

Effect of Tamsulosin and URSL on Renal Function and Stone Free Rate in Unilateral Solitary Ureteric Stone: A Prospective Interventional Study

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ABSTRACT

Introduction: Stones are common cause of obstructive uropathy which may lead to decrease in renal function. Though endourological procedure like Ureteroscopic Lithotripsy (URSL) is commonly done, yet, Medical Expulsive Therapy (MET) is often offered as a first line therapy for mid and distal ureteric stones of size less than one cm.

Aim: To compare the effect of Tamsulosin and URSL on renal function and stone free rate for solitary mid and distal ureteric stone.

Materials and Methods: This prospective interventional study was done in IPGME&R and SSKM Hospital, Kolkata, West Bengal, India, from May 2020 to October 2020, on the total study population of 50 patients with 26 patients in MET and 24 patients in URSL group. Parameters measured and compared were changes in Glomerular Filtration Rate (GFR) and stone free

rate after six weeks of intervention. Numerical variables and categorical variables were compared between two groups using independent t-test and Chi-square test respectively.

Results: The mean age of patients in MET (n=26) and URSL group (n=24) was 37.12 years and 33.63 years, respectively. GFR was significantly increased after completion of treatment in individual groups (p-value=0.01) and in final study population but change in GFR was not significant, when compared between the groups (p-value=0.372). Difference in stone clearance rate between two groups was also insignificant (p-value=0.902) whereas, within the groups was significant (p-value <0.05).

Conclusion: Tamsulosin for six weeks does not result in significant functional loss in the affected kidney and proved as effective as URSL for mid and distal solitary ureteric stone upto one cm in size with similar stone free rate.

Keywords: Glomerular filtration rate, Obstructive uropathy, Ureteroscopic lithotripsy

INTRODUCTION

The procedure of MET URSL and Extracorporeal Shock Wave Lithotripsy (ESWL) constitute the treatment modalities [1] with URSL being the gold standard in terms of stone clearance for ureteric stone. URSL is an endoscopic surgical procedure where stone is fragmented with pneumatic lithotripter or laser inserted via ureteroscope. MET is offered as an initial treatment modality in ureteric stones which are small in size, distal in location and non obstructive and sometimes as patients choice. MET is a medical management applied for lower ureteric stones where alpha blocker with or without calcium channel blocker and anti-inflammatory agents are given, which reduce the tone of ureter thus help in passage of stones [2,3]. Many studies have shown deterioration of renal function due to obstructive uropathy caused by stones [4-6]. Yang Q et al., evaluated the changes in renal function solely due to unilateral ureteric stone to compare the changes in renal function and also stone clearance rate, and compare the stone free rate between MET and URSL [7]. Aim of the present study was to measure the effect on renal function and stone free rate by comparing medical expulsive therapy using tamsulosin and URSL for solitary mid and distal ureteric stone. The null hypothesis of the study being: MET is less effective as URSL for expulsion of mid and distal ureteric stone. Alternate hypothesis: MET is as effective as URSL for expulsion of mid and distal ureteric stone.

MATERIALS AND METHODS

This prospective interventional study was done in IPGME&R and SSKM Hospital, Kolkata, West Bengal, India, after Institutional Ethics Committee clearance (IPGME&R/IEC/2020/283), from

May 2020 to October 2020. The study population included patients with ureteric stones diagnosed by Non Contrast Computerised Tomography (NCCT)- Scan of the kidneys, Ureter and Bladder (KUB).

Inclusion criteria: Patients older than 12 years, patients with single ureteric stone, stone located in mid and distal ureter of size up to one cm.

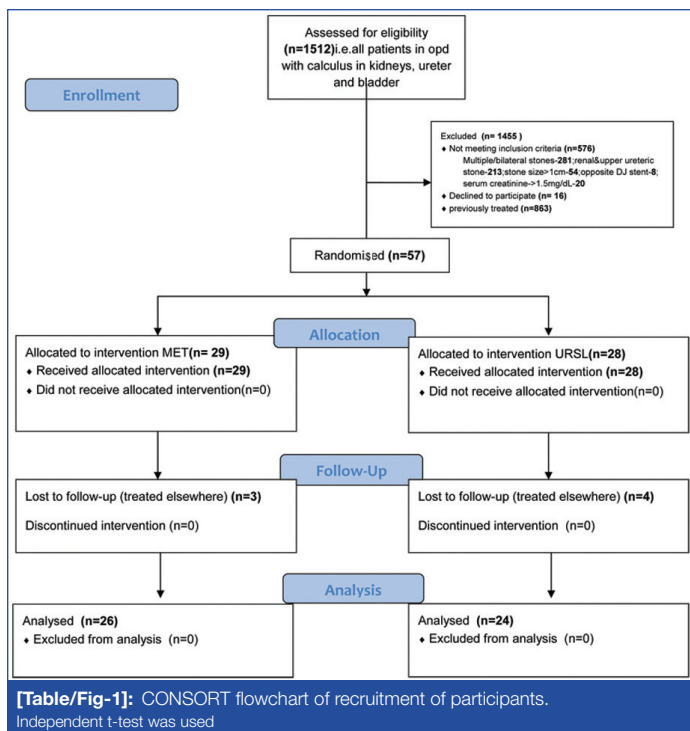
Exclusion criteria: Those patients having past history of endourological procedure, presence of kidney stones, bilateral stones, double-J (DJ) stent in-situ, patients with serum creatinine >1.5 mg/dL, chronic kidney disease (CKD), solitary kidney and patients with moderate to gross hydronephrosis (HDU) or/and hydroureteronephrosis (HDUN).

Sample size calculation: Assuming 65% expulsion rate of stone using MET [8] and power of study being 0.8, calculated sample size was 50. Considering decay in follow-up process of 5%, final sample size considered was $(50+2.5)=53$ (approximately).

As per flowchart and applying exclusion criteria and after taking written informed consent, 57 patients were allocated in two groups MET and URSL by serially numbered sealed opaque envelope technique [Table/Fig-1]. Diethylenetriaminepentaacetic acid (DTPA) scan was done as a test for renal function of affected kidney in all patients. As three patients in MET group and four patients in URSL group lost to follow-up, so, the final calculation was done for 50 patients.

Study Procedure

The URSL group patients underwent surgery by pneumatic lithotripter with DJ stent within two weeks of recruitment after



preoperative work-up. The DJ stent was removed in all patients after four weeks of surgery as per Institutional protocol. MET group patients were initiated on medication (Tamsulosin 0.4 mg tablet once daily at bed time) immediately after enrollment. MET was given for an additional two weeks arbitrarily after standard four weeks MET [9] assuming no deterioration in renal function after excluding factors leading to decreased renal function like Urinary Tract Infection (UTI), bladder outlet obstruction, medical renal disease, neurogenic abnormality and malignancy. Those patients who were not stone free after MET were advised to undergo URSL, however these patients were not included in the present study as URSL group. Follow-up of each patient in two groups was done with second NCCT-KUB and DTPA scan after six weeks of completion of treatment and these patients were removed from the concerned study group. During the study, three patient from MET group and four patients from URSL group left the study, so, finally there were 26 patients in MET group and 24 patients in URSL group. Parameters measured were:

- Stone clearance (stone presence or absence in ureter in NCCT-KUB) at six weeks postintervention,
- Change in glomerular filtration rate (GFR) of affected kidney at six weeks,
- Comparison of GFR change in both intra (MET or URSL group) and inter-groups (between MET and URSL group).

Other variables studied were: age, distribution of stones, side of occurrence of stones and presence of Hydroureteronephrosis (HDUN)/Obstruction.

STATISTICAL ANALYSIS

All data of patients were entered in Microsoft Excel spreadsheet. Data were analysed using International Business Management (IBM)- Statistical Package for Social Sciences (SPSS) software version 26.0 (IBM SPSS Statistics for Mac OS, IBM Corp, NY, version 26.0, 2019). Numerical variables were summarised as mean and standard deviation and compared between two groups with Independent t-test. Categorical variables were summarised as counts and compared between two groups by Pearson's Chi-square test. For these comparisons, p-value <0.05 was considered as statistically significant.

RESULTS

Total number of male and female patients in MET group was 21 and five, respectively. In URSL group, there were 12 male and 12 female patients, respectively. The mean age of patients in MET and URSL group was 37.12 years (ranging from 24-50 years) and 33.63 years (ranging from 26-42 years), respectively. There were no significant differences in mean age, mean calculus size and pre-treatment GFR [Table/Fig-2] between both groups.

Only stone position was significant determinant of stone clearance rate with highest removal rate in VUJ stones [Table/Fig-3].

| Parameters | Treatment group | | p-value |
|---------------------------|-----------------|-------------|---------|
| | URSL (n=24) | MET (n=26) | |
| Age (years) | 33.63±8.05 | 37.12±13.00 | 0.264 |
| Size of stone (mm) | 7.63±2.11 | 6.57±1.65 | 0.052 |
| Pretreatment GFR (mL/min) | 32.18±13.47 | 33.74±15.72 | 0.709 |

[Table/Fig-2]: Comparison of age, size of calculus and pre-treatment GFR in both treatment groups. (Student's Independent t-test for p-value)

| Parameters | | Stone clearance | | Total (N) | p-value |
|---------------------|--------------------------|-----------------|---------|-----------|--------------|
| | | Not cleared | Cleared | | |
| Gender | Males | 5 | 29 | 34 | 0.716 |
| | Females | 3 | 13 | | |
| Side of stone | Left side | 3 | 18 | 21 | 0.778 |
| | Right side | 5 | 24 | | |
| Position of stone | Mid ureteric | 3 | 4 | 7 | 0.040 |
| | Distal ureteric | 5 | 24 | | |
| | VUJ | 0 | 14 | | |
| Obstruction HDUN+/- | Non obstructive/ No HDUN | 5 | 31 | 36 | 0.514 |
| | Obstructive/Mild HDUN | 3 | 11 | | |

[Table/Fig-3]: Effect on stone clearance according to gender, side of stone, position of stone, presence of obstructive stone and presence of HDUN. Chi-square test; bold p-values are significant VUJ: Vesicoureteric junction; HDUN: Hydroureteronephrosis

The clearance of stone was compared in both the treatment groups and there was no significant difference between the two groups (p-value=0.902) [Table/Fig-4] however, it was significant when compared within the groups (p-value <0.001) [Table/Fig-5].

| Treatment modality | Stone clearance | | Total (N) | p-value |
|--------------------|-----------------|---------|-----------|---------|
| | Not cleared | Cleared | | |
| URSL | 4 | 20 | 24 | 0.902 |
| MET | 4 | 22 | | |

[Table/Fig-4]: Comparison of stone clearance among both treatment groups. Chi-square test, URSL: Ureteroscopy lithotripsy; MET: Medical expulsive therapy

| Treatment modality | Stone clearance | | p-value (Chi-square test) |
|--------------------|-----------------|---------|---------------------------|
| | Not cleared | Cleared | |
| Pre URSL | 24 | 0 | <0.001 |
| Post URSL | 4 | 20 | |
| Pre MET | 26 | 0 | <0.001 |
| Post MET | 4 | 22 | |

[Table/Fig-5]: Comparison of stone clearance within the treatment groups.

Glomerular Filtration Rate was significantly increased after completion of treatment. Similar observations were noted in individual groups but inter-group change was not significant [Table/Fig-6].

| Parameters | Treatment modality/ pre and post GFR | N | Mean | p-value |
|--|---|----|---------------|---------|
| Pre-treatment GFR (mL/min) | URSL | 24 | 32.18±13.47 | 0.792 |
| | MET | 26 | 33.74±15.72 | |
| Change in GFR among all subjects | Pre-treatment GFR | 50 | 32.996±14.558 | 0.001 |
| | Post-treatment GFR | 50 | 34.61±13.92 | |
| Change in GFR among MET subjects | Pre-treatment GFR | 26 | 33.74±15.72 | 0.010 |
| | Post-treatment GFR | 26 | 35.11±15.08 | |
| Change in GFR among URSL subjects | Pre-treatment GFR | 24 | 32.18±3.47 | 0.001 |
| | Post-treatment GFR | 24 | 34.06±12.84 | |
| Change in GFR between treatment group | URSL | 24 | 1.88±1.17 | 0.372 |
| | MET | 26 | 1.37±2.52 | |

[Table/Fig-6]: Comparison of pre and post treatment GFR in intra and inter treatment groups.
URSL: Ureteroscopic lithotripsy; MET: Medical expulsive therapy

DISCUSSION

Various minimally invasive techniques like Extracorporeal Shock Wave Lithotripsy (ESWL), URSL and even expectant management are offered in management of lower ureteric stones. The choice depends upon location, size, number as well as age, co-morbidities and laboratory parameters, surgeon's skill [10] and sometimes, patient preference. In this study, effects of MET and URSL were compared in patients with single mid to lower ureteric stone in terms of pre-determined parameters. The number of patients who completed study has indeed come out to be 50 with 5% of those randomised lost to follow-up. The burden of stone remains the guiding factor for appropriate treatment of a patient with ureteric calculi [11]. The α 1 blockers have a important impact in spontaneous removal of the stones smaller than 8 mm size located in the Vesicoureteric Junction (VUJ) [12]. In the present study, 14 patients with VUJ stone with average size of 6.5 mm had complete stone clearance after MET. Distal ureteric stones had more chances of spontaneous clearance [13]. In the present study, where 29 patients had stone on right side with an average size of 6.8 mm out of which 24 were stone free after MET.

The non invasive medical management may be associated with complications, like urinary tract infection, HDU and renal function defects [14]. However in the present study, none of the patient had such complications. The majority of ureteric stones might pass within six weeks period after the onset of symptoms [15] depending upon size, shape, location of stone and associated ureteric oedema. Different stone expulsion rate was seen in the present study; with MET for six weeks, patients with VUJ stone had maximum expulsion rate and followed by patients with distal ureteric stone. Patients with mid-ureteric stone had least stone free rate. Though standard MET with Tamsulosin is for four weeks, the extended the treatment period for additional two weeks for the final outcome assessment at six weeks in both groups. Tamsulosin did not cause serious deterioration of renal function due to non expulsiing stone with extended treatment for two weeks. According to Cervenakov I et al., [16], α 1 blockers increase the rate of passage of small stone from the terminal parts of the ureter. Dellabella M et al., [17], using tamsulosin observed an increased stone expulsion rate of 90%. Similar results were obtained in the present study with expulsion rate of 84%.

Hassanzadeh K et al., [18] observed considerable chance of recovery of renal function after surgical removal of the obstruction in patients with unilateral ureteric obstruction, if the GFR of the affected kidney was >10 mL/minute/1.73 m² or total GFR was >25 mL/minute/1.73 m². Gheissari A et al., [19] observed significant increase in post-surgery GFR after three days of surgery with pre-surgery GFR as the predictor of the post-surgery GFR. Likewise

in the present study too, postintervention GFR was significantly increased in both groups.

Studies including effect of PCNL on renal function showed significant improvement in renal function after PCNL [20,21]. Likewise an increase in GFR of affected kidney was observed after URSL in the present study. In the present study, patients were randomly allocated with minimal selection bias. End results were measurable with minimal inter-observer bias and power of study was good. The results of the present study supports the alternate hypothesis but for the null hypothesis, future studies with large sample size are needed to further validate results of the present study.

Limitation(s)

The relatively small sample size, unicentric nature and open label design are limitations of the present study. Further, the impact of stone size, presence of chronic kidney disease, anatomic abnormality and, previous intervention have not been assessed in the present study.

CONCLUSION(S)

The MET using Tamsulosin for six weeks can be safely considered as first choice in patients with mid and distal solitary ureteric stone with size upto one cm without any anatomic abnormality, chronic kidney disease or prior intervention and same may not cause any functional damage to the affected kidney.

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