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Effect of Alpha-Blocker on Distal Ureteric Calculi: A Comparative Study

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Abstract:-

➢ ***Introduction***

Silodosin is a recently introduced selective alpha-blocker in Medical Expulsive Therapy for the management of distal ureteric calculi. The efficacy and safety of silodosin compared to tamsulosin are controversial, however the former is considered to be more effective. The objective of the study is to assess the efficacy and safety of silodosin compared to tamsulosin in the treatment of ureteral stones less than 10mm.

➢ ***Methods***

This prospective randomized study was conducted in the Department of General Surgery, Navodaya Medical College, Raichur, Karnataka. Sixty patients were included in the study who presented with abdominal or loin pain and were diagnosed with unilateral solitary distal ureteric stone measuring <10mm with no complications. Participants in Group I received Tablet Silodosin 8mg OD until the passage of stone or up to two weeks, and Group II received Tablet Tamsulosin 0.4mg OD until the passage of stone or up to two weeks. Analgesic Tablet Diclofenac sodium 50mg was given to both patients on demand.

➢ ***Results***

A total of 60 patients were included in the study, divided into 30 patients in each group of Silodosin and tamsulosin respectively. In Group I (silodosin), out of 30 patients, 25 patients expelled the calculus, whereas in Group II (tamsulosin), out of 30 patients, 15 patients expelled the calculus. Group I showed a significantly higher rate of expulsion, with a p-value of 0.005. Stone expulsion time was notably shorter in Group I compared to Group II, with averages of 4.73 days versus 6.33 days (p=0.009). Additionally, analgesic use during the medical expulsive therapy was lower in Group I, averaging 8.25 compared to 4.13 (p=0.0001) in the tamsulosin group. Significant differences were observed in the outcomes such as stone expulsion time, and analgesic requirement. However, no significant differences were found when comparing the groups based on age, gender, stone size, and side of the ureter involved.

The 20 patients who failed the medical management underwent ureterorenoscopy with 100% clearance. 3 patients in Group II experienced orthostatic hypotension, and zero patients experienced any side effects in Group I. Compared to tamsulosin, silodosin provides significantly higher stone expulsion rates, fewer colic episodes, and shorter stone expulsion duration than tamsulosin.

Keywords:- *Medical Expulsive Therapy, Silodosin, Tamsulosin, Distal Ureteric Calculus.*

I. INTRODUCTION

Urolithiasis presents a significant clinical and financial challenge to modern healthcare systems. International epidemiological data indicate a rising incidence of kidney stone disease (KSD), with a lifetime prevalence of approximately 14% and a recurrence rate of 50% or more within 10 years[1]. Although KSD primarily affects individuals between the ages of 40 and 60, there is a concerning increase in diagnoses among young adults and children. Despite the growing use of minimally invasive procedures, medical expulsive therapy (MET) remains a well-established treatment option for distal ureteric stones [2].

Factors influencing spontaneous stone passage include the stone's location, size, and number; ureteric spasm; mucosal edema or inflammation; and ureteric anatomy. Ureteric spasms induced by stones can hinder stone evacuation. Recently alpha-blockers, which target alpha-1 receptors abundant in the distal ureter, and reduce basal smooth muscle tone and hyperperistalsis while preserving tonic propulsive contractions, have been used as MET [1]. Tamsulosin, a selective alpha-1 blocker, has shown good results in MET. The use of Silodosin, a more selective alpha-1 blocker, is said to demonstrate superior efficacy compared to tamsulosin for MET with fewer side effects.

Thus a prospective study was planned to compare the efficacy of silodosin to tamsulosin in the management of distal ureteric stone in terms of stone clearance rate, stone expulsion time, potent analgesic, and associated side effects.

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II. MATERIALS AND METHODS

After approval of our Ethics Committee Board, a prospective randomized controlled study was conducted from November 2022 to January 2024 in the Department of General Surgery Navodaya Medical College, Raichur.

The inclusion criteria for the study included ages between 18 years to 60 years of age, with a diagnosis of a symptomatic, unilateral, single distal ureteral calculus, diagnosed with either sonography of KUB or X-ray KUB, with a size ranging from 4mm to 10mm. Prior to the study, all patients underwent a complete hemogram, renal function test, complete urine examination, and urine culture sensitivity. Stone presence and its characteristics were noted with the help of X-ray KUB, Abdominal ultrasonography, and if required computed tomography.

Patients presenting with active urinary tract infection, fever, multiple calculi, moderate to severe hydroureteronephrosis, acute or chronic renal failure, any previous renal or endourological surgeries, associated comorbidities, hypersensitivity to alpha-blockers, and pregnant women, were excluded from the study.

A Total of 60 symptomatic patients were randomly divided into Group I (Silodosin) and Group II (Tamsulosin).

- Group I (Silodosin): 30 patients in this group received Tablet Silodosin 8mg once daily in the evening until the passage of the stone, or up to 2 weeks along with analgesics (Tablet Diclofenac Sodium 50mg) as per demand.
- Group II (Tamsulosin): 30 patients in this group received Tablet Tamsulosin 0.4mg once daily in the evening until the passage of the stone, or up to 2 weeks along with analgesics (Tablet Diclofenac Sodium 50mg) as per demand.

Weekly follow-up of patients was done until the passage of calculus or up to 4 weeks.

Age, Gender, Calculus size, side of the ureter involved, calculous passage time, failure of spontaneous expulsion of stone, analgesic requirement, and any adverse effects to the drugs were noted. Spontaneous passage of stone was considered as the primary endpoint of the study.

➢ *Statistical Analysis*

Processing of the data is done with the SPSS software. The obtained data was entered in the Excel spreadsheet and presented through tables. The descriptive statistics were calculated by arithmetical average and standard deviation. Testing of the qualitative data was done using the X^2-test, and an independent sample t-test was applied to compare quantitative parameters. The level of significance was set at 5%.

III. RESULTS

A total of 60 patients were included in this study. 30 patients were in each group, i.e., the silodosin group and the tamsulosin group. Out of the 60 patients, 46 patients were males (76.6%) and 14 patients were Females (23.3%). Their ages ranged from 18 to 65 years with mean age being 43.20 +/- SD 13.80 in Group I and 40.27 +/- SD 17.76 in Group II. The X^2-test did not show any statistical significance in both the parameters (p=0.542 and p=0.478 respectively). The average size of the stones of the patients included was 6.87 mm (SD +/- 0.77 mm) in Group I, whereas in Group II was 6.93 mm (SD +/- 1.01) with a p-value of 0.478, thus not significant.

TABLE I. AGE AND SEX DISTRIBUTION

	Group I		Group II		Total		P-value
	N	*%*	*N*	*%*	*N*	*%*	
Total	30	100	30	100	60	100	
Male	22		24		46	76.6	
Female	8		6		14	23.3	0.542
Age (Mean)	40.27 +/- 17.76		43.20 +/- 13.80		41.73 +/- 15.78		0.478
Stone Size	6.93 +/- 1.01		6.87 +/- 0.77		6.9 +/- 0.89		0.478

In 48.3% of the cases, stones were located on the left side of the ureter and 51.7% on the right side of the ureter, with no statistical significance. In the study during the follow-up, 40 patients expelled the stone with MET of which 25 were in the Silodosin Group and 15 were in the Tamsulosin Group. This observation had a significant p-value of 0.005. The patients who didn't expulse the stone underwent endourological intervention (ureterorenoscopy) with 100% stone clearance. The observation noted in the failed expulsion was mainly due to chronic pain and the larger size of the ureteric stone.

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TABLE II. STONE EXPULSION TIME AND ANALGESICS

	Group I		Group II		Total		P-value
	N	*%*	*N*	*%*	*N*	*%*	
Stone Expulsed							
Expulsed	25	83.33	15	50	40	66.67	
Not Passed	5	16.67	15	50	20	33.33	0.005
Analgesic	4.13 +/- 1.40		8.25 +/- 1.29				0.0001
Mean Expulsion Time (days)	4.73 +/- 1.31		6.33 +/- 1.03		5.53 +/- 1.17		0.009

The average time of expulsion of stone in Group I was 4.73 days with an SD of 1.313 whereas in Group II average expulsion time was 6.33 days with an SD of 1.033 showing statistical significance (p=0.009). The mean analgesic requirement was higher in Group II (8.25) than in Group I (4.13). Using the T-test, we found a statistically significant difference between the analgesic doses used across groups (P=0.0001)

TABLE III. SIDE EFFECTS OF ALPHA BLOCKERS

	Group I		Group II		Total	
	N	*%*	*N*	*%*	*N*	*%*
Dizziness	2	6.67	5	16.67	7	23.33
Hypotension	0	0	3	10	3	10
Retrograde Ejaculation	0	0	0	0		0
No Side Effects	28	93.33	22	73.33	50	83.33

IV. DISCUSSION

The lifetime prevalence of renal stones is estimated to be 1% to 15% and can vary according to age, gender, race, climate, and geographic location, with a recurrence rate being as high as 50% in the first 10 years [1]. As renal stones form, a cascade of events leads to early-stage irreversible apoptotic changes, hence the role of appropriate treatment is required[3].

Minimally endo-urological procedures such as ureterorenoscopy and SWL have proved their effectiveness in stone clearance, however, they are expensive and present multiple risks. Around 50% of DUS pass spontaneously with conservative management up to 6mm but can be associated with complications such as ureteric colic, UTI, and hydroureteronephrosis. With the introduction of MET for DUS, it has been studied to reduce pain and complications and increase the rate of stone expulsion, including stones of larger size.

The α1A- and α1D-adrenoceptors are the predominant subtypes in the distal ureter. Stimulation of these receptors increases both the frequency and force of ureteric peristalsis and contractions. In contrast, blocking these receptors reduces basal ureteric tone and decreases peristaltic frequency and amplitude, leading to lower intra-luminal pressure and increased urine transport rate, which enhances the likelihood of stone passage [4]

Highly selective α1A-adrenoceptor blockers have been developed to minimize cardiovascular side effects while preserving their efficacy on the urinary tract [5]. Tamsulosin is a selective α1-blocker with a tenfold greater affinity for the α1A- and α1D-adrenoceptor subtypes compared to the α1B-adrenoceptor subtype. Similarly, silodosin shows approximately 162-fold and 50-fold greater affinity for the α1A-adrenoceptor compared to the α1B- and α1D-adrenoceptor subtypes, respectively, which accounts for its relatively mild cardiovascular side effects.

There are multiple factors that influence spontaneous stone clearance such as the size of the stone, site, presence or absence of sub-mucosal edema, and presence or absence of spasm of the ureteric smooth muscle. A study by Coll et al[6]. showed a direct relationship between stone size and spontaneous clearance.

Our present study showed a higher clearance rate in the silodosin group compared with the tamsulosin group at 83.3% and 50%, respectively (p=0.005). These results are in agreement with a study conducted by Hazem et al.[7], who reported a stone clearance rate of 83% and 57% for their silodosin and tamsulosin groups respectively. a study by Gupta et al[8]. showed similar results of 82% and 58% of stone clearance rates respectively.

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A study by Abdullah et al [9]. reported a significant stone expulsion time in the silodosin group vs tamsulosin to be 10.15 vs 13.4 days respectively. Similarly, our study had a short stone expulsion time in the silodosin group (4.73 vs 6.33, p=0.009). A study conducted by Itoh et al. had similar findings in the expulsion time in the silodosin group of 11.33 days when compared to the tamsulosin group of 21.09 days[10]. However, Imperatore et al.[11] reported a mean stone expulsion time of 6.7 days for silodosin and 6.5 days for tamsulosin, indicating a shorter duration for both medications.

The results of the present study indicate a low mean number of pain episodes in both groups with subsequently lower analgesic requirement of 4.13 in the silodosin group as compared to 8.25 in the tamsulosin group showing statistical significance (p=0.0001). Similarly Abdullah et al[9]. reported that analgesics required by the silodosin group were significantly lesser compared to tamsulosin (5.6 vs 8.4, p=0.002). Whereas Yuksel et al[12]. found that silodosin improved the expulsion of stone but had minimal effects on ureteric colic episodes or analgesic requirements. The pain-relieving effects of α-blockers may be attributed to their action on C-fibres, which are responsible for mediating pain.

A systematic review and meta-analysis conducted by Huang et al. found that silodosin was associated with a higher expulsion rate, shorter expulsion time, and fewer pain episodes compared to tamsulosin [13]. They also noted that silodosin had a higher incidence of abnormal ejaculation than tamsulosin, although this difference was not statistically significant. In contrast, another meta-analysis of randomized controlled trials by Liu et al. reported no significant differences between silodosin and tamsulosin in terms of expulsion time, analgesic use, or retrograde ejaculation [14].

No patients were discontinued from the study due to intolerance to the medication or adverse effects. Orthostatic hypotension was reported in three (10%) patients in the tamsulosin group whereas the silodosin group of patients did not present with this complaint, which was not statistically significant.

The limitations noted in this study included a smaller sample size and a lack of in-depth assessment of other drug side effects, such as retrograde ejaculation.

V. CONCLUSION

At the end of our study, we found that silodosin was more efficient for the conservative management of distal ureteric calculus measuring less than 10mm as compared to tamsulosin. Using silodosin in our patients led to a reduction in the frequency of ureteric colic episodes and decreased the intensity of the pain. It also increased and accelerated stone expulsion rates, shortened the duration of stone expulsion, and decreased the need for analgesics. Silodosin had better patient compliance and hence should be considered for managing uncomplicated distal ureteral stones over Tamsulosin. Nevertheless, large-scale studies are required to further confirm its efficacy and safety.

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