Prospective Evaluation of Silodosin for Ureteral Stone Management in Basra: Expulsion Rates and Pain

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ABSTRACT

To find out if silodosin is a safe and effective Medical Expulsive Therapy (MET) for distal ureteral stones in Basra's urology practice. The Urology Department of Basra Teaching Hospital in Iraq conducted this prospective cohort study from May 2022 to April 2023, enrolling 137 patients with solitary distal ureteral stones that were less than 10 mm in diameter. The study excluded patients with multiple stones, severe renal impairment, previous interventions, or contraindications to alpha-blockers. Participants were given Silodosin (8 mg daily) and were monitored weekly over three weeks to assess stone expulsion as well as symptom improvement. Data collected included demographic characteristics, stone characteristics, pain scores, and adverse effects. Kaplan-Meier and log-rank tests analysis were used to estimate stone expulsion rates to examine for subgroup differences. Of the 137 participants (115 males, and 22 females with an average age of 36 years), Silodosin led to an overall stone expulsion rate of 77% within three weeks. Stone size was a significant predictor of expulsion; stones <7 mm were more likely to pass spontaneously ($p < 0.05$). Male and female patients did not significantly differ in expulsion rate ($p > 0.05$). Pain scores and analgesic requirements were lower in patients whose stone expulsion was successful. Commonly reported adverse effects were retrograde ejaculation and mild dizziness. However, both of these side effects were well tolerated. Silodosin had high efficacy and a relatively good safety profile as MET for distal ureteral stones of ≤10 mm. Higher success rates in stones <7 mm were observed. This study recommends Silodosin as a primary therapy for stones smaller than 7 mm in diameter, to reduce the need for invasive interventions. Future research with larger samples and longer follow-up is recommended to further validate these findings.

Keywords: Silodosin, Medical Expulsive Therapy, Ureteral stones, Stone expulsion, Alpha-blocker, Urology

INTRODUCTION

Ureteral stones are a significant health concern, leading to severe pain, obstruction, and potential complications such as infections and renal damage[1,2]. The management of ureteral stones has evolved, with medical expulsive therapy (MET) emerging as a non-invasive option to facilitate stone passage. MET utilizes pharmacological agents to relax the ureter, thereby easing the passage of stones[3,4]. Among various agents, alpha-blockers have shown considerable promise. The effectiveness of silodosin, a specific alpha-1A adrenergic receptor antagonist, in MET, especially for distal ureteral stones, has recently drawn attention[5,6]. The effectiveness of silodosin, a specific alpha-1A adrenergic receptor antagonist, in MET, especially for distal ureteral stones, has recently drawn attention[7]. Its action results in the relaxation of smooth muscles, reducing symptoms of BPH. The same mechanism can be beneficial in facilitating the passage of ureteral stones. The high selectivity for alpha-1A receptors belonging to Silodosin is predominantly found in the ureter, making it a promising candidate for MET[8]. Studies have shown that Silodosin can significantly enhance stone expulsion rates and reduce the time to stone passage[9].

Results from studies on silodosin as a MET for ureteral stones have been encouraging. Silodosin and tamsulosin were compared in a study conducted by Taguchi et al. (2015) in patients who had distal ureteral stones[10]. According to the study, silodosin outperformed tamsulosin in terms of stone ejection rate (80% vs. 65%) and mean time to expulsion (7.3 days vs. 10.1 days). Furthermore, silodosin demonstrated a noteworthy decrease in analgesic use and pain episodes[10]. Tamsulosin is another alpha-blocker widely studied and used in MET. Several meta-analyses, including Lu et al. (2016), have confirmed the efficacy of tamsulosin in increasing stone expulsion rates and reducing expulsion time[11]. However, higher selectivity for alpha-1A receptors of Silodosin offers potential advantages. In a head-to-head comparison, Kang et al. (2018) demonstrated that Silodosin had a superior stone expulsion rate (78% vs. 64%) and faster expulsion time compared to tamsulosin[12].

Nifedipine, a calcium channel blocker, has also been used in MET. While effective, its side effect profile, including hypotension and peripheral edema, makes it less favorable compared to alpha-blockers. Della Bella et al. (2003) highlighted that nifedipine, combined with corticosteroids, could facilitate stone passage but with a higher incidence of adverse effects compared to alpha-blockers[13]. Silodosin enhances stone ejection rates, shortens the time to expulsion, and lowers pain, according to numerous clinical investigations. A randomized controlled experiment comparing silodosin versus a placebo in individuals with distal ureteral stones was carried out by Porpiglia et al. (2010). According to the study, the Silodosin group had a far greater expulsion rate (82% vs. 48%) and a shorter mean expulsion time (8.6 days vs. 14.7 days)[14]. Additionally, compared to tamsulosin, silodosin dramatically reduced pain episodes and the need for analgesics[15].

A multicenter study assessing the effectiveness of silodosin in MET was carried out by Yilmaz et al. (2016). Silodosin had an 85% stone expulsion rate with a mean expulsion time of 6.5 days, according to the study, which included 500 participants. Additionally, the study found that patient quality of life had improved and pain levels had significantly decreased[16]. Silodosin has a good safety profile and is usually well tolerated. Dizziness, nasal congestion, and retrograde ejaculation are typical adverse effects. Bensalah et al. (2008) reviewed the safety of Silodosin in MET and found that while retrograde ejaculation was reported in 20% of patients, it was reversible upon discontinuation

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of the drug. Other side effects were mild and transient. The overall incidence of adverse effects with Silodosin was lower compared to nifedipine and comparable to tamsulosin[17].

The use of MET for the treatment of ureteral stones, especially distal stones, is supported by current clinical guidelines. According to the 2016 American Urological Association (AUA) guidelines, tamsulosin and other alpha-blockers are recommended as first-line treatments for MET[18]. Silodosin, due to its high efficacy and favorable safety profile, is increasingly being considered a viable option. The potential advantages of silodosin in MET are also acknowledged in the 2020 European Association of Urology (EAU) guidelines, especially for patients with bigger distal stones[19].

Silodosin has emerged as a potent agent for MET, offering significant advantages in stone expulsion rates, time to expulsion, and patient comfort. Its high selectivity for alpha-1A receptors in the ureter makes it particularly effective for distal ureteral stones. Comparative studies have demonstrated its superiority over other MET agents like tamsulosin and nifedipine[13,15]. With a favorable safety profile and growing clinical evidence, Silodosin holds promise for widespread adoption in the management of ureteral stones[16]. Future research should focus on long-term outcomes, optimal dosing strategies, and patient selection to further refine its use in clinical practice. 137 patients with distal ureteric stones measuring 10 mm or fewer were recruited for this prospective cohort study, which was carried out at the Urology Department of the Basra Teaching Hospital between May 2022 and April 2023. Every patient who visited the urology outpatient department was prescribed silodosin. To track stone passage, patients were monitored once a week for a maximum of three weeks.

This study aimed to assess the effectiveness of Silodosin in a real-world clinical setting as well as identify the pain experience of patients.

METHODOLOGY

A prospective cohort study was conducted at the Urology Department of Basra Teaching Hospital in Basra, Iraq, from May 2022 to April 2023. The primary goal of the study was to assess the effectiveness of silodosin as an expulsive drug for ureteric stones up to 10 mm in size that are located in the distal ureters.

The study involved 137 patients, of whom 115 were males, diagnosed with distal ureteric stones of 10mm or less. Adults aged 18 years and more and who have proven ureteric stones of up to 10 mm without previous intervention were included in the study. Patients with several stones, those who had previously undergone intervention or MET for the present stone, those who had a history of alpha-blocker hypersensitivity, those who were pregnant or nursing, and those with significant renal impairment (eGFR < 30 ml/min/1.73 m2) were also excluded.

Included individuals were given Silodosin (8 mg). Patients were instructed to take the medication once daily at the same time.

Detailed demographic data (age, gender), clinical history, and baseline stone characteristics (size, location) were recorded at the very first contact with the patients. Patients were given an appointment and their telephone numbers were taken so that they could be notified of the appointment.

Patients were called weekly to obtain information about the passage of stones and they were inquired about their symptoms. A visual analog scale (VAS) was used to measure pain. Additionally, patients were urged to report side effects. There have been reports of analgesic use and co-medications.

Individual treatment options were discussed with those who did not pass stones after three weeks.

The primary outcome measure was the stone expulsion rate within three weeks. Secondary outcomes were also sought and included time to stone expulsion, pain intensity during the treatment period as well as the occurrence of adverse effects.

Data were fed into SPSS software version 25 for tabulation and analysis. Baseline characteristics were presented as summaries. Scale variables were presented as means and standard deviations while categorical ones were shown as frequency and percentage.

A comparative investigation was conducted to assess silodosin's effectiveness in ejecting stones. The stone expulsion rate over time was estimated using the Kaplan-Meier method, and expulsion rates between subgroups were compared using the log-rank test. Pain scores and analgesic use were compared using paired t-tests or Wilcoxon signed-rank tests as appropriate. Statistical significance was defined as a p-value of less than 0.05.

The study followed the Declaration of Helsinki principles. Informed consent was obtained from all participants after fully exploring the purpose behind the study. Confidentiality was confirmed and withdrawal from the study did not imply any consequence on the treatment plan as individualized and agreed upon.

RESULTS

The study involved 137 patients with lower ureteric stones of up to 10 mm size. Male patients comprised the whole bulk of the sample (115 patients that is 84%). Neither age nor stone size showed a significant difference between male and female patients (Table 1).

Table 1. Basic characteristics of the sample

		Male (N=115)	Female (N=22)	P value
Age (mean ±SD) (years)		38.6 ±11.9	36.0 ± 13.8	0.498*
Stone diameter (mean ±SD) (mm)		7.11± 2.3	6.74±2.56	0.505**
Stone size categories	**<7 mm**	73 (63.5%)	17 (77.3%)	0.316***
	7 mm or more	42 (36.5%)	5 (22.7%)	

*Student's t-test, **Mann Whitney's test, ***Chi-squared test

Stone size appeared to be significantly influencing stone expulsion. Table 2 A and B confirm that a larger proportion of stones smaller than 7 mm in diameter were likely to pass earlier in the course of the disease. This was true in females as well.

Stone expulsion did not seem to significantly vary between male and female patients (Table 3).

Table 2-A. Expulsion rate in male

Stone size	Week 1	Week 2	Week 3	Week 4	Fail to pass	P value*
<7 mm (n = 71)	21	16	13	8	13	0.021
7 mm or more (n = 44)	8	10	7	5	14	
Total	29	26	20	13	27	

* Chi-squared test

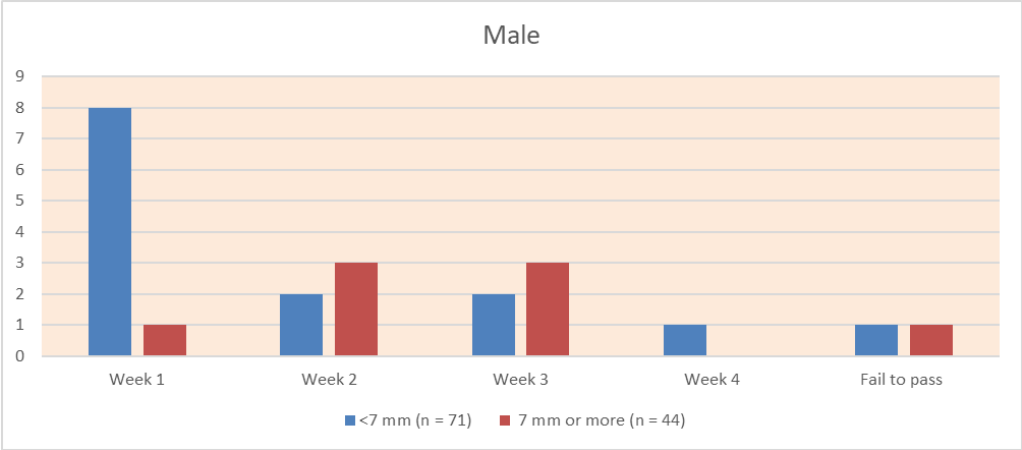

Figure 1-A. Stone expulsion rate in male patients

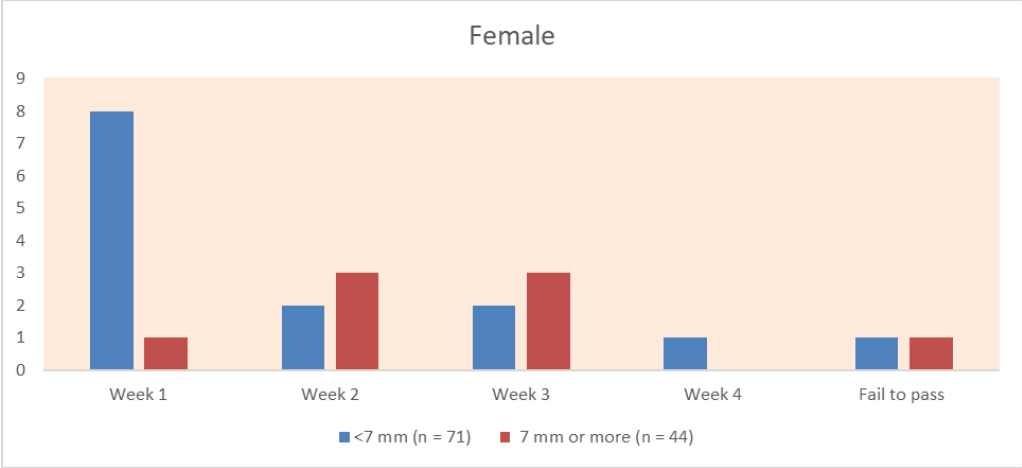

Figure 1-B. Stone expulsion rate in female patients

Table 2-B. Expulsion rate in female

Stone size	Week 1	Week 2	Week 3	Week 4	Fail to pass	P value*
<7 mm (n = 14)	8	2	2	1	1	0.006
7 mm or more (n = 8)	1	3	3	0	1	
Total	9	5	5	1	2	

* Chi-squared test

Table 3. Stone passage in male and female patients

Stone size	Week 1	Week 2	Week 3	Week 4	Fail to pass	P value*
Male	29	26	20	13	27	0.336
Female	9	5	5	1	2	

*Chi-squared test

DISCUSSION

Expulsion of ureteric stones by medical therapy varied across sex and stone size. This study explores using Silodosin as a sort of medical expulsive therapy (MET). Stone size represents a key factor in the success of expulsing ureteric stones. Hereby, this study found that stones smaller than 7 mm in diameter were significantly more likely to pass spontaneously in both sexes (p values <0.05). This finding is consistent with other studies like Segura et al. (1997) and Ueno et al. (2018) [20, 21]. Passing larger stones is a challenge to patients and doctors and it could be due to the physiological limitations of the ureters therefore stones of less than 7 mm are amenable to MET sparing larger stones to have a try keeping the plan of surgery considered all the time during the course.

Despite the anatomical and physiological differences between males and females, this study did not identify significant differences in the potential of stone passage (P value >0.05). Other studies of similar conclusions include De Coninck et al (2016) who did not find significant variation as well [22,23,24]. The hypothetical assumption that longer urethra in males can affect the passage of ureteric stones was not supported in this study.

Silodosin as an alpha blocker used as an expulsive therapy was extensively studied (Ramadhani MZ, 2023) [25,26]. This study confirms the evidence of the value of Silodosin in expulsing stones smaller than 7 mm in diameter. However, it found that stones larger than 7 mm are less likely to pass even after the lapse of 4 weeks making other interventions as valid alternative options.

This study had certain limitations including the relatively small number of female patients (n=22) opening the door for future studies with a more balanced sample size could provide more robust insights into gender differences in stone expulsion. Some confounders were not checked e.g., hydration status which can affect stone passage.

CONCLUSIONS

In summary, this study confirms the importance of stone size as a key factor in the likelihood of spontaneous expulsion especially if stones are smaller than 7 mm. Gender does not appear to significantly affect expulsion outcomes, indicating that there is no need to tailor treatment according to sex alone. It is recommended that silodosin be used as a first-line therapy for smaller size stones and spare other interventions for larger ones.

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Competing Interest: None

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