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Original Research Article **Urology**

Effect of Silodosin in the Treatment of Distal Ureteral Stone

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Abstract

Background: Ureteral stones are a common type of urinary tract stones, accounting for 20% of all cases. The majority of these stones, approximately 70%, are located in the distal ureter. Recent studies have shown that α1- Adrenergic blockers can enhance the spontaneous passage of distal ureteral stones. ***Objectives*:** This study was done to compare the outcomes of treating distal ureteral stone with Silodosin, an α1- A adrenergic blocker, versus without Silodosin. ***Materials and Methods:*** A total of 70 patients aged between 18 and 50 years, diagnosed with distal ureteral stone, were enrolled in the study, which took place at the Department of Urology, Dhaka Medical College, from October 2017 to March 2019. The patients were divided into two groups: Group A and Group B. Group A consisted of 35 patients who were instructed to drink 3 litres of water daily, while Group B received the same instruction and also received Silodosin 8 mg/day. The treatment duration was four weeks, during which patients were monitored weekly through history, serum creatinine levels, X-ray KUB, and ultrasonogram of KUB. The number of stone expulsions, duration of spontaneous stone passage through the ureter, analgesic dosages, and adverse effects were recorded. ***Results:*** The higher expulsion rate in Group B (91.4%) compared to Group A (71.4%) (P=0.031). The mean expulsion duration was significantly shorter in Group B (8.94±3.58 days) compared to Group A (13.08±7.26 days) (P<0.00298). Additionally, Group B required significantly lower analgesic dosages (115.71±75.51 mg) compared to Group A (255.71±108.31 mg) (P=0.00001). No adverse effects were observed in Group A, while two patients in Group B experienced adverse effects (retrograde ejaculation and postural hypotension). ***Conclusion:*** These results indicate that 8 mg/day of silodosin facilitates the expulsion of distal ureteral stone of about 5 to 10 mm in diameter in the largest dimension and significantly reduces the number of analgesic dosages.

Keywords: Silodosin, Distal Ureteral Stone, α1-Adrenergic Blocker, Stone Expulsion, Analgesic Dosages.

INTRODUCTION

Urolithiasis is one of the most common diseases of the urinary tract affecting about 5%-10% of the population. Of them, ureteral stones account for 20% of urinary tract stones and about 70% of them are found in the lower third of the ureter [1]. The increasing prevalence of ureteral stones is a matter of concern in this era. The incidence varies with geographic location; being greater in mountainous and desert areas that are found in the Middle East, Western India, Southern United States, Scandinavia, Mediterranean, and Central Europe which probably reflects water and soil content as well as hot weather and dehydration that exist in these areas. Mehmet *et al.*, have found that the selective alpha 1A adrenergic receptor antagonist, silodosin is more effective than the selective alpha 1D adrenergic receptor antagonist in respect of higher stone expulsion rates and faster stone expulsion times [2].

Management of ureteral stones depends on the size, location, number and presence of symptoms. Presence of ureteral spasm, mucosal edema or inflammation and ureteral anatomy also influence stone expulsion. Minimally invasive therapy, ureter lithotripsy represents efficacious treatment modality in

almost all cases. But it is costly and is not risk free. Complication rates are also high. Elgalaly *et al.*, have demonstrated that the overall complications after ureteroscopy have been estimated to be 10-20% in different studies [3]. Recently, the use of α-blocker as medical expulsive therapy (MET) has replaced minimally invasive procedures as the first line management for small ureteral stone. The clinical benefit of α-blockers for treating distal ureteral stone (DUS) has been shown in two meta- analyses with a high level of evidence, in which spontaneous stone passage in patients given α- blockers are 52% and 44%, greater than those not given such medications. Itoh *et al.*, have demonstrated that three types of alpha 1 adrenoceptor are expressed in the human ureter [4]. Antagonist of these receptors has been proved to decrease ureteral basal tone, peristaltic activity and contractions, thus decreasing intraureteral pressure and increasing urine transport. So alpha blockade has been proved to improve the likelihood of spontaneous stone passage and to decrease both the time to stone passage and analgesic requirements. Demonstration of alpha-adrenergic receptors in distal one-thirds of ureter, and evidence regarding the effects of those receptors on smooth muscle contraction shows that they play an important role in the ureter physiology. Understanding those physiologic factors enabled the use of alpha receptor blockers for medical treatment of distal ureteral stones [5]. Owing to this unique property, Silodosin also shows lesser blood pressure related adverse effects mediated by alpha 1B receptors. Both the American Urological Association and the European Association of Urology have included alpha blockers in their treatment recommendation [6].

Alpha 1-A receptors are the most important adrenoreceptors for ureteral contraction. Silodosin, which has greater specificity to alpha1-A than other alpha blockers, is the latest alpha blocker that has been approved for use. Our knowledge regarding silodosin in MET is less than that regarding other alpha blockers. So, this study is designed to observe the effect of administration of 8 mg/day of Silodosin on ureteral stone expulsion rate, duration of stone expulsion, need for analgesics and adverse effects in patients with distal ureteral stones.

OBJECTIVES

General Objectives

- To compare the outcome of treatment of distal ureteral stone with Silodosin and with that of without Silodosin.

Specific Objectives

- To observe event of stone expulsion after administration of Silodosin.
- To observe stone expulsion time after administration of Silodosin.
- To observe analgesic requirement after administration of Silodosin.
- To assess adverse effects such as retrograde ejaculation (in case of male), postural hypotension after administration of Silodosin.

MATERIALS AND METHODS

This quasi-experimental study was done from Oct 2017 to March 2019. Diagnosed cases of distal ureteral stone attending at OPD of Urology in DMCH were selected by purposive sampling followed by inclusion and exclusion criteria. After selection of the subjects, the nature, purpose and benefit of the study were explained to each subject in details. Informed written consent was taken from the participants. A total of 70 patients were included in the study and they were allocated into two groups. The participants were allocated into two groups based on their assigned case numbers. Group A consisted of 35 participants who were instructed to drink 3 L of water daily for 4 weeks. Group B consisted of 35 participants who were treated with Silodosin 8 mg once daily along with the same instruction to drink 3 L of water daily for 4 weeks. Blinding was not possible in this study as the participants and the researchers were aware of the treatment allocation. However, efforts were made to minimize bias by using objective outcome measures.

Statistical Analysis

The collected data were entered into a spreadsheet (Microsoft Excel) and analyzed using appropriate statistical software (e.g., SPSS,). Descriptive statistics such as mean, standard deviation, frequency, and percentage were calculated for the demographic variables and outcome measures. For comparative analysis, independent t-tests or Mann-Whitney U tests were performed, depending on the distribution of the data, to assess the differences between the two treatment groups. A p-value of less than 0.05 was considered statistically significant. The stone expulsion rate, stone expulsion time, analgesic requirement, and adverse effects were compared between Group A (water intake) and Group B (water intake + Silodosin) to evaluate the effectiveness of the interventions.

Ethical Considerations

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical clearance was obtained from the Ethical Clearance Committee of Dhaka Medical College. Informed written consent was obtained from all participants, and their confidentiality and privacy were ensured throughout the study. The participants were informed about the voluntary nature of their participation and their right to withdraw from the study at any time without any negative consequences.

RESULTS

A total of 70 patients of distal ureteral stone were selected from department of Urology, DMCH. They were allocated into Group-A and Group-B. Patients of Group-A were instructed to drink 3 L of

water daily for 4 weeks and patients of Group-B were treated with Silodosin 8 mg daily at night with the same instruction. No patient was dropped out during the follow up period. The different parameters of the patients have been shown in tabulated form and statistical analysis has been done in both groups to see any significant difference. *P*- value was set at 0.05 and p<0.05 was considered as significant.

Table 1: Distribution of study subjects according to age in groups.

Age (Years)	Mean ± SD	*p*-value
Group A	34.71 ± 10.74	0.48
Group B	34.49 ± 9.31	

Table 1 shows age (years) in group-A is 34.71±10.74 and in group-B is 34.49±9.31. The difference of mean (±SD) age of the two groups was not statistically significant.

Table 2: Comparison of patients according to stone expulsion time(N-57).

Stone Expulsion Time (days)	Mean ± SD	*p*-value
Group A (n=25)	13.08 ± 7.26	0.00298
Group B (n=32)	8.94 ± 3.58	

Table 2 shows the time of stone expulsion (days) in group-A is 13.08±7.26 and in group B is 8.94±3.58. The difference in stone expulsion time of the two groups is statistically significant (p<0.05).

Table 3: Comparison of analgesic requirement (mg) between groups

Analgesic Requirement (mg)	Mean ± SD	*p*-value
Group A	255.71 ± 108.31	0.00001
Group B	115.71 ± 75.51	

According to Table 3, the overall analgesic (Diclofenac sodium) requirement for group A was 255.71 ± 108.31 mg, whereas the requirement for group B was 115.71 ± 75.51 mg. The difference between the two group's analgesic requirements in mg is statistically significant (p<0.05).

Table 4: Comparison of occurrence of retrograde ejaculation (N=70)

Retrograde Ejaculation	Group A n (%)	Group B n (%)	Fisher Exact Test Value
Occurred	0 (0)	1 (2.86)	1
Not Occurred	35 (100)	34 (97.14)	
Total	**35**	**35**	

Table 4 shows adverse effect (retrograde ejaculation) occurs in 0(0%) patient in group-A and 1(2.86%) patient in group-B. The intergroup difference is not statistically significant (p>0.05).

The occurrence of postural hypotension (N=70)adverse effect (Postural hypotension) occurred in 0(0%) patient in group-A and 1(2.86%) patient in group-B. The intergroup difference is not statistically significant (p>0.05).During the study period, a number of patients developed clinical symptom such as fever, severe ureteral colic but no patient developed deterioration of renal function. The number of patients admitted in hospital was also observed. In Group A, 4(11.42%) patients experienced fever whereas 1(2.85%) patient experienced fever in Group B. All of them were admitted in hospital and treated with antibiotics according to urine C/S. In Group A, 5(14.28%) patients experienced severe ureteral colic whereas 2(5.71%) patients in Group B experienced severe ureteral colic. All of them were hospitalized and treated conservatively.

DISCUSSION

The management of ureteral stone disease involves a careful consideration of the natural course of the condition in the absence of treatment, as well as the risks associated with various treatment options. Arafat, Yassar *et al.,* found that the size of the stone directly influences its spontaneous clearance. Therefore, factors such as stone size, location, number, presence of symptoms, ureteral spasm, mucosal edema, inflammation, and ureteral anatomy must be taken into account when managing ureteral stones [7].

In recent years, there has been a shift towards a conservative approach in the management of ureteral calculi, as it minimizes patient morbidity. Conservative nonsurgical approaches are typically recommended for distal ureteral stones measuring 5-10 mm, as they are less likely to pass spontaneously. Previous studies have shown that the expulsion rate of distal ureteral stones through expectant therapy ranges from 25% to 54%, with a mean expulsion time exceeding 10 days.

Furthermore, even stones smaller than 5 mm often require high analgesic doses. To improve stone expulsion rates and reduce analgesic requirements, medical therapy, such as the use of Silodosin, is considered for distal ureteral stones.

The present study included patients between 18 and 50 years of age, with the majority falling within the 18-30 year age range. The age distribution in this study aligns with previous research conducted by [3] on the management of distal ureteral stones using Silodosin or Tamsulosin. The age ranges in these studies were comparable to those in the present study.

In our study, the stone expulsion rate was significantly higher in the Silodosin group (Group B) compared to the group without Silodosin (Group A), with rates of 91.4% and 71.4%, respectively ($p = 0.031$). These results are consistent with the findings [8], who reported higher stone clearance rates in the Silodosin groups compared to the non-Silodosin groups. However, Imperatore *et al*,. reported no significant difference in stone clearance rates between Silodosin and Tamsulosin [1]. Yasunori Itoh *et al.*, [9] reported comparable stone expulsion rates between control and Silodosin groups but noted shorter mean expulsion times in the Silodosin group, particularly for distal ureteral stones.

A similar study found that Silodosin had a significantly greater rate of passage for distal ureter stones compared to placebo, but no significant difference was observed for all ureteral stones combined [10]. Diandong Yang *et al.*, also reported superior stone expulsion rates, shorter expulsion times, and reduced analgesic requirements in Silodosin groups compared to controls [11].

In terms of stone expulsion time, our study showed a significantly shorter mean time in the Silodosin group compared to the group without Silodosin (8.94 vs. 13.08 days, respectively; $p < 0.05$). These findings align with the results of Mustafa *et al.*, (2015) and Kumar *et al.*, (2015), who reported shorter stone expulsion times in the Silodosin groups compared to the non-Silodosin groups. However, Imperatore *et al.*, (2014) reported shorter mean expulsion times for both Silodosin and Tamsulosin.

Regarding safety, Silodosin was generally well tolerated in our study. Few adverse effects were observed, with incidence of abnormal ejaculation in the Silodosin group compared to the control group. Similar findings were reported by [1] regarding the incidence of adverse effects, including abnormal ejaculation.

In terms of complications, our study observed a small number of patients who developed fever, severe ureteral colic, and required hospital admission. However, no cases of renal function deterioration or the need for surgical intervention were observed during the study period.

In summary, the present study supports the use of Silodosin in the management of distal ureteral stones. In the Silodosin group compared to the group without Silodosin, it showed a considerably higher stone expulsion rate, shorter expulsion time, and reduced analgesic requirements. These findings are consistent with previous studies that have reported favorable outcomes with Silodosin in terms of stone clearance rates and expulsion time.

It is important to note that while Silodosin shows promise as a medical therapy for distal ureteral stone, individual patient characteristics and preferences should be considered when deciding on the appropriate treatment approach. Further research and larger studies are warranted to confirm the efficacy and safety of Silodosin in the management of ureteral stone disease.

CONCLUSIONS

Stone expulsion rate is more and stone expulsion time and analgaesic requirement is less in that with Silodosin in the treatment of distal ureteral stone. Adverse effect of Silodosin is also insignificant. So, Silodosin is effective in the management of distal ureteral stone in terms of the stone expulsion rate, stone expulsion time, analgesic requirement and insignificant adverse effect.

Limitations

The present study had numbers of limitations.

- The study was conducted in a single center in Dhaka city which might not be representative to the whole population.
- Assessment of severity of pain was not done before use of analgesic.

RECOMMENDATIONS

From the results of this study, it may be recommended that, Silodosin 8 mg daily can be used in patients with single, symptomatic distal ureteral stone. However, a multicenter clinical study on larger scale is needed to confirm the effect of Silodosin in the treatment of single, symptomatic distal ureteral stone disease.

REFERENCES

1. Imperatore, V., Fusco, F., Creta, M., Di Meo, S., Buonopane, R., Longo, N., ... & Mirone, V. (2014). Medical expulsive therapy for distal ureteric stones: tamsulosin versus silodosin. *Archivio Italiano di Urologia e Andrologia*, *86*(2), 103-107.
2. Özsoy, M., Liatsikos, E., Scheffbuch, N., & Kallidonis, P. (2016). Comparison of silodosin to tamsulosin for medical expulsive treatment of ureteral stones: a systematic review and meta-analysis. *Urolithiasis*, *44*, 491-497.

3. Elgalaly, H., Sakr, A., Fawzi, A., Salem, E. A., Desoky, E., Shahin, A., & Kamel, M. (2016). Silodosin vs tamsulosin in the management of distal ureteric stones: a prospective randomised study. *Arab journal of urology*, *14*(1), 12-17.
4. Itoh, Y., Kojima, Y., Yasui, T., Tozawa, K., Sasaki, S., & Kohri, K. (2007). Examination of alpha 1 adrenoceptor subtypes in the human ureter. *International journal of urology*, *14*(8), 749-753.
5. Yuceturk, C. N., Dadali, M., Bagbanci, M. S., Ozgur, B. C., Aydogmus, Y., Yildiz, Y., & Kilinc, M. F. (2017). Efficacy of silodosin dose in medical expulsive therapy for distal ureteral stones: a retrospective study.
6. Preminger, G. M., Tiselius, H. G., Assimos, D. G., Alken, P., Buck, C., Gallucci, M., ... & Wolf, J. S. (2007). 2007 guideline for the management of ureteral calculi. *The Journal of urology*, *178*(6), 2418-2434.
7. Arafat, Y. (2016). Effectiveness of Medical Management in Spontaneous Expulsion of Lower Ureteral Calculi: A Prospective Study.
8. Yuksel, M., Yilmaz, S., Tokgoz, H., Yalcinkaya, S., Baş, S., Ipekci, T., ... & Savas, M. (2015). Efficacy of silodosin in the treatment of distal ureteral stones 4 to 10 mm in diameter. *International journal of clinical and experimental medicine*, *8*(10), 19086.
9. Itoh, Y., Okada, A., Yasui, T., Hamamoto, S., Hirose, M., Kojima, Y., ... & Kohri, K. (2011). Efficacy of selective α1A adrenoceptor antagonist silodosin in the medical expulsive therapy for ureteral stones. *International journal of urology*, *18*(9), 672-674.
10. Sur, R. L., Shore, N., L'Esperance, J., Knudsen, B., Gupta, M., Olsen, S., & Shah, O. (2015). Silodosin to facilitate passage of ureteral stones: a multi-institutional, randomized, double-blinded, placebo-controlled trial. *European urology*, *67*(5), 959-964.
11. Yang, D., Wu, J., Yuan, H., & Cui, Y. (2016). The efficacy and safety of silodosin for the treatment of ureteral stones: a systematic review and meta-analysis. *BMC urology*, *16*, 1-8.