

Meta-analysis of the efficacy of sexual intercourse for distal ureteric stones

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Abstract

Objective: This meta-analysis was performed to evaluate the efficacy of sexual intercourse for treatment of distal ureteral stones.

Methods: Randomized controlled trials (RCTs) of sexual intercourse for treatment of distal ureteral stones were searched using PubMed, EMBASE, and the Cochrane Controlled Trials Register.

Results: Three RCTs comprising 240 patients were included in the meta-analysis, which showed that sexual intercourse was effective in treating distal ureteral stones. The expulsion rate of distal ureteral stones at the second week (odds ratio [OR] = 6.61, 95% confidence interval [CI]: 3.66 to 11.94), expulsion rate of distal ureteral stones at the fourth week (OR = 4.00, 95% CI: 2.09 to 7.64), and number of analgesic injections (mean difference [MD] = -0.79, 95% CI: -1.51 to -0.08) indicated that sexual intercourse was more effective than placebo. However, the mean expulsion time of distal ureteral stones (MD = -3.98, 95% CI: -8.77 to 0.81) showed no difference between sexual intercourse and placebo.

Conclusions: Compared with placebo, sexual intercourse exhibited greater efficacy for the treatment of distal ureteral stones, whilst potentially alleviating pain.

Keywords

Sexual intercourse, distal ureteral stones, randomized controlled trials, meta-analysis, analgesics, pain

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Introduction

Urolithiasis is a frequent and multifactorial disorder in daily urological practice that affects approximately 5% to 10% of people worldwide.^{1,2} Of all urinary stones, ureteric stones comprise 20%, with 70% of these ureteric stones located in the distal ureteric segment.³ The spontaneous passage of distal ureteral calculi varies between 50% and 95%, depending on the localization and size of the calculi.⁴ Using α -adrenoceptor antagonists, medical expulsive therapy (MET) has been exploited as an alternative strategy for initial treatment of small distal ureteral stones.⁵ In addition to its ability to increase the incidence of stone expulsion, a significant reduction was observed in the costs, labor loss, and risks caused by invasive interventions, as well as stone expulsion time, duration of hospitalization, and complications in patients with ureteral stones.⁶⁻⁸

MET involves the use of various drugs, such as α -blockers, calcium channel blockers (e.g., nifedipine), corticosteroids, and phosphodiesterase type 5 inhibitors (PDE5i) acting on the ureter by different mechanisms.⁹ α -blockers could be beneficial to the patient when used for distal ureteral stones more than 5 mm in size. However, the quality of randomized controlled studies of MET remains low, based on the Consolidated Standards for Reporting Trials (CONSORT) criteria. Several studies have shown that PDE5i facilitates ureteral stone expulsion through a nitric oxide (NO)-mediated pathway.¹⁰ MET should be used with caution in children and pregnant women. NO is a crucial neurotransmitter in both ureteral peristalsis and erection physiology. During sexual intercourse, NO is abundantly released in cavernosal tissues, as well as in the distal ureter, causing ureteric smooth muscle relaxation.¹¹⁻¹⁴ Recently, some studies have suggested a role for sexual intercourse

as an alternative therapeutic option in the management of distal ureteral calculi.¹⁵⁻¹⁷

Thus far, there has been no meta-analysis regarding the efficacy of sexual intercourse versus placebo in treatment of distal ureteral stones. Therefore, we performed a meta-analysis to assess the effects of sexual intercourse in patients with distal ureteral calculi.

Methods

Search strategy

PubMed (from 1987 to April 2018), EMBASE (from 1987 to April 2018), the Cochrane Controlled Trial Register of Controlled Trials, and the reference lists of the retrieved studies were searched to identify randomized controlled trials (RCTs) that assessed the efficacy of sexual intercourse for treatment of ureteral calculi. The search terms used were: Sexual intercourse, ureteral stones, ureteral calculi, ureteric stones, distal ureteral stones, and randomized controlled trials.

Trial selection

RCTs that met the following criteria were included: (1) they studied the efficacy of sexual intercourse for treatment of distal ureteral stones, (2) they provided sufficient data for analysis, including the expulsion rate of distal ureteral calculi, number of analgesic injections, or mean expulsion time of distal ureteral calculi, and (3) the full text of the selected study was accessible. If the same group of researchers studied a group of subjects with multiple experiments, then each study was included. The selection process is shown in Figure 1.

Quality assessment

The Jadad Scale was used to evaluate the quality of searched RCTs. The research methods (patient allocation, concealment

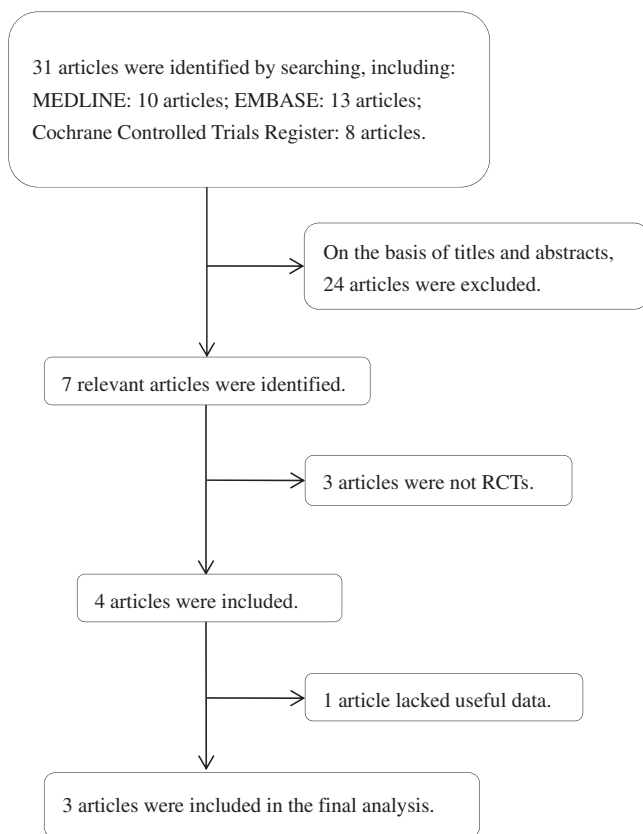


Figure 1. Flow diagram of the study selection process. RCT, randomized controlled trial.

of allocation, blinding method, number of cases lost to follow-up) were used to determine the quality of an individual study. Afterwards, the studies were distributed on the basis of guidelines set in the *Cochrane Handbook for Systematic Reviews of Interventions* v.5.1.0.¹⁸ Each study was rated and assigned to one of the three following quality categories based on the quality assessment criteria: –, high risk of bias; +, low risk of bias; ?, unclear risk of bias. Differences were settled by discussion among the authors.

Data extraction

Usable information was collected from each article, including (1) the name of the first

author and year of article publication, (2) study design, (3) therapy in the experimental and control groups, (4) sample size, (5) follow-up time, and (6) the study population.

Statistical analysis

Data were analyzed using Review Manager 5.1.0 (The Cochrane Collaboration, London, UK). Fixed effects (Mantel-Haenszel method) and random effects (DerSimonian and Laird method) models were used to assess the mean difference (MD) for continuous data and the Odds Ratio (OR) for dichotomous results pooled across studies, with corresponding 95% confidence intervals (CIs). A random effects model was used if heterogeneity was

detected, whereas a fixed effects model was used if there was no conspicuous heterogeneity. Chi-squared tests were used to assess heterogeneity, and $p < 0.05$ was considered statistically significant. We combined forest plots by using Adobe Photoshop CS (Adobe Systems, San Jose, CA, USA).

Results

Characteristics of individual studies

On the basis of the exclusion and inclusion criteria, three RCTs¹⁵⁻¹⁷ including 240 patients were considered eligible for

the analysis. Relevant characteristics of the articles are listed in Table 1.

Quality of individual studies

All included articles were double-blinded RCTs, and each described their randomization processes. All included articles reported a power calculation to determine the optimal sample size (Table 2). The level of quality of each identified article was A (Table 2).

Expulsion rate of distal ureteral stones

Three RCTs including 240 patients (125 in the sexual intercourse group and 115 in the

Table 1. Characteristics of randomized controlled trials (RCTs) included in the present meta-analysis.

Study	Design	Therapy in experimental group	Therapy in control group	Sample size		Follow-up time	Inclusion population
				Experiment	Control		
Abdel-Kader 2017	RCT	Sexual intercourse 3-4 times/week + symptomatic treatment	Symptomatic treatment	28	28	4 weeks	Married males, from 26 to 55 years of age, with radiopaque distal ureteral stones or intramural stones 5-10 mm in size.
Bayraktar 2017	RCT	Sexual intercourse at least 3 times/week	Symptomatic treatment	66	64	4 weeks	Married males over the age of 18 years with radiopaque distal ureteral stones 5-10 mm in size.
Doluoglu 2015	RCT	Sexual intercourse at least 3 times/week	Symptomatic treatment	31	23	4 weeks	Married males over the age of 18 years with radiopaque distal ureteral stones ≤ 6 mm in size.

Table 2. Risk of bias for included randomized controlled trials.

Study	Sequence generation	Allocation concealment	Blinding	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias
Abdel-Kader 2017	+	+	+	+	?	+
Bayraktar 2017	+	+	+	+	+	?
Doluoglu 2015	+	+	+	+	+	?

+, low risk of bias; ?, unclear risk of bias; -, high risk of bias.

placebo group) (Figure 2) were identified. Compared with placebo, sexual intercourse therapy was associated with a significantly higher expulsion rate at the second week (OR=6.61, 95% CI: 3.66 to 11.94, $p < 0.0001$). Moreover, at the fourth week, a statistically higher expulsion rate of distal ureteral stones was also observed in the group undergoing sexual intercourse therapy (OR = 4.00, 95% CI: 2.09 to 7.64, $p < 0.0001$).

Need for analgesic injections

All patients received nonsteroidal anti-inflammatory drug injection (e.g., ketorolac and diclofenac) on demand as analgesic. Therefore, the number of analgesic

injections was used to measure pain control within the patients. All three RCTs including 240 patients (125 in the sexual intercourse group and 115 in the placebo group) (Figure 3) were used for analysis of the number of analgesic injections. Compared with placebo, sexual intercourse therapy significantly reduced the number of analgesic injections required by patients (MD = -0.79, 95% CI: -1.51 to -0.08, $p = 0.03$).

Expulsion time of distal ureteral stones

Additionally, all three RCTs including 240 patients (125 in the sexual intercourse group and 115 in the placebo group) (Figure 4) were used for analysis of the expulsion time of distal ureteral stones.

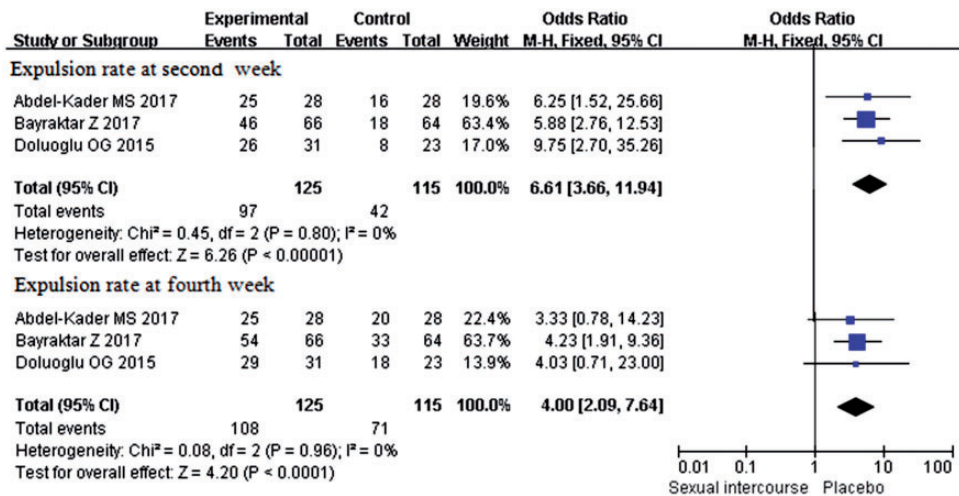


Figure 2. Forest plots showing expulsion rate of distal ureteral stones.

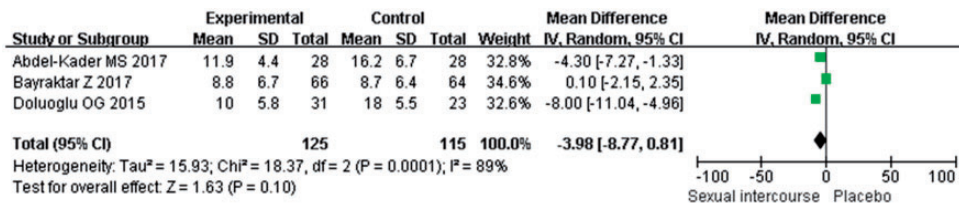


Figure 3. Forest plots showing the requirement for analgesic injections.

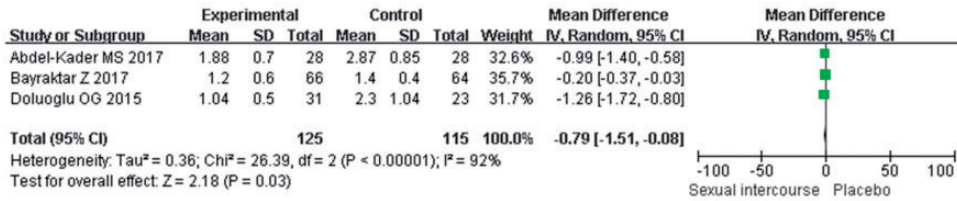


Figure 4. Forest plots showing expulsion time of distal ureteral stones.

Sexual intercourse therapy showed no difference in expulsion time, compared with placebo (MD = -3.98, 95% CI: -8.77 to 0.81).

Discussion

MET has become a well-established modality of treatment by virtue of a wide array of drugs acting on the ureter, which promotes stone passage and circumvents invasive surgery.⁶ Current European Association of Urology guidelines recommend the use of MET for all ureteral stones, while American Urological Association guidelines recommend MET only for patients with distal ureteral stones ≤ 10 mm. A recent systematic meta-analysis of MET studies by Hollingsworth et al.¹⁹ concluded that MET increased the likelihood of stone passage for stones ≥ 5 mm, regardless of location. Furyk et al.²⁰ found that MET increased the likelihood of spontaneous stone passage in a subset of larger stones 5–10 mm in size ($p=0.03$). These conflicting data have generated some doubt regarding the efficacy of MET.

Currently, sexual intercourse is regarded as a novel therapeutic option for MET of distal ureteric stones. Doluoglu first demonstrated that sexual intercourse 3 or 4 times per week increased the spontaneous passage of ureteral stones, reduced the analgesic requirement, and shortened the expulsion time.¹⁵ Nitroergic fibers were shown in human and porcine intravesical ureters,

approximately 20 years ago.^{21,22} Studies have suggested that both exogenously released and endogenously administered NO can cause relaxation of the porcine intravesical ureter.²³ NO is an important neurotransmitter in both ureteral peristalsis and erection physiology;¹⁴ notably, NO is released from the endothelium and directly from nitroergic nerves. Upon stimulation of the cavernous nerve, nitroergic nerve fibers are activated and NO is released from the nerve endings, which ultimately causes penile smooth muscle relaxation.²⁴ The level of NO in the body increases during sexual intercourse. This can inhibit ureteral tonus and ureteral peristalsis via the NO-mediated pathway; thus, the analgesic requirements of patients are reduced, facilitating the passage of ureteral stones. Therefore, sexual intercourse is considered an effective method to treat ureteral peristalsis. Furthermore, the proposed mechanism indicates that masturbation may not achieve the same benefits as sexual intercourse with regard to ureteral peristalsis; further research is required.

Our results indicate that, for patients with distal ureteric stones, performing sexual intercourse 3 or 4 times per week increases the expulsion rate at the second week or fourth week; moreover, it reduces the requirement for analgesic injections, compared with placebo. Thus, it improves the quality of life for patients with stones. Furthermore, this meta-analysis is the first to assess the efficacy of sexual intercourse

versus placebo for treatment of distal ureteral stones. Following this comprehensive assessment, our meta-analysis suggests that sexual intercourse therapy is superior to placebo in regards to efficacy for treatment of distal ureteral calculi, and that it provides better control of pain.

This meta-analysis included only studies in which all data were derived from randomized double-blind, placebo-controlled trials. Though the quality of the individual studies in the meta-analysis conformed to the quality assessment scale that we developed, our study contains some limitations. First, the number of included studies was not large. Second, the baseline characteristics of the patients were not uniform, especially with regard to stone size. Third, the long-term efficacy of this therapy cannot be determined in our analysis. Finally, data from unpublished studies were not used in this analysis. These factors may contribute to bias in the results. Additional high-quality articles with larger samples are required to further evaluate the efficacy of sexual intercourse for treatment of distal ureteral stones.

Conclusions

Sexual intercourse is superior to placebo with respect to its efficacy for treatment of distal ureteral calculi; moreover, it provides better control of pain. Our meta-analysis demonstrates that sexual intercourse may offer an alternative therapeutic option for distal ureteral stones.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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