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RESEARCH ARTICLE
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SILODOSIN AS A MEDICAL EXPULSIVE THERAPY FOR DISTAL URETERAL STONES IN THE PAKISTANI POPULATION

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Abstract

Purpose: Renal stones are a one of leading problems in today's world. Along with renal stones, ureteral stones also cause significant disturbance in daily living. Objective of this research is to determine the efficacy of Silodosin, a selective alpha receptor blocker, in the Pakistani population for treatment of distal ureteral stones.

Materials and methodology: This Prospective Cohort study was conducted at Urology Department, KRL Hospital Islamabad from May 2021 to April 2022. Our study comprised 160 individuals with distal ureteric stones of 10mm or less. Silodoso (Silodosin) was prescribed to all patients who came to the urology outpatient department, and their contact information was recorded. Patients were called for follow-up on a weekly basis for up to 3 weeks to make sure that the stone was passing through their urine. The significance of p-value less than 0.05 and odds ratios were examined using the Chi-square test and risk variables for distal ureteral stones. Quality of life was assessed using the Wisconsin Stone (WISQOL) questionnaire.

Results: A whopping 94% of the stones were expelled taking an average of 7.17 days. There are 6.6 times increased risks of forming a stone that is at least 5 mm in diameter in patients between the ages of 41 and 80. Men were 1.4 times more likely than females to have ureteric stones (odds ratio = 1.486, 95 per cent confidence interval [CI] = 1.302-1.696">OR = 1.486). The average quality of life improved after the treatment was 38.87.

Conclusion: According to the results of this study, silodosin is regarded as safe and effective in the treatment of non-complicated distal ureteral stones ranging from 4 to 7 mm in diameter. The cost-effectiveness of silodosin gives it an edge over other alpha-blockers for medical expulsive therapy.
Research Registration: Chinese Clinical Trial Registry (ChiCTR2200060517)

Keywords: Medical Expulsive Therapy, Renal Colic, Silodosin, Ureteral Calculi, Urolithiasis, Alpha-blocker, Lifestyle

Introduction:

Renal stones are one of the leading problems in today's world, leading to multiple urologist consultations as it carries along notable morbidity and affects lifestyle.[1] Along with renal stones, ureteral stones also cause significant disturbance in daily living as well as a common problem faced in the primary healthcare system.[2] Ureteral stones have an incidence of 3%-18% in various geographical areas.[3]

The four main types of ureteral calculi which combinedly are associated with more than 20 underlying etiologies include calcium stones, struvite (magnesium ammonium phosphate) stones, uric acid, and cysteine stones. Management options for ureteral stones include watchful waiting for spontaneous expulsion, extracorporeal shock wave lithotripsy, medical expulsive treatment, and open and laparoscopic uretero-lithotomy.[4]

Various pharmacological agents are used in medical expulsive therapy (MET), which include calcium channel antagonists, alpha-blockers, phosphodiesterase inhibitors, and corticosteroids. Among these, alpha-blockers are most effective and commonly used one is tamsulosin.[5] Since tamsulosin is widely used in studies and has been proven to play an important role in the treatment of MET for a long time, it has been widely accepted. Silodosin (Silodoso), a drug with higher alpha 1a selectivity that is increasingly being used in MET, may be more effective than tamsulosin, according to recent research. Clinical trials on the medical treatment of ureteral stones are scarce and controversial to date.[6]

As a selective alpha-blocker, silodosin is another effective medication for relieving symptoms of the lower urinary tract by determining smooth muscle relaxation in bladder and prostate tissue. Stone expulsion time is improved and analgesic use is reduced by silodosin. Distal ureteral stones between 4 and 10 millimeters in diameter can be more easily expelled with silodosin, according to research.[7],[8],[9] Moreover, silodosin showed greater efficacy and safety in comparison with tamsulosin.

After a comprehensive literature search about the emerging drug and its efficacy, we aim to determine the efficacy of silodosin drug for the treatment of distal ureteric stones. This is the first research done on the Pakistani population for determining the efficacy of silodosin.

Material and Methodology:

This Prospective Cohort study was conducted at Urology Department, KRL Hospital Islamabad from May 2021 to April 2022. A sample size of 160 cases was calculated with a confidence interval of 95%, a margin of error of 5% having a prevalence of ureteric stones at 15%.[3] The non-probability consecutive sampling technique was used. Our study has been registered on Chinese Clinical Trial Registry with the following registration number: ChiCTR2200060517.[10] In accordance with the STROCSS 2021 recommendations,[11] we conducted this study. As an added bonus, a detailed STROCSS 2021 check list may be found in the supplemental materials

Inclusion and Exclusion criteria:

All the patients regardless of gender coming to the urology outpatient department of KRL hospital with distal ureteric stone of 10mm or less as confirmed by ultrasonography kidney ureter bladder were included in our study. Patients previously taking any medication or any other invasive procedure were excluded from our study. Patients with pyelonephritis, fever, interactable pain, or having creatinine deranged were also excluded from our study.

Data collection procedure:
The data collection was approved by the hospital's ethical committee, Ref ERC: KRL-HI-ERC/May/16-05 Dated: 16th May 2021. Silodoso (Silodosin) was prescribed to all patients who came to the urology outpatient department, and their contact information was recorded. Patients were called for follow-up on a weekly basis for up to 3 weeks to make sure that the stone was passing through their urine. Record of the exact day when the stone was passed, size, number, and time of presentation were among the data gathered. Additionally, quality of life was recorded before starting the treatment & at the end of treatment.

Data analysis:
Data was analysed using SPSS Version 26. Quantitative variables included age, gender, stone size & stone-free rate were presented as frequencies and percentages. Pearson's Chi-square test was applied to see the significance considering a p-value less than 0.05 & Odds ratios to assess risk factors of distal ureteral stones. Wisconsin Stone (WISQOL) questionnaire was used to assess the quality of life.

Results:
There were 35 (21.87%) females and 125 (78.13%) males in our study. The average age was 38.25 years old, as shown in Table I.

Variables	Frequency	Percentages
Gender		
Male	125	78.13
Female	35	21.87
Age		
19-40 years	91	56.87
41-80 years	69	43.13

The diameter of the stones ranged from 3mm to 10mm. The most prevalent stone sizes were between 4 to 7 milli meters. The average number of days between removing a stone was 4-7. 22(13.75%) patients reported the stone expelled after four days, 25(15.62%) patients reported having their stones ejected after five days, 35(21.87%) patients after six days, and 26(16.25%) patients after seven days, while 6(3.75%) and 7(4.37%) patients had their stones expelled after 13 days and 21 days, respectively, according to the data provided. After three weeks, ten patients (6.25%) reported that the stone had not passed, and five of those had surgery, as shown in Figure I..

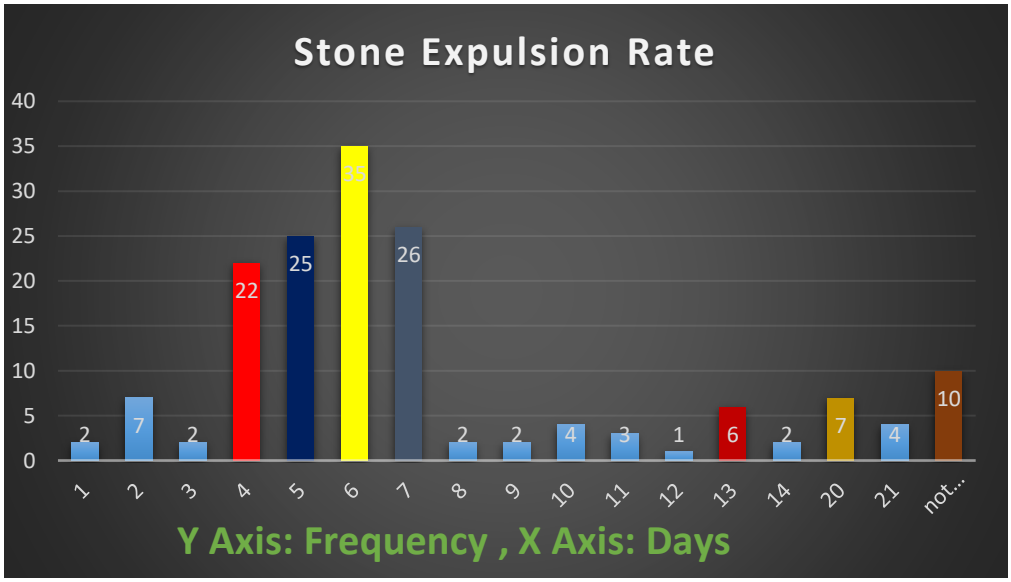

Figure I: Bar Graph Showing Stone Expulsion Rate

Stone size was compared to the expulsion rate, gender & age group of patients. Stone size less than 5mm was expelled out in 20(37.7%) patients during 6-10 days & 12(22.64%) patients during 11-15 days who belonged to 41-80 years age group specifically males in dominance. Whereas 58(54.20%) patients expelled during 1-5 days and 49 (45.80%) expelled during 6-10 days out of which 72(67.28%) were males and 35(32.72%) were females, which mostly belonged to 19-40 years age group (85.04%) and 16(14.96%) from 41-80 years age group. Having a significant p value 0.00, as shown in Table II.

Stone Size	**Stone Expulsion in Days** 1-5	6-10.	11-15.	16-20.	not expelled	**Gender** Male.	Female	**Age (in Years) 19-40.**	**41-80**	**P value**
less than 5mm	0	20	12	12	9	53	0	0	53	0.00
More than 5mm	58	49	0	0	0	72	35	91	16	

Table II: Comparison of Stone Size, Stone Expulsion Rate with Gender & Age Group

Patients with age group41-80 years have 6.6 times more chances of developing the stone preferably more than 5mm in size (OR = 6.688, 95% CI = 4.256-10.508). whereas male patients were 1.4 times more prone to develop the ureteric stones (OR = 1.486, 95% CI = 1.302-1.696), as presented in Table III.

Variables	**Odds ratio**	**95% Confidence Interval**	**P Value**
Age (41-80) years	6.688	4.256-10.508	0.00
Gender (Male)	1.486	1.302-1.696	0.00

Table III: Odds Ratio & Confidence Interval of Age & Gender

Average Quality of life scoring was 41.61 before starting the treatment whereas it increased to an average of 87.25 after the treatment, as shown in Figure II.

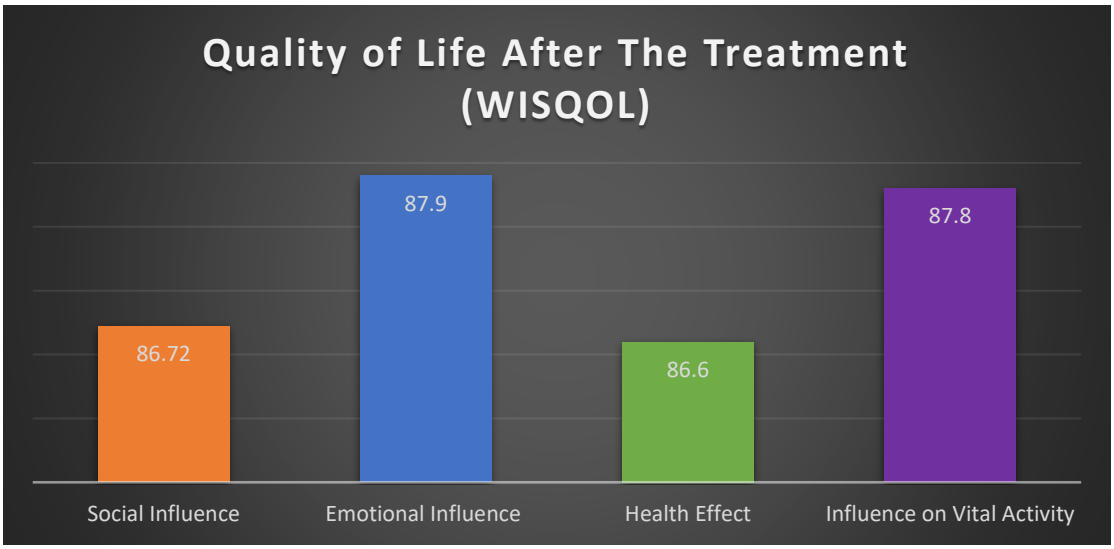

Figure II: Quality of Life Scoring After the treatment according to WISQOL Scoring

Discussion:

Our study provides details on the safety and efficacy of silodosin as a selective alpha-1a adrenergic antagonist. To the best of our knowledge, this is the first study conducted in Pakistan with this aim.

According to our study, all the patients having distal ureteral stones greater than 5 mm were able to expel it/them within 10 days of medication. This is in accordance with the findings of a meta-analysis by Ding et al. where distal ureteral stones greater than 5 mm had a significant expulsion rate.[12]
The total expulsion rate in our study is way higher than the expulsion rate in a study conducted by Sahin et al. where the expulsion rate was 75%.[13] Our study also reported a significant association between stone size and expulsion rate which was in accordance with the findings of Yuceturk et al.[14]
Participants having stones less than 5mm and greater than 5mm shows much improved efficacy in our study than the one conducted by Bayar et al. where expulsion rates were 66.7% and 64.3% for stones less than 6mm and equals to or greater than 6mm respectively.[8]
The efficacy of silodosin in our study was also better than the study conducted by Arda et al. where the stone expulsion rate was 78.6%.[6] The only study that shows better expulsion rates than our study was by Imperatore et al. where it was 95.8% for less than or equal to 5mm and 80.8% for greater than 5mm stones.[15]
Our study reported 1.48 times increased chances of developing ureteral stones in males than in females which is contrary to the findings of another study where no significant gender difference was noted.[14] The findings of Arda et al. are in accordance with ours as they had more men.[6]
Bayar et al. reported the mean days of stone expulsion as 7.1 days, which is similar to that of our study[8] but way lesser than another study[14] where they reported it to be 16 days on average which proves better efficacy of silodosin in our study. The only study to report lesser mean days for expulsion as compared to our study is by Imperatore et al [15] who reported it as 6.7 days although the value was insignificant. Quality of life improved after treatment with silodosin in our study but alpha-blockers (including silodosin) did not show any promising results in a meta-analysis performed by Oestreich et al.[16] A recent meta-analysis by Hsu et al. includes certain Randomized control trials (RCTs) that displayed silodosin as a superior drug to tamsulosin.[17] Post-treatment retrograde ejaculation was found to be a common side effect amongst 2 meta-analyses.[12],[17] Manjunatha et al. in their prospective analysis compared the cost-effectiveness of Silodosin with other alpha-blockers, where they reported it to be somewhat cost-effective but not as much as alfuzosin.[18]

Strengths and Limitations:
Being the first study in Pakistan to comment on silodosin's efficacy on distal ureteral treatment conducted gives it an edge. The limitations of our study include the small sample size; we did not compare silodosin's efficacy with other alpha-blockers.

Conclusion:
According to the results of this study, silodosin is regarded as safe and effective in the treatment of non-complicated distal ureteral stones ranging from 4 to 7 mm in diameter. Young males should avoid silodosin due to the chances of retrograde ejaculation.
Further research comparing silodosin with other drugs of the same class will yield more conclusive results on the effectiveness and side effects of the two drugs.
Lifestyle guidance is the major method of preventing recurrence in patients who have formed calcium and/or uric acid/urate stones. The cost-effectiveness of silodosin gives it an edge over other alpha-blockers for medical expulsive therapy.

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