate. The best results from MET were seen in cases with size ranging from 5-10 mm. Most of the cases in present study had calculi measuring between 5-10 mm with mean size in cases of silodosin and tamsulosin group as 7.21 mm and 7.28 mm respectively. The comparison of stone size as observed in the studies by other authors is as follows:

Table 17 : Mean Stone size in different studies

Author	Stone Size (mm)	
	Silodosin	Tamsulosin
Kumar S et al. 68	7.5	7.44
Elgalaly H 77	5.4	5.6
Gupta S 78	6.6	7.0
Present study	7.21	7.28

Stone Expulsion

Mean expulsion time of calculi was significantly earlier in patients managed by silodosin as compared to tamsulosin (13.1 vs 16.92 days; $p<0.05$). Complete expulsion was seen in 82% cases on silodosin as compared to 66% cases on tamsulosin (p-0.109). Higher expulsion rate was observed in cases of silodosin across all stone sizes, however the difference was statistically significant for smaller stones. Poor stone expulsion rate was seen in both groups for stone size over 8 mm (Silodosin: Tamsulosin: 57%: 46%).

The stone expulsion rate in the study by Kumar S [11] was significantly higher in the Silodosin group than in the tamsulosin group (83.3% vs. 64.4%).Sharma G et al.[12] in their study observed stone expulsion arte of 83% in silodosin group as compared to 57% in tamsulosin group. In a similar study by Elgalaly et al. [17], the stone clearance rate was also significantly higher with silodosin (83%) as compared Tamsulosin (57%) ($p<0.01$). While Gupta S et al. [18] observed stone expulsion arte of 82% in silodosin group as compared to 58% in tamsulosin group.

The rate of expulsion was observed to be significantly faster with silodosin in most of the studies .[11,12,17,18]

Table 18 : Stone Expulsion Rates across various studies

Author	Expulsion Rate	
	Silodosin	Tamsulosin
Kumar S et al.68	83.3%	64.4%
Sharma G et al. 69	83%	57%
Elgalaly H 77	83%	57%
Gupta S 78	82%	58%
Present Study	82%	66%

Table 19 : Stone Expulsion Time in days across various studies

Author	Expulsion Time (days)	
	Silodosin	Tamsulosin
Kumar S et al.11	14.8	16.2
Sharma G et al.12	11.3	17.8
Elgalaly H17	13.3	16.5
Gupta S 18	12.5	19.5
Present study	13.10	16.92

COLICKY PAIN & HOSPITAL VISITS

Mean analgesic use (269.4 vs 181.0 mg; $p<0.05$) and episodes of colicky pain (1.41 vs 0.43; $p<0.05$) were significantly higher in patients managed by tamsulosin. The number of hospital visits required during treatment were also more with tamsulosin, but the difference did not reach significance levels (2.56 vs 2.02 days; p-0.06).MET not only facilitates stone passage, but also decreases the colicky pain episodes and analgesic requirement.

Kumar S et al al.[11], who had compared tamsulosin with silodosin, demonstrated a significantly fewer colicky pain episodes (0.8 vs. 1.7, $p<0.01$), and significantly less analgesic use (195 mg vs. 220 mg, $p<0.01$) with Silodosin. Similarly Gupta et al.[18] was also able to demonstrate lower analgesic use for the silodosin group. On the contrary, Sharma G et al. [12] and Imperatore et al.[19] showed no significant difference in terms of mean number of pain episodes and need for analgesics while Dell'atti et al. [21] reported infrequent and mild colic episodes in both groups that were manageable with analgesics that allowed continuation of MET.

Colicky pain in ureteral stones occurs owing to an increase in intraureteral pressure above the site of ureteral obstruction. Kinnman et al. [20] demonstrated that -blockade relieves ureteric colic by blocking the C-fibers responsible for mediating pain. Both drugs are thought to decrease the frequency and amplitude of phasic peristaltic contractions that accompany ureteric obstruction and to decrease the need for analgesia. In the present study, these parameters were lower in silodosin group.

ADVERSE REACTIONS

The various side effects noted during the study period in patients on Silodosin and tamsulosin group were headache (8% vs 6%), dizziness (8% vs 6%), backache (6%vs 8%), hypotensive episodes (4% vs 6%) and abnormal ejaculation (0% vs 4%). No difference was seen in the adverse effect profile of both drugs. Similar incidences of side effects were reported in most of the studies with no significant difference between the two groups [11,12,17,18]. Elgalaly H et al.[17] reported six patients had orthostatic hypotension, two in the silodosin group (3.8%) and four in the tamsulosin group (7.8%), which was not statistically significantly different. Kumar et al. [68] reported orthostatic hypotension in 3.3% and 6.6% in the silodosin and tamsulosin groups. Imperatore et al. [19] also observed a nonsignificant difference in orthostatic hypotension of 2% and 6% in the silodosin and tamsulosin groups, respectively. However Imperatore et al. [19] reported that retrograde ejaculation was significantly different between silodosin (2%) and tamsulosin (8%).

CONCLUSION:

Silodosin also provides early stone expulsion due to its specific action,early onset of action, a greater decrease in colicky pain episodes, and a greater decrease in analgesic requirement

Conflict of interest

None declared.

Source of Funding

None.

REFERANCE

1. Soundararajan P, Mahesh R, Ramesh T, Hazeena Begum V. Effect of Aerva Lanata on calcium oxalate urolithiasis in rats. Indian journal of experimental biology, 44, 2006, 981-986. 2.
2. Ueno A, Kawamura T, Ogawa A, Takayasu H. Relation of spontaneous passage of ureteral calculi to size. Urology. 1977;10:544–546.
3. Porpiglia F, Vaccino D, Billia M, Renard J, Cracco C, Ghignone G, et al. Corticosteroids and tamsulosin in the medical expulsive therapy for symptomatic distal ureter stones: single drug or association? Eur Urol. 2006;50:339–344.

4. G.M. Preminger, H.G. Tiselius, D.G. Assimos. Guideline for the management of ureteral calculi. J Urol, 2007.178, pp. 2418-2434.
5. Wang CJ, Huang SW, Chang CH. Efficacy of an alpha1 blocker in expulsive therapy of lower ureteral stones. J Endourol. 2008;22:41–46.
6. Gratzke C, Uckert S, Reich O, et al. PDE5 inhibitors. A new option in the treatment of ureteral colic? Urologe A. 2007;46:1219–1223.
7. Pricop C, Novac C, Negru D, Ilie C, Pricop A, T nase V.Rev Med Chir Soc Med Nat Iasi. 2004 Jan-Mar; 108(1):128-33.
8. Sur RL, Shore N, L'Esperance J, et al. Silodosin to facili- tate passage of ureteral stones: A multi-institutional, randomized, double-blinded, placebo-controlled trial. Eur Urol. 2015;67:959–964.
9. Itoh Y, Okada A, Yasui T, et al. Administration of the selective alpha 1A-adrenoceptor antagonist Silodosin facilitates expulsion of size 5-10mm distal ureteral stones, as compared to control. Int Urol Nephrol. 2013;45:675–678.
10. Gupta S, Lodh B, Singh AK, et al. Comparing the effi- cacy of tamsulosin and silodosin in the medical expul- sion therapy for ureteral calculi. J Clin Diagn Res. 2013;7:1672–1674.
11. Kumar S, Jayant K, Agrawal MM, Singh SK, Agrawal S, Parmar KM. Role of tamsulosin, tadalafil, and silodosin as the medical expulsive therapy in lower ureteric stone: a randomized trial (a pilot study). Urology. 2015 Jan 31;85(1):59-63.gupta
12. Sharma G, Khadav B, Sadasukhi TC, Gupta M, Gupta HL. comparative analysis of silodosin and tamsulosin in distal ureteric calculus treatment. Journal of Evidence Based Medicine and Healthcare. 2016 Jan 1;3(85):4647-9.
13. Hubner WA, Irby P, Stoller ML. Natural history and current concepts for the treatment of small ureteral calculi. Eur Urol. 1993;24:172–176.
14. Seitz C, Liatsikos E, Propiglia F, et al. Medical therapy to facilitate the passage of stones: what is the evidence? Eur Urol. 2009;56:455–471.
15. Bensalah K, Pearle M, Lotan Y. Cost effectiveness of medical expulsive therapy using alpha-blockers for the treatment of distal ureteral stones. Eur Urol. 2008;53:411–418.
16. Wolf JS., Jr Treatment selection and outcomes: ureteral calculi. Urol Clin N Am. 2007;34:421–430.
17. Elgalaly H, Sakr A, Fawzi A, Salem EA, Desoky E, Shahin A, Kamel M. Silodosin vs tamsulosin in the management of distal ureteric stones: A prospective randomised study. Arab journal of urology. 2016 Mar 31;14(1):12-7.
18. Gupta S, Lodh B, Singh AK, Somarendra K, Meitei KS, Singh SR. Comparing the efficacy of tamsulosin and silodosin in the medical expulsion therapy for ureteral calculi. Journal of clinical and diagnostic research:JCDR.2013,Aug;7(8):1672.
19. Imperatore V, Fusco F, Creta M, Di Meo S, Buonopane R, Longo N, Imbimbo C, Mirone V. Medical expulsive therapy for distal ureteric stones: tamsulosin versus silodosin. Archivio Italiano di Urologia e Andrologia. 2014;86(2):103–107.
20. Kinnman E, Nygards EB, Hansson P. Peripheral alpha-adrenoreceptors are involved in the development of capsaicin induced ongoing and stimulus evoked pain in humans. Pain 1997;69:79-85.
21. Dell'Atti L. Silodosin versus Tamsulosin as medical expulsive therapy for distal ureteral stones: a prospective randomized study. Urologia. 2015 Jan 1;82(1).
22. Jayant K, Agrawal R, Agrawal S. Tamsulosin versus tamsulosin plus tadalafil as medical expulsive therapy for lower ureteric stones: a randomized controlled trial. International Journal of Urology. 2014 Oct 1;21(10):1012-5.