

A Prospective Study Of Comparison Between Alfuzosin, Tamsulosin, Silodosin And Tadalafil As A Medical Expulsive Therapy For Lower Ureteric Stones Of Size ≤ 10 Mm

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I. Introduction:

Stone disease is one of the most common affections of modern society and it has been described since antiquity. Urolithiasis is a chronic disease, a substantial economic consequence and great public health importance^{1, 2}. 20% of all urinary tract stones are found in the ureter and of all ureteric stones, 70% are found in the lower third of the ureter. For lower ureteric stones there are many modalities like watchful waiting^{3,4}, MET (medical expulsion therapy), ESWL and Ureteroscopic removal depending on many factors like size of stones, presence and grade of hydronephrosis, sepsis, duration of the stone present. Stone expulsion and the time of the expulsion of ureteric stones depend on stone size and location³.

⁹. Urologist intervention is recommended for ureteric stones that persist for more than two months¹⁰. MET is an option in selected patients and many studies are in favour of this¹¹⁻¹⁷. Alpha 1 Blocker¹⁴⁻¹⁷ and calcium channel blockers, Deflazacort, and Tadalafil have been used in various studies. The Deflazacort density of alpha 1 adrenergic receptors in the ureteral smooth muscle wall is significantly greater than other adrenergic receptors. Alpha 1 adrenergic antagonist inhibits basal tone peristaltic frequency and ureteric contraction¹⁸. TAMSULOSIN and ALFUZOSIN are alpha 1 selective whereas SILODOSIN is an alpha 1 A selective agent. PDE 5 (Tadalafil) acts on NO/cGMP pathway urethral relaxation. We did this study to know the efficacy and effectiveness of Alfuzosin, Silodosin, Tadalafil, and Tamsulosin as MET

II. Material Method :

From August 2022 to November 2021 prospectively we enrolled a hundred patients randomly from 18 to 60 years of age of both sexes. Diagnosis of stone is confirmed with NCCT KUB.

Inclusion Criteria:

Stone size ≤ 10 mm, Stone distance $10 \leq$ cm from VUJ, Either site of stone (Left / Right)

Exclusion Criteria:

B/L stones, multiple ureteric stones, Ureteric stones with renal stones, Stones with hydronephrosis, Stones with CKD / AKI or both, Stones with sepsis with features of high-grade fever with chills and rigour.

Approval from the ethical committee was taken down. Informed consent of MET and alternative method is done.

Drug used are Alfuzosin 10gm/day (FLOTAL), Tamsulosin 0.4 MG (VELTAM, URIMAX), Silodosin 8mg/day (RAPILIF, GERIPOD), Tadalafil 5mg/day (MODULA). Tab ACECLOFENAC PARACETAMOL SOS in pain.

Patients who had uncomfortable MET, the option of URSL was given. Demographic data of age, sex, weight, height, and BMI were noted with the site of stones. Patient having symptoms of ureteric stones and having USG suggestive of ureteric stones underwent NCCT KUB region on 128 Slice CT scan machine. Stone distance from VUJ, stone diameter, stone volume with HU, HUD noted. CT scan reporting did by the different radiologists as per the radiology department rotation. All the radiologists were faculty ranks of assistant

professors and above. The largest stone diameter was measured on Longitudinal, transverse and axial images.HU and stone volume were calculated with CT. HU was calculated as HU divided by the stone diameter.

For the study, we have arranged the 4 drugs in alphabetical order (Alfuzosin, Silodosin, Tadalafil, and Tamsulosin) and prescribed them to the patients in the same order cycles so that there are least chances of interviewer/selection bias. We followed the patient after 6 weeks; patients who did not turn up at 6 weeks were communicated with the phone call. At 6 weeks, we did the NCCT KUB test.

III. Results:

A total of 100 patients were included in the study and randomized into 4 equal groups of 25 patients each by the use of a computer-based data entry system. Out of 100 patients, 88 patients were continued till the study was completed except 12 patients who absconded from the study. Out of 100 patients, 63 were male and 37 were female, 46 were on the left side and 54 are on the right side. Stone diameter, stone volume and distance from VUJ were measured from NCCT KUB. Tables 1, 2 and 3

Table-1: Comparison of Anthropometry and Stone Characteristics among Drugs Advise

Parameters	Alfuzosin		Silodosin		Tadalafil		Tamsulosin		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F-value	p-value
AGE	41.44	8.87	36.84	10.71	41.28	8.98	37.64	13.30	1.280	.286
HEIGHT	166.92	5.87	167.04	5.95	167.12	4.82	167.16	5.26	.009	.999
WEIGHT	73.60	6.78	71.72	7.64	70.68	7.77	72.20	9.17	.592	.622
BMI	26.46	2.40	25.66	2.13	25.36	3.06	25.78	2.67	.792	.501
STONE DIAMETER	6.17	1.88	6.72	1.85	7.08	1.70	6.34	1.47	1.382	.253
STONE VOLUME	116.88	89.99	142.39	83.78	160.82	89.17	115.87	80.88	1.589	.197
DISTANCE	6.72	1.79	6.44	1.94	6.80	1.69	6.42	1.97	.280	.840

Table – 2: Comparison of Sex, Stone Position and Surgical Interventional among Drugs Applied

Drug		Alfuzosin		Silodosin		Tadalafil		Tamsulosin		chi sq	p-value
		No.	%	No.	%	No.	%	No.	%		
SEX	Female	6	24.0%	9	36.0%	8	32.0%	14	56.0%	5.96	0.113
	Male	19	76.0%	16	64.0%	17	68.0%	11	44.0%		
STONE SITE	LEFT	10	40.0%	10	40.0%	17	68.0%	9	36.0%	6.60	0.086
	RIGHT	15	60.0%	15	60.0%	8	32.0%	16	64.0%		
SURGERY PERFORMED	No	25	100.0%	25	100.0%	24	96.0%	24	96.0%	2.04	0.564
	YES	0	0.0%	0	0.0%	1	4.0%	1	4.0%		

Alfuzosin group had 25 patients out of which 22 turned up at 6 weeks and 15 patients expelled the stone, in 7 patients the stone was not expelled and 3 patients didn't turn up for the follow-up. Expulsion rate was 68.2 %.

Silodosin group had 25 patients out of which 23 turned up at 6 weeks and 18 patients has expelled the stone, in 5 patients the stone was not expelled and 2 patients didn't turn up for the follow-up. The expulsion rate was 78.3 %.

Tadalafil group had 25 patients out of which 21 turned up at 6 weeks and 12 patients expelled the stone, in 8 patients the stone was not expelled and 4 patients didn't turn up for the follow- up and 1 patient opted for the surgical intervention. The expulsion rate was 60%.

Tamsulosin group had 25 patients out of which 22 turned up at 6 weeks and 17 patients expelled the stone, in 4 patients the stone was not expelled and 3 patients didn't turn up for the follow-up and 1 patient opted for the surgical intervention. The expulsion rate was 81%. Table 4

Table – 4: Association of Stone Expulsion with Drug Applied

Stone Expulsion	DRUG								chi sq	p- value
	ALFUZOSIN		SILODOSIN		TADALAFIL		TAMSULOSIN			
	No.	%	No.	%	No.	%	No.	%		
Yes	15	68.2%	18	78.3%	12	60.0%	17	81.0%		
No	7	31.8%	5	21.7%	8	40.0%	4	19.0%		

Total	22	100.0 %	23	100.0 %	20	100.0%	21	100.0%	2.88	0.411
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IV. Discussion:

Lower ureteric stones and small stones have the property of self-expulsion and little assistance to them with medicine can enhance their expulsion. The likelihood of ureteral stone passage is dependent on several factors which include the stone size, location of stones and ureteral conditions. Watchful waiting with drugs and interventions like ureteroscopic removal have their pros and cons. A watchful waiting approach can result in complications such as UTI, repeated ureteric colic, hydronephrosis and renal function deterioration and in complete obstruction kidney may be irreversible damaged in 4 weeks. Problem-related to interventions are hospitalisation and anaesthesia risk. Overall complication rate with ureteroscopic lithotripsy is in the range of 10 to 20% with major complications like; ureteral perforation, ureteral avulsions and strictures occurring in 3-5 % of cases¹⁹. Veno et al in their study shows that in stones <4 mm, 4-6mm and >6 mm the rate of spontaneous passage was 80%, 59%, and 21% respectively. Proximal ureteric stone spontaneous passage rates are 10%

- 25% and for distal ureteric stones 25% - 53%. Several drug-like alpha-adrenergic blockers, calcium channel blockers, prostaglandins synthesis inhibitors, glyceryl nitrate and steroids have been used as MET^{13,18,20,21}. The role of the adrenergic receptor in the ureter was first described in 1970²². Alpha-adrenergic antagonist decreases the amplitude and frequency of peristalsis, which results in a decrease in intra-ureteral pressure. They prevent uncoordinated muscle activity which is seen in renal colic while maintaining ureteral peristalsis without facilitating a spontaneous stone passage²³ and increasing urine transport²⁴. Alpha-adrenergic receptors were classified into 3 different subtypes α 1A α 1B α 1D and in ureteric distribution is α 1D > 1A > α 1B²⁵. There are many studies with different drugs which showed that these drugs are effective in the expulsion of stones with their selection criteria¹¹⁻¹⁷.

In our study we observed these drugs(Alfuzosin, tamsulosin, silodosin and tadalafil) with slightly different mechanisms of action have a great impact on stone expulsion with our strict inclusion criteria but statistical significance was not proved. The expulsion rate was lowest with tadalafil and highest with tamsulosin and no drug is significantly better than others.

Limitation of study. The sample size is small

V. Conclusion.

All four drugs have good outcomes as MET in selected patients. Our results are comparable to other studies. Our sample size is small and needs a larger sample size for generalisation of results.