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WHEN? WHERE? AND ON WHOM? A STUDY TO HAND PICK PATIENTS SUITABLE FOR MET USING METSS.

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ABSTRACT **Background:** Ureteric stones represent a significant clinical burden, with distal ureteral stones accounting for the majority of cases. Medical expulsive therapy (MET) using alpha-blockers such as tamsulosin has been recommended as a non-invasive management option. However, patient selection and optimal duration of therapy remain unclear. **Objective:** To validate the Medical Expulsive Therapy Stone Score (METSS) for predicting MET success and to determine the optimal duration of MET in patients with distal ureteral stones sized 5–10 mm. **Methods:** A prospective study was conducted between January and June 2024 including 90 patients with symptomatic distal ureteral stones (5–10 mm). Eight patients were lost to follow-up, leaving 82 for analysis. Patients received tamsulosin 0.4 mg daily for 4 weeks. Clinical and CT-derived parameters (stone size, density, ureteral wall thickness [UWT], ureteral diameter [UD], periureteral stranding [PUS], diabetes mellitus [DM]) were scored using METSS. Patients were stratified into low (0–3), intermediate (4–5), and high (6–10) risk groups. Stone-free status was assessed weekly.**Results:** Stone-free rates were 28.4% in week 1, 29.26% in week 2, 10.9% in week 3, and 8.5% in week 4. Nineteen patients (23.1%) remained stone-bearing after 4 weeks. METSS accurately predicted outcomes: low-risk patients had 100% success, intermediate-risk 92.34%, and high-risk 0%. Prolonged MET beyond 3 weeks was associated with increased emergency visits and renal colic attacks (p=0.005 and p=0.011, respectively). **Conclusion:** The METSS scoring system effectively identifies patients suitable for MET. MET should be limited to 3 weeks, as longer durations increase complications and reduce quality of life. High-risk patients should be directed to interventional management early.

KEYWORDS : MET, METSS, Renal Colic, Ureteric stones.

INTRODUCTION

Ureteric stones pose a significant problem with its incidence confering to a rapidly growing burden in terms of financial and human resources in every healthcare system.. The overall reported incidence of renal stones is approximately 4% out of which ureteral stones constitute 20% of them [1,2]. 70% of these ureteric stones seem to locate in the distal part of the ureter [3,4] and warrants to be the major chunk of the patients visiting OPDs seeking management.

Approach to ureteric stones include multiple interventional options which include antegrade or retrograde ureteroscopic lithotripsy, extracorporeal shock wave (ESWL) lithotripsy, laparoscopic or open surgery and ureterolithotomy and many more with the advent of rising technology . Rational approach needs to be made based on the stone and patient related factors. Due to the risk of complications during interventional procedures (ureteral perforation, avulsion, and stenosis) and cost issues, MET is presented as a valid option by European guidelines for patients with ureteral stones, particularly with distal ureteral stones ≥5 mm, under the effect of alpha-blockers . Similarly, American guidelines recommend strongly the MET option with alpha-blockers administration for patients with distal ureteral stones≤10 mm. [5]

Hence, Medical expulsive therapy (MET) is an attractive option for ureteral stone management and comprises a non-invasive expectant strategy, to spontaneously pass out ureteral stones under the effect of pharmaceutical agents.

MET with alpha-blockers, calcium channel blockers, corticosteroids and phosphodiesterase-5 inhibitors (PDE5) has been identified as an effective treatment option for pharmacotherapy [6]. Of all the alpha-blockers used with this aim, tamsulosin has been the most commonly prescribed one on OPD basis with the mechanism of action being smooth muscle relaxation without disrupting the physiologic ureteral peristalsis, relieve colic pain and eliminate edema as well as inflammation in the ureteral wall.

The effect of pharmaceutical agents, the success of the MET approach is expected to be dependent on the individual characteristics of the urinary stone, and other clinical parameters. Multiple studies have contributed to this understanding which has been consolidated in the study by Uzun et al [7], where significnt parameters were considred and a scoring system was materialised. This was based on clinical and computed tomography (CT)-derived data, which claims to predict the success of MET approach.

Regarding the duration of the MET,a period varying between 2 and 6 weeks period has been suggested by various authors particularly based on a study published in 1999 by Miler and Kane [8].The EAU guidelines also advises MET as a valuable medical therapeutic option (with strong recommendation) for distal ureteric stones however no discrete time period has been mentioned and/or recommended regarding the optimal duration of this therapy[9].

Hence we intend to find the patients on whom MET works best by:

1) Validating the METSS(medical expulsive therapy stone score.
2) Identifying the optimal duration of MET in the medical treatment of distal ureteral stones sizing 5–10 mm.

METHODS

Between January 2024 and June 2024, 90 patients with symptomatic, distal ureteral stones (detected between the lower border of the sacroiliac joint and the vesico-ureteral junction on non-contrast CT) sizing 5 to 10 mm were included in the study. The study protocol was approved by the local ethical committee and an informed consent was obtained from all patients.

A total of 82 patients completed the study and 8 patients were lost to follow-up. 62 (75.6%) of the patients were male, 20 (24.4%) were female with an age range of 22–74 (mean; 43 ± 11) years. Patients with bilateral ureteral stones, multiple stones, urinary tract anomalies, lower urinary tract dysfunction, previous endoscopic or open ureteral surgery and patients under the age of 18 years were all excluded.

Demographic (age, sex) and clinical (history of stone passage, presence of diabetes mellitus [DM] data of all patients were obtained from hospital information database. According to CT, stone size, stone density, stone laterality (right–left), presence of hydronephrosis, ureteral wall thickness, ureteral diameter, presence of periureteral stranding were assessed. Distal ureteral localization was defned as above or below the iliac vessels. Stone size was calculated by measuring the longest axis of the ureteral stone.

The longest dimension.UWT (ureteric wall thickness) was calculated by measuring the thickest ureteral wall at the localization of the stone in the ureter on axial CT section. Periureteral stranding (PUS) was defned as increased density or stranding in the surrounding periureteral adipose tissue. Ureteral diameter (UD) was calculated by measuring the diameter of the ureter 3 mm above the stone on axial CT section.

All patients were administered tamsulosin 0.4 mg once a week for a duration of 4 weeks after which they were re-evaluated. Success was defned as the absence of ureteral stone. Acute urinary tract infection due to the stone, the patient's request for active treatment due to severe pain, and failure to pass the stone were defined as failure.

Patients with missing data, congenital genitourinary anomaly, solitary kidney, bilateral ureteral stone, multiple stones, history of previous kidney or ureteral surgery, acute renal failure, urinary tract infection, fever, severe pain, need for emergent intervention with double J (DJ) stent or nephrostomy tube were excluded.

Based on the MET scoring system, 1 point for stone size>6.5 mm, 2 points for stone density > 1078 HU, 2 points for UWT>2.31 mm, 3 points for UD >9.24 mm, 1 point for presence of PUS and 1 point for presence of DM were assigned to patients. Patients were classified into 3 risk groups according to METSS: low risk (0–3 points); intermediate risk (4–5 points) and high risk (6–10 points).

Patients were called for weekly evaluation with urine analysis, KUB radiography for radiopaque, and urinary system ultrasonography or for non-opaque stones. A NCCT was also performed in cases with suspicion of stone passage either on KUB of sonographic examination. The total follow-up period was 4 weeks and if stone-free status could not be achieved during this conservative treatment period, alternative management options such as URS or ESWL were recommended.

The size of the study was assessed by using the G-power 3.1 program and possible correlation between the duration of stone passage and gender, age, stone size, HU, UWT and hydronephrosis parameters was evaluated by using Spearman flash analysis test. Ap value less than 0.05 was considered to be meaningful. Results were evaluated using Spearman correlation and Kruskal–Wallis tests.

RESULTS

Evaluation of the data obtained in our study revealed following findings; while there was no relationship between stone expulsion time and gender; a relationship was found between patient age, stone size, HU, UWT, hydronephrosis and stone expulsion time which was not statistically significant.

24 (29.26%) patients were Stone free (SF) within the second week, 9 (10.9%) patients within the third week and lastly 7 (8.5%) patients passed within the fourth week period. 19 (23.1%) patients could not become stone-free after 4 weeks and were directed to alternative treatments such as URS and ESWL (Table 1).

					Non stone free	P
Stone free (weeks)	1st week	2nd week	3rd week	4th week		
Gender (Male/female)	17/7	18/5	6/3	6/1	16/3	0.204
Age (mean +/- SD)	44.4+/-12	38.3+/-9	51.2+/-15	45.2+/-8	43.8+/-7	0.027
Total	23	24	9	7	19	
Stone free rate	28.4	29.26	10.9	8.5	23.1	

A statistically insignificant relationship was found between stone-passage period and the age, stone size and UWT parameters.

Time period required for stone period tended to increase parallel to the age, stone size, and UWT values (p = 0.027, p = 0.043, p = 0.013, respectively) (Table 2).

					Non stone free	P
Stone free week	1st	2nd	3rd	4th		
Stone size (mm +/- SD)	5.95+/-1.02	6.3+/-1.2	7+/-1.4	6.57+/-1.6	6.42+/-1.5	0.043
Hounsfield units (HD+/- SD)	564+/-348	746+/-376	541+/-282	869+/-505	896+/-345	0.902
Urteral wall thickness (mm+/- SD)	2.09+/-0.4	2.16+/-0.9	2.38+/-0.7	2.16+/-0.6	2.08+/-0.7	0.013

No statistically significan relationship could be shown between time period for stone-free status and gender, hydronephrosis and HU values.

Mean number of visit to the emergency department ranged between 0 and 10. While 82.6% of those passing the stone within 1st week, 83.7% of those within the 2nd week, and 88.9% of those within the 3rd week had no or only once ED visit, 71.5% of the cases expulsing the stone within the 4th week visited the emergency room more at least two or two or more times. As shown in Table 3, the average number of emergency department visits was lower in cases passing the stones during the 3 weeks duration of management when compared to those who passed the stones with in the 4th week follow-up period as well as in those who did not pass any stones at all. Kruskal–Wallis (KW) multiple comparison test analysis of the data on this aspect clearly showed a significant difference between those who passed their stones in the first 3 weeks and those who could not pass during a 4 week follow-up period (p = 0.005) (Table 3).

	Stone free (weeks)				Non stone free	P
	1st week	2nd week	3rd week	4th week		
Mean no of visits to the emergency department	0.91+/-0.9	1.09+/-1.3	1.44+/-1.1	3.0+/-2.0	2.89+/-2.2	0.005
Mean no of renal colic attack	1.65+/-2.1	1.69+/-1.4	1.88+/-1.9	4.29+/-2.8	2.53+/-2.0	0.0011

On the other hand, again mean number of renal colic attacks ranged between 0 and 10 in our group. These values were 0, 1, or 2 in 82.5% of the patients passing stones during the 1st week and in 78.2% of the cases passing during the 2nd week and lastly 77.7% in those being stone free within 3 weeks, respectively. Mean renal colic number was 3 or more in 57.9% of those who had passed the stone within the 4th week. Similar to ED visits again, average renal colic number was found to be lower in cases passing their stones spontaneously under MET when compared to those who passed their stones during the 4th week evaluation along with the ones who were not stone free despite these measures.

Again comparative evaluation of the values in all groups with Kruskal–Wallis (KW) multiple comparison test, demonstrated a significant difference in the number of renal colic between those who passed their stones in the first 3 weeks and those who could not pass in the 4th week. p = 0.011 (Table 3).

In other words, our data clearly shown that if MET therapy prolongs to 4 weeks period or more, a significant increase could be noted in the mean number of renal colic attacks and mean emergency department visits in these patients. To support this observation, of the 26 patients who could not pass their stones within the first 3 weeks period, only 26.9% of them did pass their stones further during 4th week follow-up and the remaining 73.1% of the cases required interventional removal due to the problems affecting the life quality of the patients.

Applying, METSS system onto these patients showed 42 (51.21%) were categorised into Low Risk Group, 21(25.6%) into Intermediate group and 19 (23.1%) in the high risk groups. All the 19 non stone expulsors were under the high risk group and had to undergo an intervention for the clearance of the stone. Majority (84.25%) of the Low risk group expulsed stone within the first 2 weeks and the remaining in the subsequent weeks. 92.34 % in the Intermediate group had stone clerance. This is indicated in Table 4 below.

Variables	Points	METTS	MET success percentage	Risk Group	Recommnedations according to Uzun et al
Stone sixe>/=6.5 mm	1	0-3	100%	Low	Offer MET
Stone density>1078 HU	2				
UWT >2.31mm	2	4-5	92.34%	Inter-mediate	Offer MET after explaining the risk of unsuccessful passage
UD> 9.24mm	3				
Prescence of periureteral stranding	1				
Presence of DM	1	6-10	0%	High	Offer intervention

DISCUSSION

MET aims to relieve colic pain, eliminate submucosal edema and inflammation in the ureteral wall which will in turn accelerate the spontaneous passage of stone(s) with higher expulsion rates in relatively shorter time period.

The requirement of a daily office based easy to use scoring system such

as METSS is lacking in the face of dealing with ureteric calculi has to be accepted in view of the burden of this disease. Impact of this and its application at the tertiary care centers and implementation into the referral systems has a potential that can be certified with more validating studies.

The association of stone size, presence of moderate hydronephrosis, and UD with MET outcome was a fnding, which can be extrapolated from the physics of the stone impaction . Stone density, UWT, PUS, and DM being factors that predict the complication and clearance chances.

The METSS scoring system seems to separate successfully the patients with a favorable or adverse constellation of factors and predict the ones needing intervention. Applying the scoring on the same person at different intervals of time is another factor that could have been added in this study but could not be in view of difficulty in getting all the patients to undergo CT multiple number of times during the course of the study.

METSS system in our study has accurately predivted the stone expulsion probability in our study and our study strongly recommends its usage.

It is clear that the time period need for spontaneous stone expulsion with MET application cannot be prolonged as it becomes detrimental for the patient and challenging for the trating doctor after complications set in. Regarding this issue however, although some randomized clinical studies have shown the safe and effective use of these agents to accelerate stone expulsion and limit the associated problems affecting the quality of life [10]; contradictory outcomes have also been reported in other studies which makes the issue still debatable.

Generally a time period of 2 to 6 weeks is being recommended particularly for distal ureteral stones sizing 5–10 mm. Regarding this issue again, in the only study published in 1999, a follow-up period of 6 weeks has been recommended as the optimal duration by Miller and Kane [8]. In other words, although the efficacy and safety of MET have been well evaluated with various trials, the optimal duration of MET application for distal ureteric stones sizing 5–10 mm under observation is still to be clarified. Thus, an optimal duration regarding the efficacy rates on an application time based manner seems to be certainly needed.

From the above findings MET application seems to be unsuccessful after 3 weeks need to be directed to other stone removal procedures in an attempt to provide a good life quality, limit the risk of upper tract changes due to the varying degrees of obstruction and of course limit the total costs without any loss of time. In addition, the risk of side effects induced by MET will be limited if the medication could be stopped on time.

Thus our findings indicate that it could be rational and appropriate to apply MET for 3 weeks period and terminate MET it if the stone(s) do not pass during this period. Plan for other interventions if the waiting period fails.

This study does have its own limitations. This is a small short term study with limited the number of patients included. However, taking the relative difficulty of close-follow-up as well as documentation in such patients, we believe that our group with a perfect follow-up documentation will be help add to further research from multiple other institutes in the future whose additive efforts could help unearthing things that could be missed in this study.

RESULTS

Higher medical expulsive therapy stone score (METSS) indicated lower MET success. A positive relationship was found between the time period elapsed for stone passage and UWT along with the degree of hydronephrosis. SFR for distal ureteric stones sizing 5–10 mm was higher within the first 3 weeks under MET application. Thus, waiting for a longer period of time may result in increased analgesic and unnecessary MET treatment with increased risk of complications. Hence, METSS high risk and MET duration of > 3 weeks would need inteventions.

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