

# Effect of medical expulsive therapy on the health-related quality of life of patients with ureteral stones: a critical evaluation

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## Abstract

**Purpose** To evaluate the possible effects of medical expulsive therapy (MET) on the health-related quality of life (HRQOL) of the patients under watchful waiting for ureteral stones.

**Patients and methods** A total 120 patients with ureteral stones were included into this study program. Patients were divided into two subgroups. While patients in group 1 received medical therapy only for colic pain if needed, patients in group 2 received MET (tamsulosin 0.4 mg/once daily) in addition to medical therapy. All cases were evaluated weekly during 1-month period, and the patients with persistent stones after this period in both groups were evaluated with respect to the analgesic requirement, number of renal colic attacks as well as emergency department (ED) visits along with the QOL scores.

**Results** Mean values of patient age and stone burden were  $37.14 \pm 2.46$  years and  $42.04 \pm 2.03$  mm<sup>2</sup>, respectively. Evaluation of the cases with residing stones after 4 weeks (28 cases in group 1 and 27 cases in group 2) with or without MET revealed following findings; renal colic, total amount of analgesic required and the mean number of ED visits were significantly lower in cases receiving MET. Evaluation of the mean HRQOL in terms of EQ-5D index and EQ-5D VAS values in both groups again demonstrated higher mean values in patients undergoing MET ( $p < 0.05$ ).

**Conclusion** Our findings indicated that MET for ureteral calculi during watchful waiting period could increase the HRQOL scores by lowering the number of both renal colic attacks and ED visits resulting in decreased analgesic need.

**Keywords** Ureteral stone · MET · QoL · Alpha-blocker

## Introduction

As a worldwide common pathology, urolithiasis affects about 5–10 % of the population [1, 2]. Although a certain percentage of the stones may be asymptomatic; ureteral calculi may cause obstruction and colic pain requiring an immediate medical care to relieve these distressing symptoms and accelerate the spontaneous passage rates. Such approach is commonly needed particularly for the stone(s) sizing <10 mm in an attempt to decrease the use of invasive procedures for stone removal and to increase the life quality in these cases [3–8].

Regarding this issue, published data demonstrated that a vast majority of smaller stones in the ureter (<5 mm) will pass spontaneously during close follow-up under standard therapy. However, distressing symptoms necessitating analgesic use and emergency department (ED) visits caused by relatively larger stones (>5 mm) could be a serious health problem with significant effects on the health-related quality of life (HRQOL) in such cases during the observation period for spontaneous passage [1, 2, 4]. Evaluation of the published data on this aspect will clearly show that the HRQOL of patients with ureteral stones under medical expulsive therapy (MET) therapy and the possible positive effects of MET on this critical factor have not been evaluated in detail so far.

HRQOL is an estimate of freedom from impairment, disability or handicap [6]. The concept of HRQOL is

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multidimensional and includes psychosocial, physical and emotional status, as well as patient autonomy and is applicable to a wide variety of medical conditions [7].

Thus, it is clear that MET will not solely increase the stone passage rates in an effective manner, but may also diminish the associated symptoms and morbidity induced by the stone(s) during this close follow-up period that may affect the HRQOL of the cases in a significantly manner [9]. This brings the issue into the agenda that irrespective of the stone-related factors, urologists should not solely focus on the stone-free rates obtained but also on the possible effects of the stone-induced distressing symptoms on the psychological and social life of the affected patients [5]. Related with this subject, although various studies focused on the stone-free rates and stone-related problems to some extent during the watchful waiting period, to our knowledge, no study so far has investigated the HRQOL in patients with ureteral calculi receiving MET therapy under follow-up for spontaneous passage.

In this present prospective controlled study, we aimed to evaluate the possible effects of MET on the HRQOL of the patients under watchful waiting for ureteral stones.

## Patients and methods

Between January 2014 and January 2015, a total of 120 adult patients (>18 years, 84 males and 36 females, M/F: 2.33) being on the elective operational list for 5–10 mm single radio-opaque ureteral stones were included into this study program. Patients with multiple stones, previous stone-related procedures, obstruction, stent placement, congenital anomalies, active urinary tract infection, pregnancy or renal insufficiency were excluded. Additionally, patients requiring urgent stone removal and/or auxiliary procedures for intractable pain, obstruction, infection and other related complications during follow-up period were also excluded from the study program.

Prior to the treatment, a detailed information regarding the use of tamsulosin (an alpha-receptor blocking agent) and related side effects were explained to all patients after which a written informed consent was obtained. In addition to a detailed history and a thorough urogenital examination, biochemical evaluation, urinalysis and urine culture sensitivity tests were performed. All patients with positive urine culture were treated by proper antibiotic regimen. The study protocol has been approved by ethics committee of the institution.

Although a non-contrast computed tomography (NCCT) was performed in all cases, plain X-ray of the kidney, ureter and bladder (KUB), ultrasound and excretory urography were done when necessary. The density of all stones in terms of Hounsfield unit (HU) has been evaluated in all

cases. In addition to the age and gender; the body mass index (BMI) of all cases was also noted.

Following these assessments, during the observation period for spontaneous passage (4 weeks), patients were further divided into two groups. While patients in group 1 ( $n:60$ ) received medical therapy only for colic pain if needed (diclofenac sodium, enteric-coated tablets of 75 mg), patients in group 2 ( $n:60$ ) received MET (tamsulosin 0.4 mg. once daily) in addition to medical therapy for pain. Following the formation of these two groups, a further randomization with respect to the localization of the stones (upper–lower ureter) with a simple randomization method by generating a random digit (0–60 in each group) has been used within each group. Even numbers have been used for cases using MET, and odd numbers have been used for cases without MET therapy.

All patients were well followed and evaluated weekly during these 4 weeks of watchful waiting period for spontaneous stone expulsion rates in the whole group. While cases passing the stones spontaneously and the cases requiring intervention due to certain reasons mentioned above were excluded from the evaluation, cases with persistent stones in the ureter after 4 weeks were well evaluated with respect to the analgesic requirement, number of renal colic attacks as well as emergency department visits along with the HRQOL scores assessed by using EQ-5D index and EQ-5D VAS scoring values [10].

Data are presented as mean  $\pm$  standard error of mean. By using prism 5.0 (GraphPad Software, San Diego, CA), unpaired t test, Mann–Whitney test and Chi-square tests were used to evaluate both the overall statistical significance and also the correlation between subgroups.  $p < 0.05$  was considered to be significant.

## Results

Of the 120 patients evaluated (84 men and 36 women; M/F: 2.33), while 60 cases had upper ureteral stones (50 %), 60 cases (50 %) had lower ureteral stones. In total, 66 stones were located in the right (55 %) and 54 stones (45 %) were in the left ureter. Patients as well as stone-related characteristics in the whole group are being summarized in Table 1. During a 4-week, follow-up period, although a total of 22 cases (36.66 %) passed the stones under standard therapy in group 1, 26 cases (43.33 %) receiving MET passed the stone in group 2. Additionally, while ten cases in group 1 required stone removal (16.66 %) during this period, seven cases (11.66 %) from the patients receiving MET required stone-removal procedures. The stone passage rates along with the patients requiring intervention are being given in Table 2.

Evaluation of the cases with residing stones (28 cases in group 1 and 27 cases in group 2) in the ureter with or

**Table 1** Evaluation of patient and stone characteristics in both groups

	Medical expulsive therapy		<i>p</i>
	No (group 1) <i>n</i> = 60	Yes (group 2) <i>n</i> = 60	
	Mean ± SD	Mean ± SD	
Age (year)	37.23 ± 1.56	37.07 ± 2.26	0.625
Body mass index (kg/m <sup>2</sup> )	24.76 ± 0.32	24.12 ± 0.23	0.132
Stone burden (mm <sup>2</sup> )	40.04 ± 1.93	43.71 ± 2.10	0.217
HU (Hounsfield unit)	614.5 ± 19.68	582.4 ± 22.34	0.264

without medical expulsive therapy clearly demonstrated that MET application was found to be significantly effective in lowering the mean number of renal colics that may eventually result in relatively higher analgesic need and also ED visits ( $p = 0.0001$ ). However, as seen in Table 3, MET did not lower the VAS score during colic attack in these cases ( $p = 0.11$ ).

In addition to these findings, most importantly, our results did also show that this approach may significantly improve the HRQOL of these cases which may be particularly affected by the factors mentioned above. Evaluation of the mean HRQOL in terms of EQ-5D index demonstrated a significantly higher mean index value in cases undergoing MET when compared with the others ( $p = 0.0006$ ). Additionally, evaluation of mean EQ-5D VAS values in both groups again demonstrated higher mean values in patients undergoing MET ( $p = 0.0001$ ) (Table 4). These data again further clearly emphasized the significantly improving effects of MET on the life quality of the cases with ureteral stones under observation for spontaneous passage.

## Discussion

Of all the stones treated, ureteral stones are a common problem in daily practice by causing urinary obstruction and severe colic pain which may significantly affect the life quality in the majority of these cases. Regarding the management, while relatively smaller (<5 mm), uncomplicated

**Table 3** Evaluation of the mean number of colic attacks, analgesic requirement, ED visits and VAS in both groups during 4-week follow-up period

	Medical expulsive therapy		<i>p</i>
	No (group 1) <i>n</i> = 28	Yes (group 2) <i>n</i> = 27	
	Mean ± SD	Mean ± SD	
No. of renal colic	4.92 ± 0.37	3.59 ± 0.33	<b>0.02</b>
No. of ED visit	2.42 ± 0.28	1.51 ± 0.32	<b>0.01</b>
Analgesic required (mg)	507.1 ± 31.10	313.0 ± 28.10	<b>0.0001</b>
VAS during pain	7.64 ± 0.12	7.33 ± 0.10	0.11

Bold values indicate statistical significance ( $p < 0.05$ )

**Table 4** Evaluation of the mean EQ-5D index and EQ-5D VAS values in both groups, during 4-weeks follow-up period

	Medical expulsive therapy		<i>p</i>
	No (group 1) <i>n</i> = 28	Yes (group 2) <i>n</i> = 27	
	Mean ± SD	Mean ± SD	
EQ-5D index	0.72 ± 0.02	0.80 ± 0.001	<b>0.0006</b>
EQ-5D VAS	55.71 ± 1.19	70.37 ± 1.64	<b>0.0001</b>

Bold values indicate statistical significance ( $p < 0.05$ )

and asymptomatic stones may be treated in an expectant manner [9], larger stones causing obstruction, colic pain and infection will require active removal preferably by using the minimal invasive management alternatives available today. However, it is well known that although minimally invasive and effective, these procedures are not risk free and are considerably expensive.

Published data in the literature demonstrated that depending on the size and location of the ureteral stone, a considerable percentage of the stone may pass spontaneously without any intervention [4, 11]. A well conducted meta-analysis of the studies assessing the spontaneous passage rates reported a median probability of stone passage of 68 % for stones <5 mm and 47 % for those 5–10 mm [12, 13]. Moreover, European Association of Urology

**Table 2** Stone passage rates and required interventions in both groups

	Overall <i>n</i> = 120 <i>n</i> (%)	Medical expulsive therapy		<i>p</i>
		No (group 1) <i>n</i> = 60 <i>n</i> (%)	Yes (group 2) <i>n</i> = 60 <i>n</i> (%)	
Stone free	48 (40.0 %)	22 (36.6 %)	26 (43.3 %)	0.264
Not stone free	55 (45.8 %)	28 (46.7 %)	27 (45.0 %)	0.207
Requiring intervention	17 (14.2 %)	10 (16.7 %)	7 (11.7 %)	0.579

guidelines indicate observation as the initial treatment option for patients with controlled symptoms harboring ureteral stones <10 mm [12]. Taking the relatively lower rates of spontaneous passage rates along with associated problems in ureteral calculi sizing >5 mm and the growing understanding of ureteric function and pathophysiology into account, MET mainly with alpha-blockers has recently emerged as an alternative treatment option to increase the spontaneous passage rates, decrease the rate of complications as well as the need for invasive interventions and eventually decrease the healthcare costs [14, 15].

Regarding this subject, in their well-prepared meta-analytic study, Campschroer et al. did review 32 studies including 5864 cases. The stone-free rates were significantly higher in cases receiving an alpha-blocker (RR 1.48, 95 % CI 1.33–1.64) when compared with the cases under standard therapy. Stone expulsion time was 2.91 days shorter with the use of alpha-blockers. Use of alpha-blockers did clearly reduce the number of pain episodes, the need for analgesic medication (diclofenac) and hospitalization [16]. Additionally, Hermanns et al. [11] demonstrated that 76 and 84 % of the patients in the tamsulosin and control groups passed the distal ureteral stones <5 mm in a successful manner.

On the other hand, it is well known that ureteral calculi could be a serious health problem resulting from the associated distressing symptoms (mainly colic pain necessitating analgesic use and ED visits) and obstruction caused by relatively larger stones (>5 mm). These symptoms may induce significant adverse effects on the HRQOL of the cases during the observation period for spontaneous passage [1, 2, 4]. Thus, in addition to the well-documented data regarding the effective use of these agents for spontaneous passage in appropriate cases, clinical use of these agents may give us additional advantages to lower the risk of stone-induced distressing symptoms which will have negative effects on the life quality of these cases.

Although the life quality of the cases suffering from stone disease is an important issue, “at least from patients perspective,” this issue has not been subjected to well-documented studies in detail. Concerning this critical issue of the limited data reported in the literature so far, Penniston and Nakada reported that patients with urolithiasis showed decreased HRQOL when compared to healthy adults. Using the SF-36 validated QOL questionnaire, they specifically found that stone-bearing patients had lower scores on the general health and bodily pain domains, and female stone formers reported lower average QOL scores than male respondents [17]. In 2009, again, Bensalah et al. [18] reported multiple factors affecting HRQOL in patients with urolithiasis, including BMI, age and the number of surgical procedures performed. Lastly, Rabah et al. [19] examined HRQOL of patients after lithotripsy procedure and stated that HRQOL of these cases was similar to the healthy

controls. In light of these data reported so far, it will be clear that the HRQOL of patients with ureteral stones during watchful waiting period for spontaneous passage and the possible positive effects of MET on this critical factor have not been evaluated so far.

HRQOL is an estimate of freedom from impairment, disability or handicap [6]. The concept of HRQOL is multi-dimensional and includes psychosocial, physical and emotional status, as well as patient autonomy and is applicable to a wide variety of medical conditions [7].

In light of the data given above, one can easily claim that, in addition to increasing the stone-free rates, MET application will further be advantageous by diminishing the associated symptoms and morbidity caused by the stone(s) that may significantly affect the HRQOL of the cases during this period. This observation will further strengthen the judicious use of these agents in such cases. With this concept, we may realize and say that urologists should not solely focus on the stone-free rates obtained but also on the possible effects of the stone-induced distressing symptoms on the psychological and social life of the patients [5]. Related with this subject, to our knowledge, no study so far has investigated HRQOL in patients with ureteral calculi under close follow-up for spontaneous passage and possible effects of MET on the HRQOL of the cases treated.

In this present study, we aimed to evaluate the possible effects of MET on the HRQOL of the patients under watchful waiting for ureteral stones, and obtained data clearly demonstrated that use of alpha-blockers did significantly lower the mean number of renal colics which may normally result in a relatively higher use of analgesic and subsequent ED visits. In addition to these observations, most importantly, our current findings well demonstrated that this approach will significantly improve the HRQOL of the cases with ureteral calculi which may be particularly affected by the stone-induced factors mentioned above. Higher scores of EQ-5D index along with higher EQ-5D VAS values noted in cases treated with MET further supported our hypothesis. All these findings clearly demonstrate the improving effects of MET on the HRQOL of the cases with ureteral stones under observation for spontaneous passage.

Our current study may have only one certain limitation; the number of cases evaluated in this study might be small, but in light of the highly limited published data available in the literature, we believe that our current findings will be contributive enough to a considerable extent.

## Conclusion

Our current data clearly show that in addition to the increased spontaneous stone passage rates, MET for ureteral calculi could increase the HRQOL scores in these cases by lowering

the number of both renal colic attacks and ED visits along with decreased analgesic need during watchful waiting period for spontaneous passage. With this approach, the need for stone removal as well as auxiliary procedures which may also further affect the HRQOL scores will certainly be diminished.

#### Compliance with ethical standard

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical standard** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

#### References

1. Tiselius HG (2003) Epidemiology and medical management of stone disease. *BJU Int* 91:758–767
2. Scales CD, Smith AC, Hanley JM, Saigal CS (2012) Prevalence of kidney stones in the United States. *Eur Urol* 62:160–165
3. Hollingsworth JM, Norton EC, Kaufman SR, Smith RM, Wolf JS Jr, Hollenbeck BK (2013) Medical expulsive therapy versus early endoscopic stone removal for acute renal colic: an instrumental variable analysis. *J Urol* 190:882–887
4. Coll DM, Varanelli MJ, Smith RC (2002) Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. *Am J Roentgenol* 178:101–103
5. Seitz C, Liatsikos E, Porpiglia F, Tiselius HG, Zwergel U (2009) Medical therapy to facilitate the passage of stones: what is the evidence? *Eur Urol* 56:455–471
6. Pedro RN, Hinck B, Hendlin K, Feia K, Canales BK, Monga M (2008) Alfuzosin stone expulsion therapy for distal ureteral calculi: a double-blind, placebo controlled study. *J Urol* 179:2244–2247
7. Lee SR, Jeon HG, Park DS, Choi YD (2012) Longitudinal stone diameter on coronal reconstruction of computed tomography as a predictor of ureteral stone expulsion in medical expulsive therapy. *Urology* 80:784–789
8. Hollingsworth JM, Wolf JS Jr, Faerber GJ, Roberts WW, Dunn RL, Hollenbeck BK (2010) Understanding the barriers to the dissemination of medical expulsive therapy. *J Urol* 184:2368–2372
9. Resim S, Ekerbicer H, Ciftci A (2005) Effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus. *Int J Urol* 12:615–620
10. EuroQol Group (2008) EQ-5D available versions. [http://www.euroqol.org/web/users/language\\_a.php](http://www.euroqol.org/web/users/language_a.php)
11. Hermanns T, Sauer mann P, Rufibach K, Frauenfelder T, Sulser T, Strebel RT (2009) Is there a role for tamsulosin in the treatment of distal ureteral stones of 7 mm or less? Results of a randomised, double-blind, placebo-controlled trial. *Eur Urol* 56:407–412
12. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck C, Gallucci M et al (2007) Guideline for the management of ureteral calculi. *J Urol* 178:2418–2434
13. Miller OF, Kane CJ (1999) Time to stone passage for observed ureteral calculi: a guide for patient education. *J Urol* 162:688–691
14. Lotan Y, Gettman MT, Roehrborn CG, Cadeddu JA, Pearle MS (2002) Management of ureteral calculi: a cost comparison and decision making analysis. *J Urol* 167:1621–1629
15. Zheng S, Liu LR, Yuan HC, Wei Q (2010) Tamsulosin as adjunctive treatment after shockwave lithotripsy in patients with upper urinary tract stones: a systematic review and meta-analysis. *Scand J Urol Nephrol* 44:425–432
16. Campschroer T, Zhu Y, Duijvesz D, Grobbee DE, Lock MT (2014) Alpha-blockers as medical expulsive therapy for ureteral stones. *Cochrane Database Syst Rev* 4:CD008509
17. Penniston KL, Nakada SY (2007) Health related quality of life differs between male and female stone formers. *J Urol* 178:2435–2440
18. Bensalah K, Tuncel A, Gupta A, Raman JD, Pearle MS, Lotan Y (2008) Determinants of quality of life for patients with kidney stones. *J Urol* 179:2238–2243
19. Rabah DM, Alomar M, Binsaleh S, Arafa MA (2011) Health related quality of life in ureteral stone patients: post-ureterolithiasis. *Urol Res* 39:385–388