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Factors Influencing the Success of Medical Expulsive Therapy for Lower Ureteric Stones: An Observational Study

[1]Dr Yashpal Ramole, Professor, Department of General Surgery, Gandhi Medical College, Bhopal (M.P)
[2]Dr Archana Ramole, Assistant Professor, Department of Pathology, Gandhi Medical College, Bhopal (M.P)
[3]Dr Anuradha Chaudhry, Associate Professor, Department of General Surgery, Gandhi Medical College, Bhopal (M.P)
[4]Dr Priyanka Singh, Assistant Professor, Department of Microbiology, Gandhi Medical College, Bhopal (M.P)
[5]Dr Umang Dudeja, Resident, Department of General Surgery, Gandhi Medical College, Bhopal (M.P)
[6]Dr Namrata Pandey, Resident, Department of General Surgery, Gandhi Medical College, Bhopal (M.P)
[7]Dr Deepak Kumar Nayak, Resident, Department of General Surgery, Gandhi Medical College, Bhopal (M.P)
Corresponding Author: Dr Deepak Kumar Nayak, Resident, Department of General Surgery, Gandhi Medical College, Bhopal (M.P)

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Abstract

Purpose: This study aimed to assess the factors influencing the success of Medical Expulsive Therapy (MET) in managing lower ureteric stones, with particular focus on stone size, location, and patient-specific characteristics. Methodology: A prospective observational study was conducted at Gandhi Medical College and Hamidia Hospital, Bhopal, from August 2022 to December 2023. A total of 107 patients aged 18-50 years with lower ureteric calculi (5-10 mm), confirmed via ultrasonography (USG) and non-contrast computed tomography (NCCT), were included. Patients with pregnancy, solitary kidney, severe comorbidities, or opting for immediate surgery were excluded. MET treatment included hydration, NSAIDs, and alpha-blockers. Patients were reassessed at 2 and 4 weeks, with MET success defined as spontaneous stone passage within 4 weeks. Results: The study cohort had a mean age of 35.17 years, with 72.9% male participants. The majority of stones were located in the left distal ureter (56.1%). The mean stone size was 6.92 mm (SD=1.26). The overall MET success rate was 86.9%. Stone size was the most significant predictor of MET success, with smaller stones (<8 mm) exhibiting higher spontaneous passage rates. No significant associations were found between MET success and age and gender. Conclusion: MET is an effective conservative treatment for lower ureteric stones, particularly for stones smaller than 8 mm. Stone size is the most critical factor influencing treatment success. This study supports the use of MET as a first-line treatment for lower ureteric stones, especially in resource-limited settings.

Keywords: Medical Expulsive Therapy, Ureteric Stones, Stone size, Alpha-blockers

Introduction: Ureteric stones, or calculi, are a common urological condition globally, with a lifetime incidence of

up to 15% in developed countries [1] and approximately 12% in India [2]. Several factors, including diet, metabolic conditions, climate, and genetics, contribute to their formation [3]. The acute onset of renal colic, marked by severe flank pain, nausea, and vomiting, presents a significant burden on patients and healthcare systems. The global economic impact of kidney stones exceeds $5 billion annually [4,5], and studies in India highlight significant direct and indirect costs associated with ureteric stone treatment [6]. Managing lower ureteric stones is particularly challenging due to the need to balance conservative treatments with the risk of complications like obstruction, infection, and renal damage [7]. This dilemma is further complicated in resource-limited settings like India, where access to specialized care and socioeconomic factors can influence treatment outcomes [8]. Medical Expulsive Therapy (MET) has emerged as a key conservative approach to promote the spontaneous passage of lower ureteric stones, offering a cost-effective, less invasive alternative, especially in such settings [9]. MET primarily involves the use of medications, such as alpha-blockers (e.g., tamsulosin or alfuzosin), which relax ureteral smooth muscle, facilitating stone passage and reducing pain [10-12]. Calcium channel blockers like nifedipine have also shown efficacy, though their mechanism is less understood [11,12]. The success of Medical Expulsive Therapy (MET) in managing lower ureteric stones is influenced by several key factors. Stone size plays a significant role, with smaller stones (<5mm) having a high spontaneous passage rate of over 70%, while stones between 5-10mm show a lower success rate, ranging from 25-50%. Stones larger than 10mm are unlikely to pass with MET alone. [10,13,14] Stone location is another important determinant, as stones located in the distal ureter tend to respond more favourably to MET compared to those in the proximal ureter. [15] Patient-specific factors, including age, gender, body mass index (BMI), and prior history of stone passage, may also influence the effectiveness of MET, though the precise impact of these factors is still under investigation. [16] Additionally, anatomical considerations such as ureteral strictures or other abnormalities can affect the likelihood of successful stone passage. [17] Despite the known influence of stone size, location, and patient characteristics on MET outcomes, there remains uncertainty regarding how these factors interact and the specific thresholds where MET success significantly decreases. This study aims to assess the factors associated with the success of MET in patients with lower ureteric stones and to correlate these factors with therapy outcomes. these factors with therapy outcomes.

Materials and methods

This prospective observational study was conducted in the Department of General Surgery, Gandhi Medical College & Hamidia Hospital, Bhopal, from August 2022 to December 2023 after approval from the Institutional Ethics Committee.

The study included all patients who presented to the department during the study duration (sample size=107); aged 18-50 years presenting with acute colicky pain due to lower ureteric calculi, measuring 5-10 mm, confirmed by ultrasonography (USG) and non-contrast computed tomography (NCCT). Exclusion criteria included pregnancy, solitary kidney, impaired renal function, severe comorbid conditions (e.g., cardiac illness, respiratory diseases, chronic renal failure), immunocompromised status, and those opting for immediate surgical intervention.

After obtaining written informed consent, eligible patients were evaluated through clinical history, physical examination, and imaging (X-ray KUB, USG, and

NCCT). All patients underwent non-surgical management consisting of adequate hydration, NSAIDs, and alpha-1 blockers. They were reassessed at 2 and 4 weeks using clinical assessment, X-ray KUB, and USG, with NCCT if required. Persistence of the stone at 4 weeks was considered a failure of MET, and these patients were planned for surgical intervention.

Data were collected and analysed using Epi Info Version 6. Frequency distribution and cross-tabulation were employed to summarize the data. Continuous variables were expressed as mean ± standard deviation, while categorical data were presented as percentages. The Pearson Chi-Square test was used for normally distributed data, and the student's t-test for non-normally distributed data, with a p-value of <0.05 considered statistically significant.

Results

The study cohort consisted of 107 patients with a mean age of 35.17±8.07 years. Males constituted the majority, comprising 72.9% (n=78), while females accounted for 27.1% (n=29). The age distribution was as follows: 14.0% (n=15) were ≤25 years, 34.6% (n=37) were aged 26-35 years, 41.1% (n=44) were aged 36-45 years, and 10.3% (n=11) were ≥46 years. All patients presented with flank pain as the primary symptom. Additionally, 15.0% (n=16) experienced nausea, and 30.8% (n=33) reported vomiting. Notably, none of the patients had a fever at the time of presentation. Majority of ureteric stones were located in the left distal ureter (56.1%, n=60), while the right distal ureter accounted for 43.9% (n=47). The mean stone size measured by USG was 6.92±1.26 mm. NCCT further revealed a mean transverse diameter of 6.43±1.08 mm and a mean longitudinal diameter of 7.05±1.22 mm. Hydroureteronephrosis (HUN), characterized by dilation of the ureter and renal collecting system due to obstruction, was assessed using NCCT KUB findings. Among the patients, 48.6% (n=52) showed no evidence of HUN, 24.3% (n=26) had mild HUN, and 27.1% (n=29) presented with moderate HUN. A statistically significant association was found between the severity of HUN and both the mean stone size on USG (p=0.001) as well as the mean transverse and longitudinal diameters of the calculi on NCCT KUB (p=0.000). The significant difference in stone size across HUN severities suggests that the size of the obstructing calculi influences both the presence and extent of HUN, as depicted in Table 1. The primary endpoint of this study was the success of medical expulsive therapy (MET), defined as spontaneous stone expulsion within 4 weeks. An impressive 86.9% of patients (n=93) achieved successful MET, underscoring the efficacy of this conservative approach, as shown in Table 2. Further analysis revealed that the success of MET was significantly influenced by stone size (Table 3). Specifically, all patients with stones measuring between 6.1 mm and 8 mm experienced successful outcomes, whereas the failure rate escalated to 50% for stones ≥9.1 mm. Interestingly, stone location (left vs. right distal ureter) exhibited association with MET success, and all patients with stones located in the left lower ureter, right distal ureter, or right lower ureter achieved successful outcomes. Notably, neither age nor gender demonstrated a statistically significant association with MET success. To discern the independent predictors of MET success, a multivariate logistic regression model was employed. This analysis unequivocally identified stone size as the sole significant predictor (p=0.016, odds ratio = 5.129), indicating that for each 1 mm increase in stone size, the odds of successful MET decrease by a factor of 5.129. Furthermore, Spearman's rank correlation analysis revealed a moderate positive correlation between both the transverse and longitudinal diameters of calculi and the

outcome of MET (ρ = 0.30 for both), reinforcing the influence of stone size on treatment success.

Table 1: Association between hydroureteronephrosis severity and stone size on various investigations

Parameters	Hydroureteronephrosis			p-value
	Absent (N=52)	Mild (N=26)	Moderate(N=29)	
Mean stone size (mm) on USG KUB	5.863±0.5987	7.181±0.3200	8.583±0.5801	0.001*
Mean transverse diameter (mm) on NCCT KUB	5.529±0.442	6.654±0.358	7.844±0.532	0.000*
Mean longitudinal diameter (mm) on NCCT KUB	6.027±0.502	7.285±0.308	8.683±0.586	0.000*

*p-value significant

Table 2: Distribution of patients according to outcome of Medical Expulsion Therapy

Outcome of Medical Expulsion Therapy	Number of Patients	Percentage
Successful MET	93	86.9%
Failed MET	6	5.6%
Loss to follow up	8	7.5%
Total	107	100%

Table 3: Association between MET outcome and size of ureteric stone and its location

Parameters	Outcome of MET		Total N (%)	p-value
	Successful N (%)	Failed N (%)		
Stone Size (mm) on USG KUB				
≤6	27 (29%)	1 (16.7%)	28 (28.3%)	0.000*
6.1-7	30 (32.3%)	0 (0.0%)	30 (30.3%)	
7.1-8	20 (21.5%)	0 (0.0%)	20 (20.2%)	
8.1-9	15 (16.1%)	2 (33.3%)	10 (17.2%)	
≥9.1	1 (1.1%)	3 (50.0%)	4 (4.0%)	
Mean±S.D	6.823±1.1736	8.717±1.5171	-	0.027*
Transverse diameter (mm) on NCCT KUB				
≤6	46 (49.5%)	1 (16.7%)	47 (47.5%)	0.000*
6.1-7	27 (29.0%)	0 (0.0%)	27 (27.3%)	
7.1-8	19 (20.4%)	0 (0.0%)	19 (19.2%)	
8.1-9	1 (1.1%)	5 (83.3%)	6 (6.1%)	
Mean±S.D	6.336±1.00	7.950±1.221	-	0.027*
Longitudinal diameter (mm) on NCCT KUB				
≤6	26 (28.0%)	1 (16.7%)	29 (27.3%)	0.000*
6.1-7	30 (32.3%)	0 (0.0%)	30 (30.3%)	
7.1-8	21 (22.6%)	0 (0.0%)	21 (21.2%)	

8.1-9	13 (14.0%)	1 (16.7%)	14 (14.1%)	
≥9.1	3 (3.2%)	4 (66.7%)	7 (7.1%)	
Mean±S.D	6.944±1.134	8.866±1.436	-	0.027*
Diagnosis/Location				
Left distal ureteric calculi	50 (53.8%)	6 (100%)	56 (56.6%)	0.027*
Right distal ureteric calculi	43 (46.2%)	0 (0.0%)	43 (43.4%)	
Total	93 (100%)	6 (100%)	99 (100%)	

*p-value significant

Discussion

The findings of this prospective observational study offer compelling evidence supporting the efficacy of medical expulsive therapy (MET) in the management of lower ureteric stones. In the present study, the mean age of participants was 35.17 years (SD=8.07), with 72.9% being male. The age distribution and gender ratio were similar to other studies, including Ramesh A et al. (2016) [18] with a mean age of 34.94 years, and Moon YJ et al. (2015) [19], who reported a mean age of 46.04 years and a male-to-female ratio of 64.6% to 35.4%. Similarly, Hari Bahadur KC et al. (2016) [20] reported a mean age of 31.72 years with a male-to-female ratio of 1.5:1, consistent with the male predominance observed in our study.

Regarding stone characteristics, the majority were located in the left distal ureter (56.1%) with a mean size of 6.92 mm (SD=1.26), which is consistent with previous studies such as Hari Bahadur KC et al. (2016) [20], where the mean stone size was 7.09 mm. The stone size distribution and location in the present study align with other reports, including Ibrahim AK et al. (2013) [21], who found the majority of stones in the lower ureter, and Ramesh A et al. (2016) [18], who observed stones predominantly ranging from 4-7 mm in size. Symptomatically, all patients presented with flank pain, and 15.0% experienced nausea, while 30.8% reported vomiting, with no incidence of fever. This symptom profile is similar to findings by Abedinzadeh M et al. (2021) [22], who noted mild and moderate hydronephrosis in 54.1% and 28.1% of patients, respectively, and flank pain as the most common symptom. In terms of MET outcomes, the overall success rate was 86.9%, with 88.8% of patients asymptomatic by 2 weeks. This success rate is higher than that reported in some other studies but comparable to Moon YJ et al. (2015) [19] and Ibrahim AK et al. (2013) [21], who noted expulsion rates of 85% with tamsulosin. Ramesh A et al. (2016) [18] also found that MET with tamsulosin and deflazacort led to a significantly higher expulsion rate of 84% for stones ≥5 mm. Stone size was identified as a significant predictor of MET success (p=0.016), with larger stones less likely to pass spontaneously. Both transverse and longitudinal diameters of calculi showed a moderate positive correlation with MET outcomes ($\rho = 0.30$). These findings align with previous studies, including Moon YJ et al. (2015) [19] and Khereddine MD et al. (2020) [15], who found that stone diameter was a significant predictor of MET failure, particularly for stones larger than 7 mm. Overall, this study confirms that stone size is a critical determinant of MET success, while factors such as age and gender were not found to be significant predictors, consistent with findings from similar studies.

Study Limitations

While this study provides valuable insights into the factors influencing MET success, it is essential to acknowledge certain limitations that may impact the

generalizability and interpretation of the findings. First and foremost, the study's relatively small sample size of 107 patients might limit the statistical power to detect subtle associations between variables and MET outcomes. Additionally, the single-centre design of the study raises the possibility of selection bias and limits the applicability of the results to other populations or healthcare settings. Furthermore, the 4-week follow-up period, although sufficient to assess the primary outcome of spontaneous stone expulsion, might not capture longer-term complications or recurrence rates. Future studies with larger, multi-centre cohorts and extended follow-up durations are warranted to address these limitations and provide a more comprehensive understanding of MET's efficacy and safety profile.

Clinical Implications

The findings of this study carry significant clinical implications for the management of lower ureteric stones. The robust association between stone size and MET success underscores the importance of careful patient selection. For patients with smaller stones, particularly those measuring less than 8 mm, MET emerges as a compelling first-line treatment option, offering a non-invasive approach with high success rates. This can potentially reduce the need for surgical interventions, thereby minimizing associated risks, complications, and healthcare costs. Conversely, for patients with larger stones, particularly those exceeding 8 mm, the likelihood of successful MET diminishes considerably. In such cases, early consideration of alternative treatment modalities, such as ureteroscopy or shock wave lithotripsy, may be warranted to avoid prolonged obstruction and potential complications. The study's findings can thus guide clinicians in making informed treatment decisions, tailoring the approach to individual patient and stone characteristics. Furthermore, the lack of association between age, gender, and MET success suggests that this conservative approach can be offered to a wide range of patients, irrespective of their demographic profile. This inclusivity is particularly relevant in resource-constrained settings where access to specialized urological care may be limited. By identifying stone size as the primary determinant of MET success, this study provides clinicians with a practical and readily applicable tool for optimizing treatment selection and improving patient outcomes. While this study sheds light on the pivotal role of stone size in MET success, it also underscores the need for further exploration. Future research should focus on elucidating the impact of stone location with greater precision, potentially employing advanced imaging techniques to map stone position in relation to ureteral anatomy. Additionally, investigating the influence of patient-specific factors, such as comorbidities and genetic predispositions, on MET responsiveness could enhance personalized treatment strategies. Long-term follow-up studies are also warranted to assess the durability of MET success and the potential for stone recurrence. Finally, comparative effectiveness research comparing MET with other treatment modalities could provide valuable insights into the optimal management of lower ureteric stones across diverse patient populations and healthcare settings.

Conclusion

In conclusion, this prospective observational study reaffirms the efficacy of medical expulsive therapy (MET) as a valuable tool in the management of lower ureteric stones. Our findings highlight a remarkable success rate, particularly notable given the inclusion of patients with stones up to 10 mm in size. The study unequivocally establishes stone size as the most critical determinant of MET success, with larger stones

exhibiting a significantly lower likelihood of spontaneous passage. The absence of a significant association between age and gender with MET success broadens the potential applicability of this non-invasive approach. It suggests that MET can be considered a viable first-line treatment for a diverse range of patients, as long as stone size is carefully evaluated. While our study provides compelling evidence supporting the use of MET, it also underscores the need for further research to refine patient selection and optimize treatment protocols. Future investigations should delve deeper into the impact of stone location, patient-specific factors, and long-term outcomes to enhance the precision and effectiveness of MET in the management of lower ureteric stones.

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