

Sexual intercourse as a new option in the medical expulsive therapy of distal ureteral stones in males: a prospective, randomized, controlled study

Zeki Bayraktar^{1,2}  · Selami Albayrak¹

Received: 10 July 2017 / Accepted: 7 August 2017 / Published online: 12 August 2017
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Abstract

Purpose To investigate the effect of sexual intercourse on the spontaneous passage of distal ureteral stones 5–10 mm in size.

Methods A total of 190 male patients with distal ureteral stones were randomly divided into three groups. Patients in group 1 were administered tamsulosin 0.4 mg/day ($n = 60$). Patients in group 2 were asked to have sexual intercourse at least three times a week ($n = 66$). Patients in group 3 received standard medical therapy alone and acted as the controls ($n = 64$). The expulsion rate was controlled after 2 and 4 weeks. Differences between the groups were analyzed statistically by the Chi-square and Student's t test. $p < 0.05$ was considered as statistically significant.

Results The mean ages of the patients in groups 1, 2, and 3 were 34.4 ± 13.5 (18–60), 38.6 ± 14.1 (18–63), and 36.92 ± 12.4 (18–59) years, respectively ($p > 0.05$). The mean stone size was 7.09 ± 1.4 mm in group 1, 7.01 ± 1.4 mm in group 2, and 7.1 ± 1.3 mm in group 3 ($p > 0.05$). Spontaneous passage rates in groups 1, 2, and 3 were 81.6, 81.8, and 51.5%, respectively, and it was significantly higher in group 1 ($p = 0.0394$) and group 2 ($p = 0.0350$). There was no significant difference between groups 1 and 2 ($p = 0.9925$). The analgesic needs in groups 1, 2, and 3 were found to be 1.3 ± 0.4 , 1.2 ± 0.6 , and

1.4 ± 0.4 times, respectively, and were significantly lower in the sexual intercourse group than in the control group ($p = 0.0276$).

Conclusions Tamsulosin and sexual intercourse increase the spontaneous passage of distal ureteral stones 5–10 mm in size. At least three sexual intercourses per week seem to be at least as effective as tamsulosin. Sexual intercourse also reduces the need for analgesics in ureteric colic due to ureteral stones.

Keywords Medical expulsive therapy · Sexual intercourse · Tamsulosin · Ureteral stone

Abbreviations

cAMP	Cyclic adenylylate monophosphate
cGMP	Cyclic guanylylate monophosphate
ESWL	Extracorporeal shockwave lithotripsy
MET	Medical expulsive therapy
NANC	Non-adrenergic non-cholinergic
NO	Nitric oxide
PDE5i	Phosphodiesterase type 5 inhibitors
URS	Ureterorenoscopic lithotripsy

Introduction

Ureterolithiasis is one of the most prevalent urological diseases all over the world [1]. Therapeutic options for ureteral stones include different invasive and noninvasive therapeutic options such as conservative management, observation/spontaneous passage, medical expulsive therapy (MET), extracorporeal shockwave lithotripsy (ESWL), and ureterorenoscopic lithotripsy (URS) [2, 3].

MET is a noninvasive method used in the management of ureteral stones [3, 4]. MET is a safe therapeutic option

✉ Zeki Bayraktar
zbayraktar@medipol.edu.tr

Selami Albayrak
salbayrak@medipol.edu.tr

¹ Department of Urology, School of Medicine, Istanbul Medipol University, Istanbul, Turkey

² Çamlık Mah. Piri Reis Cad. Papatya Sitesi No: 48, Pendik, 34890 Istanbul, Turkey

which has been mostly preferred in recent years because it increases the likelihood of stone expulsion and decreases the stone expulsion time, hospitalization duration, labor loss, costs, need for invasive intervention, risks associated with interventions, and complications in patients with ureteral calculus who are suitable for conservative treatment [3–5]. Furthermore, it is suggested that the application time of MET should not exceed 4 weeks and that the patient should be checked on the 1st and 14th days in terms of stone localization and especially hydronephrosis [6].

For the MET decision, the anatomical state and preference of the patient as well as the localization and size of the stone are also important [3, 7]. While the lower limit for MET was previously accepted as 5 mm, the lower limit which is now expressed in the new guidelines is 6 mm, and the upper limit is 10 mm. In other words, the recommended stone size for MET is 6–10 mm [3, 6, 7]. Hence, MET is mainly preferred in practice for distal ureteral stones 5–10 mm in size [3], because ureter stones between 2 and 4 mm in size are already expelled by the spontaneous passage at the rate of 95% [3, 4]. However, the spontaneous passage ratio decreases by 50% in stones between 5 and 10 mm in size [8, 9]. Thus, multicenter, randomized, placebo-controlled studies show that the spontaneous passage of ureteral stones varies between 50 and 95% depending on the size and localization of the stone [10].

The drugs used for MET are alpha blockers, calcium channel blockers (nifedipine), corticosteroids, and phosphodiesterase type 5 inhibitors (PDE5i) [3]. However, a significant part of the studies carried out shows that the most successful result is achieved with alpha blockers. Therefore, current guidelines mostly suggest alpha blockers [3, 6, 7], because the distal ureter is rich in alpha-1 adrenergic receptors and the alpha-1 adrenergic receptor blockage reduces the peristaltic movements (frequency) and basal ureteral tonus of the ureter [11, 12]. In other words, the likelihood of the spontaneous passage of ureter stones increases with the use of alpha blockers [3, 11]. Hence, many studies have shown that distal ureteral stones are successfully treated with alpha blockers, and MET has become the first-line treatment option for the treatment of ureteral stones in patients who do not need a surgery [4, 9, 15–17]. In practice, the most preferred alpha blocker for MET is tamsulosin [3, 12–17].

Some recent studies have reported that sexual intercourse may be an alternative therapeutic option in the medical expulsive therapy of ureteric stones [17, 18]. However, these studies have some limitations such as small stone size [17] and limited patient numbers [18]. In the present study, we examined the efficiency of sexual intercourse in the treatment of distal ureteral stones 5–10 mm in size.

Methods

The study protocol was approved by the institutional ethics committee of the School of Medicine, Istanbul Medipol University, Turkey (December 2015). Between December 2015 and May 2017, 211 married males with radiopaque distal ureter stones 5–10 mm in size were included in the study. Stones under the iliac artery–ureter cross were considered to be distal ureteral stones. Patients were randomly divided into three groups according to the order of arrival (1:1:1 ratio). As a standard medical therapy, all patients were recommended a daily intake of liquids to urinate at least 1.5–2 l, and 75 mg of diclofenac was injected when they needed due to pain. Furthermore, the patients in the first group were administered with a single dose of tamsulosin of 0.4 mg daily. The patients in the second group were recommended to have sexual intercourse at least three times a week. The patients in the third group were administered standard medical therapy alone and acted as the controls. The patients in groups 1 and 3 were asked to avoid sexual intercourse and masturbation for 4 weeks. The patients who reported more than one sexual intercourse or masturbation per week were excluded from the study.

The age and stone size of all patients were noted. The stone size was measured with the longest diameter in the X-ray and tomography. At the beginning of the follow-up, hemogram, urine analysis, serum urea–creatinine level, direct urinary system graphy, urinal ultrasonography, and unenhanced urine tomography studies were performed in all patients. The patients were followed up until the stone was passed or for a maximum of 4 weeks. For all patients, the urine analysis, direct urinary system graphy, and urinal ultrasonography were performed in the 2 weeks of the follow-up (on days 14 and 16), and the urine analysis and tomography were performed again in the fourth week. All patients were asked to note the number of pain, need for injection, and the number of masturbation and sexual intercourses during the follow-up. All patients were asked to follow-up urine to determine the potential passage of the stone. However, whether the stone was passed was not determined only by the patient's statement. Moreover, all tomography and direct urinary system graphy of the patients were analyzed and confirmed by a urologist blinded to the group of the patients.

The data obtained at the end of the 4-week follow-up were statistically analyzed. Statistical analyses were performed with the MedCalc statistical software program (version 16.4.3, MedCalc Software bvba, Ostend, Belgium). The Chi-square test and Student's *t* test were used for comparison between the groups. $p < 0.05$ was considered as significant.

Inclusion criteria

Married male patients over the age of 18 years with opaque distal ureteral stones 5–10 mm in size.

Exclusion criteria

Proximal or intermediate ureter stones (stones on the ureter–iliac artery cross), stones <5 mm in size, stones ≥10 mm in size, multiple ureter stones, being <18 years of age, urinary infection, fever, renal insufficiency, high creatinine level, pregnancy, severe hydronephrosis, endoscopic or open ureteral surgery history, ureteral stenosis, vesicoureteral reflux, neurogenic bladder, unmarried patients, patients with erectile dysfunction, patients with more than one sexual intercourse and masturbation statement per week

for group 1 and group 3, and patients with less than three sexual intercourse statements per week for group 2.

Results

The findings are summarized in Table 1. A total of 211 male patients with distal ureteral stones were randomized to group 1 ($n = 71$), group 2 ($n = 70$), and group 3 ($n = 70$). A total of 13 patients, 6 in group 1, 4 in group 2, and 3 in group 3, were excluded from the study because they were lost in follow-up. Furthermore, 5 patients in group 1 and 3 patients in group 3 were also excluded from the study because they declared more than one sexual intercourse or masturbation per week. Apart from this, there were no patients who were dropped out of the protocol for any other reasons such as

Table 1 Overall results in groups 1, 2, and 3

	Group 1; tamsulosin ($n = 60$)	Group 2; sexual intercourse ($n = 66$)	Group 3; control ($n = 64$)	p values (1–2, 1–3, 2–3)
Age/years	34.4 ± 13.5 (18–60)	38.66 ± 14.1 (18–63)	36.92 ± 12.4 (18–59)	$p = 0.0909$ $p = 0.2808$ $p = 0.4569$
Stone size (mm)	7.09 ± 1.4 (5–9.9)	7.01 ± 1.4 (5–9.9)	7.1 ± 1.3 (5–9.9)	$p = 0.7492$ $p = 0.9672$ $p = 0.7049$
<i>Expulsion rate after 2 weeks (n, %)</i>				
Stone size ≤7 mm	25/34 (73.5%)	32/46 (69.5%)	13/43 (30.2%)	$p = 0.8355$ $p = 0.0037^*$ $p = 0.0091^*$
Stone size >7 mm	17/26 (65.4%)	14/20 (75%)	5/21 (23.8%)	$p = 0.8501$ $p = 0.0382^*$ $p = 0.0299^*$
Total (after 2 weeks)	42/60 (70%)	46/66 (69.7%)	18/64 (28.1%)	$p = 0.9838$ $p = 0.0008^*$ $p = 0.0007^*$
<i>Expulsion rate after 4 weeks (n, %)</i>				
Stone size ≤7 mm	29/34 (85.3%)	36/46 (78.2%)	23/43 (53.4%)	$p = 0.7301$ $p = 0.0917$ $p = 0.1515$
Stone size >7 mm	20/26 (76.9%)	18/20 (90%)	10/21 (47.6%)	$p = 0.6287$ $p = 0.2112$ $p = 0.1007$
Total (after 4 weeks)	49/60 (81.6%)	54/66 (81.8%)	33/64 (51.5%)	$p = 0.9925$ $p = 0.0394^*$ $p = 0.0350^*$
Expulsion time (day, mean ± SD)	9.3 ± 5.8	8.8 ± 6.7	8.7 ± 6.4	$p = 0.6565$ $p = 0.5862$ $p = 0.9308$
Need for analgesic (number of injections, daily)	1.3 ± 0.4	1.2 ± 0.6	1.4 ± 0.4	$p = 0.2781$ $p = 0.1667$ $p = 0.0276^*$
Ureterorenoscopic lithotripsy	11/60 (18.3%)	12/66 (18.1%)	31/64 (48.4%)	$p = 0.9841$ $p = 0.0040^*$ $p = 0.0027^*$

* Statistically significant, $p < 0.05$

an emergency operation and patient request. Ultimately, the study was completed with 60 patients in group 1, 66 patients in group 2, and 64 patients in group 3. The mean ages of the patients in groups 1, 2, and 3 were 34.4 ± 13.5 (18–60), 38.6 ± 14.1 (18–63), and 36.92 ± 12.4 (18–59) years, respectively. The mean stone size was 7.09 ± 1.4 mm in group 1, 7.01 ± 1.4 mm in group 2, and 7.1 ± 1.3 mm in group 3. There was no statistically significant between the groups in terms of age and stone size.

At the end of the fourth week, 49 of 60 patients (81.6%) in the tamsulosin group, 54 of 66 patients (81.8%) in the sexual intercourse group, and 33 of 64 patients (51.5%) passed their stones. There was no significant difference between group 1 and group 2 in terms of spontaneous passage ($p = 0.9925$). However, when compared with the control group, the spontaneous passage rate was significantly higher in group 1 ($p = 0.0394$) and group 2 ($p = 0.0350$).

The mean stone expulsion time was 9.3 ± 5.8 days in group 1, 8.8 ± 6.7 days in group 2, and 8.7 ± 6.4 days in group 3 ($p > 0.005$). The analgesic needs in groups 1, 2, and 3 were found to be 1.3 ± 0.4 , 1.2 ± 0.6 , and 1.4 ± 0.4 times, respectively, and were significantly lower in group 2 ($p = 0.0276$). The patients that could not pass their stones at the end of 4 weeks (11 patients in group 1, 12 patients in group 2, and 31 patients in group 3) were treated successfully with ureterorenoscopic lithotripsy. The number of patients requiring additional treatment (URS) was significantly lower in group 1 ($p = 0.0040$) and group 2 ($p = 0.0027$).

Discussion

The findings of the present study are consistent with results from previous studies that reported that sexual intercourse may be an alternative therapeutic option in the medical expulsive therapy of ureteric stones [17, 18]. Doluoglu et al. [17] reported that having sexual intercourse three or four times a week increased the spontaneous passage of ureteral stones, shortened the expulsion time, and decreased the analgesic requirement, and as a result, they reported that sexual intercourse could be an alternative therapeutic option. But this study had an important limitation because the stone size in their study was ≤ 6 mm. In contrast, the stone sizes in our study were 5–10 mm.

In another study, Abdel-Kader reported that practicing sexual intercourse for 3–4 times/week for male patients with distal ureteric stone (5–10 mm) increases the expulsion rate (23/28; 89% in the sexual intercourse group, 20/28; 71% in the control group) and decreases the frequency of renal colic and the needs for analgesic [18]. But this study also had an important limitation due to the small sample size (56 patients). But nevertheless, the results of these two previous

studies are consistent with our results. Therefore, it can be said that sexual intercourse is an alternative therapeutic option in the medical expulsive therapy of distal ureteric stones.

Ureteral peristalsis is essentially regulated by myogenic mechanisms. However, neurogenic factors also play an important role in this process. In fact, at the distal ureter and ureterovesical junction, smooth muscle activity is regulated by the autonomic nervous system, via noradrenergic, cholinergic, and non-adrenergic non-cholinergic (NANC) nerves [17–20]. For this reason, sexual intercourse may also be effective in ureteral peristalsis. Another factor that is effective in the peristaltic movements of the ureter is nitric oxide (NO), which plays a role in the physiology of erection [21]. NO is an important neurotransmitter in both erection physiology and ureteral peristalsis [21–24]. NO, originally identified as an endothelium-derived relaxing factor, is considered to be the main regulatory gaseous molecule involved in a wide range of biological processes, acting as a second messenger and neurotransmitter [20–22]. Strong evidence shows that the gaseous mediator NO would be involved in the NANC inhibitory transmission to the distal ureter, ureterovesical junction, and bladder outflow region [22].

NO released from nerve endings by parasympathetic activation causes cavernosal relaxation and consequently penile erection by increasing the levels of cyclic guanylate monophosphate (cGMP) and cyclic adenylylate monophosphate (cAMP) in cavernous smooth muscle cells [24]. In other words, the NO level increases during penile erection. This reduces the ureteral peristalsis and ureteral tonus by the NO effect during sexual intercourse (erection), the passage of ureteral stones is facilitated, and the analgesic requirements of patients are decreased. That is, sexual intercourse does not only increase the spontaneous passage of ureteral stones, but also it shortens the expulsion time and decreases the frequency of renal colic and the needs for analgesic [17, 18]. All of this increases the quality of life of patients because Eryildirim et al. [25] reported that MET for ureteral calculi during watchful waiting period could increase the health-related quality of life of patient scores by lowering the number of both renal colic attacks and emergency department visits resulting in decreased analgesic need.

The fact that patients with ureteral stones have sexual intercourse has the same effect as oral PDE5i due to, probably, NO that increases during erection. Hence, it is observed that spontaneous passage rates ranging from 66.7 to 93.3% were obtained in the studies carried out with sildenafil and tadalafil in ureteral stones; in other words, oral PDE5i was at least as effective as tamsulosin and decreased the need for analgesic in these patients [26, 27].

The spontaneous passage rates in this study are 80% in the tamsulosin group and 81.8% in the sexual intercourse group. These rates obtained with tamsulosin in distal ureteral

stones vary between 53 and 100% [3, 12, 15, 28], depending on stone size and follow-up time. Nevertheless, the current guidelines do not recommend the follow-ups longer than 4 weeks for MET due to the risk of hydronephrosis [6].

Conclusion

Tamsulosin and sexual intercourse increase the spontaneous passage of distal ureteral stones 5–10 mm in size. At least three sexual intercourses per week seem to be at least as effective as tamsulosin. Furthermore, sexual intercourse reduces the need for analgesics in ureteric colic due to ureteral stones. It seems that the increased NO during erection facilitates the passage of stones and reduces the need for analgesic by reducing the ureteral peristalsis and tonus. These findings indicate that sexual intercourse may be a new natural therapeutic option in the medical treatment of distal ureteral stones. However, there is a need for more comprehensive studies on this subject. The effects of sexual intercourse, masturbation, orgasmic contractions and relaxations on the ureteral tonus should be examined, and their clinical implications should be investigated in large patient groups.

Compliance with ethical standards

Conflict of interest Both the authors declare that they have no conflict of interest in the study.

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

Human and animal rights This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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