The Efficacy of Sexual Intercourse or Masturbation For The Expulsion Of Distal Ureteral Stones In Men: A Systematic Review And Meta-analysis of Randomized-controlled Trials

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Purpose: Several randomized-controlled trials (RCTs) were performed to compare the efficacy of sexual intercourse or masturbation with no sexual activity in treating distal ureteral stones, indicating conflicting results. The meta-analysis was conducted to assess the role of sexual intercourse or masturbation in the treatment of distal ureteral calculi.

Materials and Methods: PubMed, Cochrane Library, EMBASE, Scopus, Clinicaltrail.gov, and Web of Science were searched by October 2021. Men who were instructed of no sexual intercourse or masturbation, and those who only received standard symptomatic treatment are comparators. Relative risk (RR), weighted mean difference (WMD), and their 95% confidence intervals (CIs) were calculated using random or fixed effects models.

Results: Five RCTs including 500 subjects were analyzed in the study. Compared with controls, subjects in experimental group had significantly higher expulsion rate at 2nd and 4th week (95%CI: 1.334 to 2.638, RR: 1.876, I^2 = 73.6%, P < .001; 95%CI: 1.148 to 1.752, RR: 1.418, I^2 = 55.9%, P < .001), significantly decreased requirement for analgesic injections (95%CI: -1.071 to -.126, WMD: -.598, I^2 = 90.3%, P = .013), and significantly shorter expulsion time (95%CI: -6.941 to -.436, WMD: -3.689, I^2 = 83.7%, P = .026).

Conclusion: Performing sexual intercourse or masturbation 3 or 4 times a week can be an alternative treatment option of distal ureteral calculi (0-10 mm in size). However, more clinical evidence with better designs aiming to solve raised concerns is warranted.

Keywords: distal ureteral calculi; masturbation; meta-analysis; randomized-controlled trial; sexual intercourse

INTRODUCTION

Urolithiasis, a common and multifactorial disease affecting around 5-10% of people worldwide, is now increasing with an incidence of 1% per year.[1-3] Ureteral stones account for approximately one in the fifth of all urinary calculi, 70% of which are distal ureteral calculi.[4] Therapies for urolithiasis consists of invasive and non-invasive options including spontaneous passage, conservative therapy, medical expulsive therapy (MET), extracorporeal shockwave lithotripsy (ESWL), etc.[5] The rate of spontaneous passage of distal ureteral stones varies from 50% (5-10 mm in size) to 95% (2-4 mm in size), which depends on the size and location of the stone.[6-9] Therefore, MET is more preferred in the treatment of distal ureteral calculi with a size of 5-10 mm10. Currently, Tamsulosin is the most frequently used α-blockers in MET.[11-13]

The MET is based on the wide distribution of α-receptors in the distal ureter. Nitric oxygen (NO) plays a crucial role in erection as well as ureteral peristalsis. Anatomical and pharmacologic studies had indicated the distribution and the role of nitrergic fibers in the human intravesical ureter.[14] During sexual intercourse or masturbation, NO is abundantly released in these nerve endings, causing ureteral muscle relaxation, providing a possible alternative option for the management of ureteral stones.[15] Studies have indicated the efficacy of sexual intercourse or masturbation in the treatment of distal ureteral calculi, while findings are controversial.[16-18] A previously published meta-analysis conducted by Xu et al. only included 3 RCTs and now new findings were available.[26] Therefore, we conducted the meta-analysis to make a summary of evidence to date.

PATIENTS AND METHODS

Data sources

We made detailed inclusive criteria according to the well-established report guidelines before we searched the literatures.[19,20] In October 2021, all available evidence in PubMed, Web of Science, Cochrane library, Scopus, ClinicalTrail.gov website, and EMBASE was

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Table 1. Characteristic of included studies

Study	Study Design	Country	Subjects	Stone Features	Interventions In The Experimental Group	Treatment In The Control Group	Sample Size		Total Follow-up, Weeks	Main Outcomes
							Experimental Group	Control Group		
Doluoglu 2015	RCT	Turkey	Men aged over 18 with active partners	Radiopaque distal ureteral stones ≤ 6 mm in size.	Sexual intercourse at least 3-4 times a week and essential symptomatic treatment	Standard symptomatic treatment alone and instruction of no sexual intercourse or masturbation	31	23	4	Expulsion rate at 2nd and 4th week, expulsion time, and need for analgesics
Abdel-Kader 2017	RCT	Egypt	Married males aged 26-55	Radiopaque distal ureteral stones 5–10 mm in size.	Sexual intercourse 3-4 times/week and symptomatic treatment	Standard symptomatic treatment alone and instruction of no sexual intercourse or masturbation	28	28	4	Expulsion rate at 2nd and 4th week, expulsion time, need for analgesics, and frequency of colicky attacks
Bayraktar 2017	RCT	Turkey	Married males aged 26 to 55	Radiopaque distal ureteral stones or intramural stones 5–10 mm in size.	Sexual intercourse at least 3 times/week	Standard symptomatic treatment alone	66	64	4	Expulsion rate at 2nd and 4th week, expulsion time, need for analgesics, and need for ureterorenoscopic lithotripsy
Li 2019	RCT	China	Men aged 21 to 50 who received shockwave lithotripsy for stones	Radiopaque distal ureteral stones 7-15 mm in size.	Sexual intercourse 3-4 times/week and symptomatic treatment	Standard symptomatic treatment alone	70	68	2	Stone free rate, time to stone expulsion, pain score at admission, number of hospital visits for pain and steinstrasse
Turgut 2021	RCT	Turkey	Men aged over 18 having distal ureteral stones ≥ 5 mm and < 10 mm in size.	Distal ureteral stones 5–10 mm in size.	Masturbation at least 3–4 times a week and instruction to avoid sexual intercourse	Standard symptomatic treatment alone and instruction to avoid sexual intercourse and masturbation	43	44	4	Rates of expulsion, need for analgesic, and ureterorenoscopic lithotripsy

Abbreviation: RCT, Randomized Controlled Trial.

systematically searched. No restrictions on language were made when searching for evidence. No observational studies were found and only randomized controlled trials (RCTs) were included. References and citations of related articles were also searched carefully. The search process was performed independently by 3 authors. The keywords for the search were "sexual behavior", "masturbation", "sexual intercourse", and "distal ureteral stones". Details about search methods were summarized in Supplementary **Table 1**. The protocol of the study was registered in PROSPERO (CRD42021273390).

Inclusion and exclusion criteria

Studies that met the following criteria were included. (a) Population: men with distal ureteral stones; (b) Interventions: sexual intercourse or masturbation alone, or combined with standard symptomatic treatment; (c) Comparators: men who were instructed of no sexual intercourse or masturbation, and only received standard symptomatic treatment; (d) Outcomes: providing sufficient data for analysis, including at least the expulsion rate of stone, number of analgesic injections, or mean expulsion time of stone; (e) Study design: only RCTs; (f) Article type: only original articles; (g) Studies with a sample size of more than 50 and follow-up duration of at least 2 weeks. Studies which failed to meet the inclusive criteria were excluded.

Data collection

Three authors screened retrieved literature independently. Information including the first author, publication year, study design, regions, demographic and stone features, interventions and controls details, and outcomes were recorded from included studies. Missing or unclear information was collected by contacting the article authors. When there is no reply from authors, corresponding information will be considered as "not available".

Risk of bias (RoB) assessment

The Cochrane Collaboration's tool for assessing the risk of bias in the trial was used to evaluate the RoB by 3 authors independently.[21] Disagreements in the assessment were solved by discussion among the 3 authors and communication with the article authors.

Statistical analysis

Weighted mean difference (WMD) and its 95% CI were used for continuous results by follow-up analysis and pooled relative risks (RRs) and their 95% confidence intervals (CIs) for dichotomous data that complies with normality assumption. Random effect model was applied when there was a significant heterogeneity (I^2 > 50%), otherwise fixed effect model will be used.[22] Sensitivity analyses were conducted by excluding one study at each time. All statistical analyses were performed by using STATA 12.0 (Stata-Corp.) and R software (version 4.1.1). Two-tailed $P < .05$ was considered as statistically significant.

RESULTS

Literature selection

Under the established search strategy, we found 36

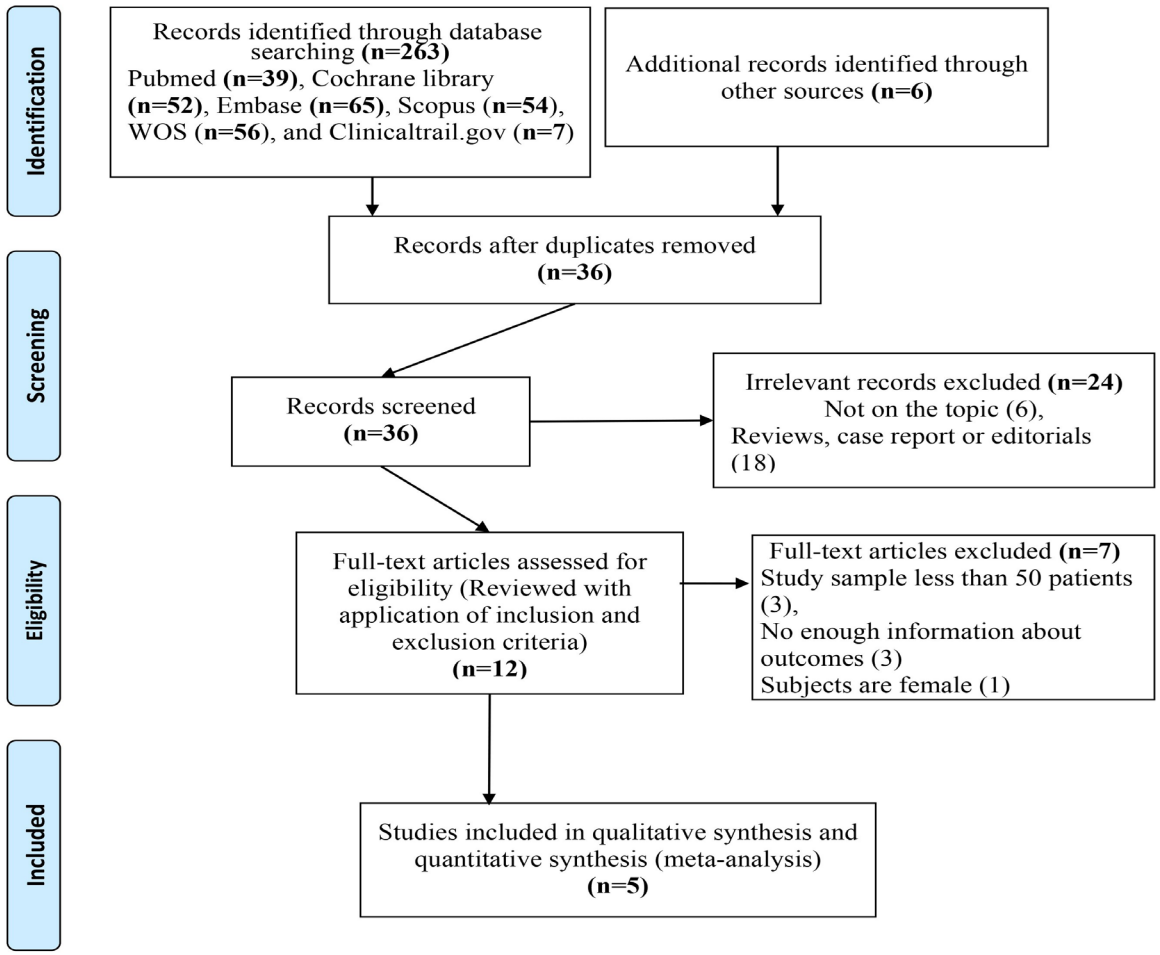

Figure 1. PRISMA flow chart of the data search.

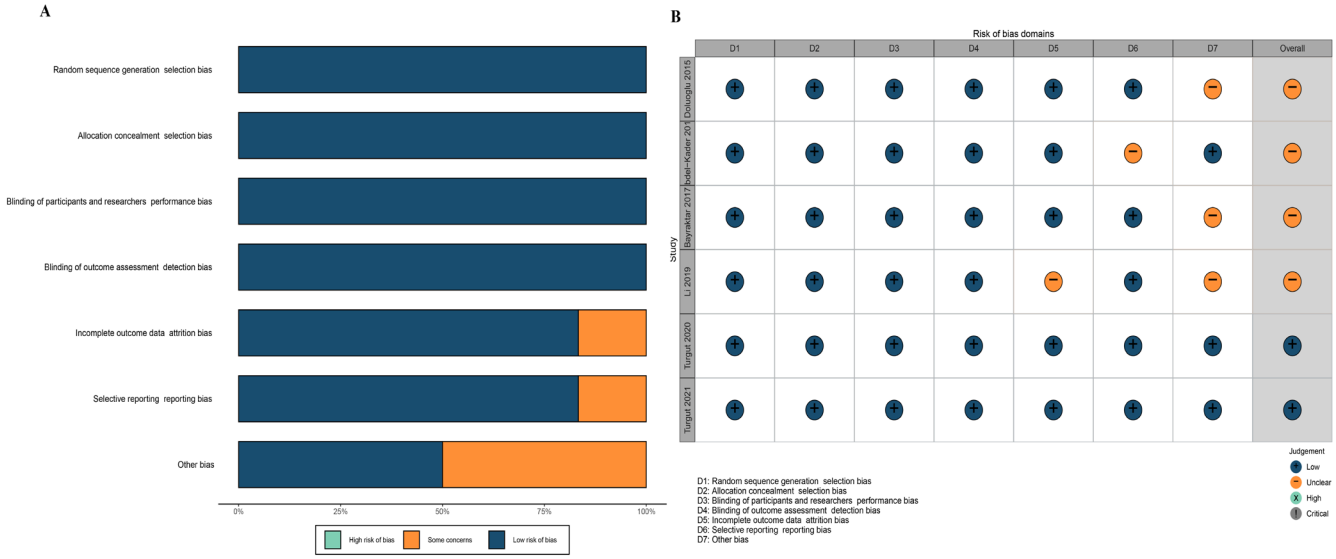

Figure 2. Risk of bias analysis **(A):** percentage; **(B):** traffic light.

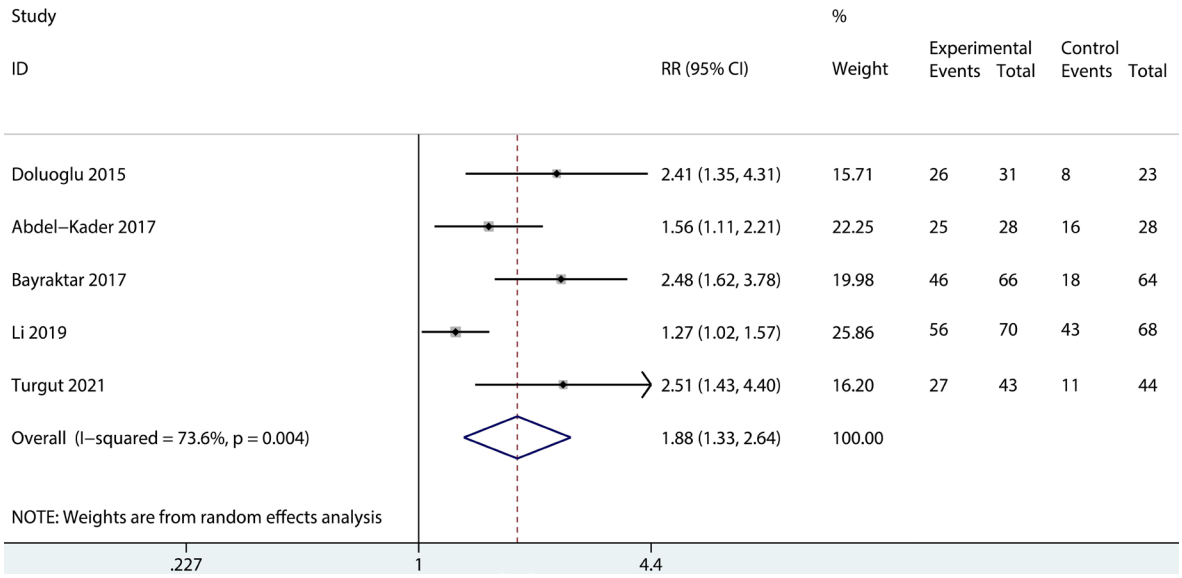

Figure 3. Pooled results of expulsion rate at 2nd week.
RR: relative risk; CI: confidence interval.

non-repeated records. After the screening and eligibility evaluation, 5 RCTs were included in the meta-analysis (shown in **Figure 1**).[16-18,23-25]

Characteristics of included studies

Five double-blinded RCTs published in recent 6 years were included in the analysis (shown in **Table 1**). All the follow-up durations were longer than 2 weeks. Among these studies, three were conducted in Turkey, one was in Egypt, and one in China. From the pooled results, no differences between experimental and control group were observed in terms of age and stone size (95%CI: -1.576 to 1.460, WMD: -.063, I^2 = .0%, P = .674; 95%CI: -.291 to .164, WMD: -.052, I2 = 11.7%, P = .542). The RoB analysis indicated that all studies had high qualities (shown in **Figure 2 A and B**).

Expulsion rate and expulsion time of distal ureteral stones

500 individuals, including 238 in the sexual intercourse or masturbation group and 227 in the control group, were included. Compared with controls, individuals in sexual intercourse or masturbation groups had significantly higher expulsion rate at both 2nd and 4th week (95%CI: 1.334 to 2.638, RR: 1.876, I2 = 73.6%, P < .001; 95%CI: 1.148 to 1.752, RR: 1.418, I^2 = 55.9%, P < .001) (shown in **Figure 3 and Figure 4**). Objects in the experimental group also had significantly shorter expulsion time than those in the control group (95%CI:

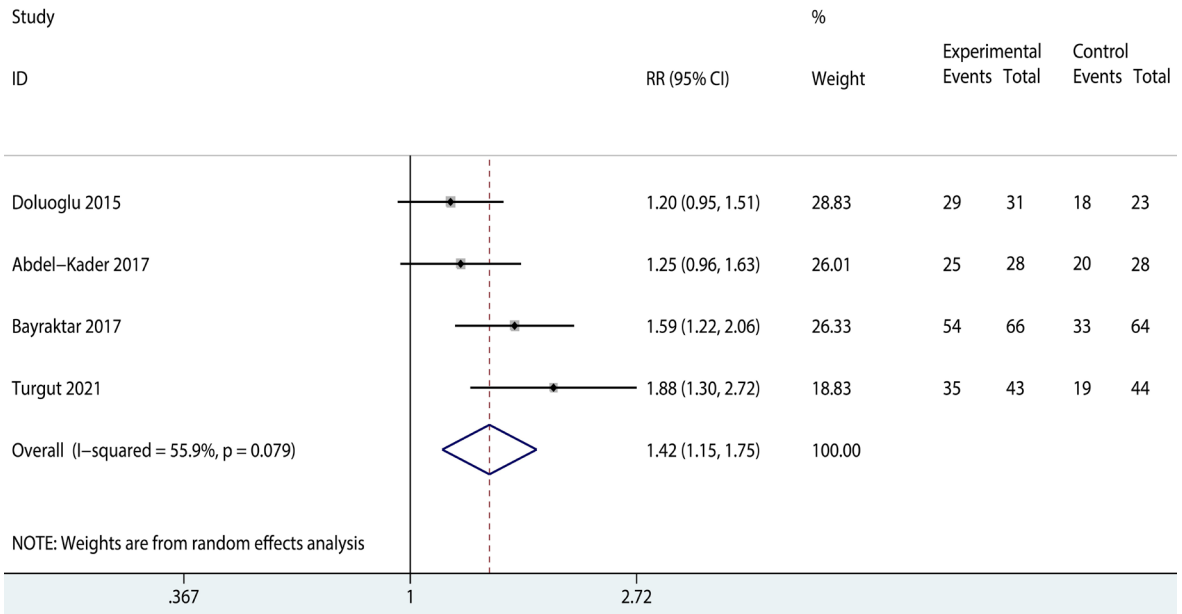

Figure 4. Pooled results of expulsion rate at 4th week.
RR: relative risk; CI: confidence interval.

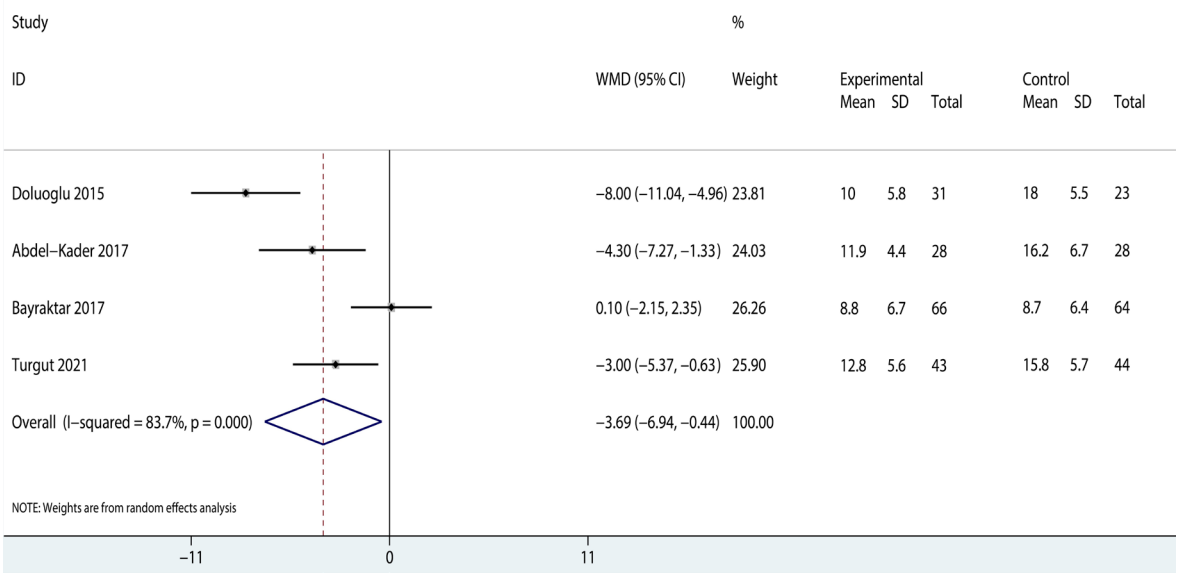

Figure 5. Pooled results of expulsion time.
WMD: weighted mean difference; CI: confidence interval.

-6.941 to -.436, WMD: -3.689, I^2 = 83.7%, *P* = .026) (shown in **Figure 5**).

Requirement for analgesic injections (per day)

The number of analgesic injections was considered as a measurement for stone related pain in four studies.[16-18,23,25] The research performed by Li et al. was not included in the pooling because they used a quantified visual analog scale to evaluate pain.[24] The pooled results demonstrated that controls had statistically more injections than subjects in experimental group (95%CI: -1.071 to -.126, WMD: -.598, I2 = 90.3%, *P* = .013) (shown in **Figure 6**).

Subgroup analysis

Details were summarized in Supplementary Table 2.

Sensitivity analysis

Studies were extracted subsequently in each analysis and no study could affect pooled results, indicating the results were reliable (Supplementary **Figure 1 and Supplementary Figure 2**).

DISCUSSION

A comprehensive meta-analysis containing 5 RCTs with 500 individuals was conducted to evaluate the efficacy of sexual behavior, including sexual intercourse and masturbation in the expulsion of distal ureteral stones. Results indicated that compared with controls, sexual intercourse and masturbation can increase expulsion rate, reduce expulsion time, and sexual intercourse can further lower the demand for analgesic injections. In the meta-regression analysis, no factors were found to significantly influence the pooled results. Results were robust. This study builds on a previous meta-analysis that only investigated the role of sexual intercourse

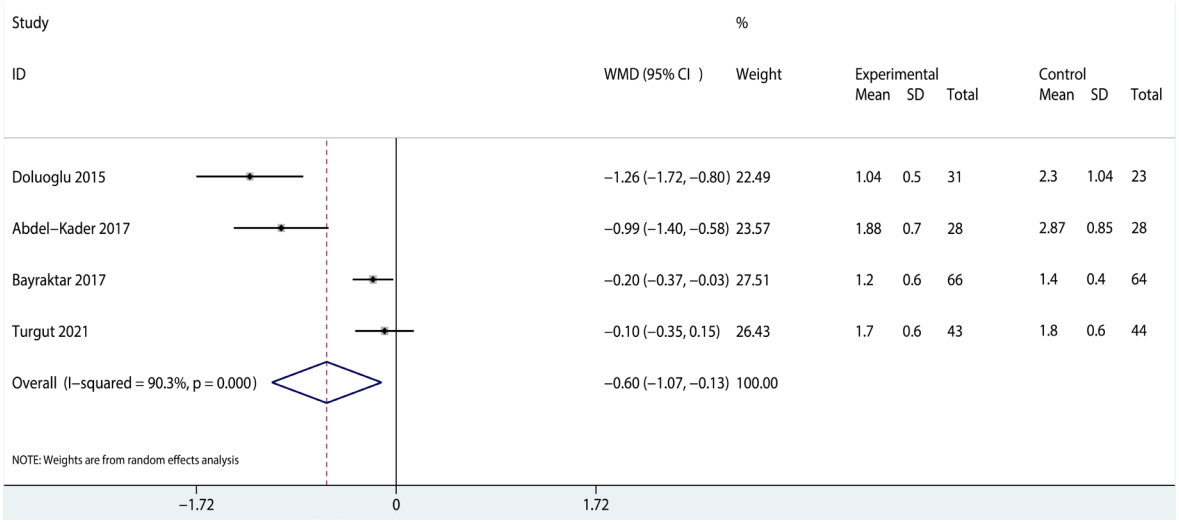

Figure 6. Pooled results of requirement for analgesic injections.
WMD: weighted mean difference; CI: confidence interval.

in the expulsion of distal ureteral stones and includes all available high-quality evidence to date.[26]

Since 2015, a series of studies have reported the expulsion role of sexual intercourse. Doluoglu et al. firstly demonstrated that men having at least 3 sexual intercourses a week had significantly shorter median expulsion time and higher expulsion rate than controls.[16] Subsequent two RCTs examined the efficacy of sexual intercourse in treating patients with larger ureteral stones in size (5-10 mm) and found consistent findings.[17,23] Li and his colleagues extended it further by investigating the role of sexual intercourse after shockwave lithotripsy for men with 7-15 mm distal ureteral stones.[24] They indicated that having more than 3 sexual intercourse a week after shockwave lithotripsy can be a treatment choice for lower ureteral stones.[24] Former studies have some limitations such as only male subjects are included and only sexual intercourse were examined. To fill the gap, Turgut et al. conducted a RCT investigating the role of masturbation in expulsion of distal ureteral stones in men.[18,25] However, the level of compliance in these studies is hard to measure and the loss to follow-up between groups is different in some studies.

The underlying mechanisms lie in the role of nitric oxide (NO). NO is a non-adrenergic and non-cholinergic neurotransmitter which plays an inhibitory role in signal transmission.[27,28] Previous studies had shown that both exogenous and endogenous NO can cause relaxation of intravesical ureter in pigs.[29,30] The ureter is innervated by sympathetic nerves originating from T11-L1 and para-sympathetic nerves come from S2-4.[31] Erection can be induced by the stimulation of cavernous nerves and pelvic plexus, whereas detumescence can be caused by sympathetic system excitation.[32] NO is the main neurotransmitter that is helpful in erection, masturbation, and sexual intercourse.[32] When cavernous nerves were stimulated, they will activate nitrergic nerves which can release NO from its end, leading to penile smooth muscle relaxation and erection. Furthermore, the endothelium can also release NO. The hypothesis that erection and sexual intercourse induced NO release leads to ureteric muscle relaxation may be supported by the following two points. Previous studies indicated that nitrergic nerve endings in the distal ureter can produce NO.[33,34] Moreover, many clinical trials reported that the stone expulsion rate of the sexual intercourse group is as high as the tamsulosin group.[16,23-25] Therefore, sexual intercourse or masturbation can reduce analgesic demand and increase stones passing through NO/ cGMP pathway during erection.

Our findings may have some clinical and research implications. Firstly, performing sexual intercourse or masturbation 3 or 4 times a week can increase expulsion rate of distal ureteral stones (diameter less than 10 mm) at 2nd or 4th week and reduce stone-related pain in men. This may be used for patient counselling and lifestyle modification. Secondly, more evidence is required for the role of masturbation in stone passage. Thirdly, given the fact that healthy men usually have morning or nocturnal erection, the confounding factor should be considered in further studies. Fourthly, how, when, and if the NO/cGMP pathway can be effectively used in treatment need further exploration. Moreover, a comparison of the efficacy of sexual intercourse and masturbation in the treatment of distal ureteral stones may help better understand the problem.

The most notable strength of the meta-analysis is the origin of evidence. Only high quality randomized double-blind, placebo-controlled trails were included in the meta-analysis, making the final conclusions relatively reliable and solid. However, some limitations also should be mentioned. Firstly, the diverse stone sizes may influence the application of findings. While we pooled stone sizes data and found that the experimental group is comparable with the control group. We think that the findings in the study are applicable to distal ureteral stones 0-10 mm in size. Secondly, there is still lack of long-term outcomes. Thirdly, the compliance of subjects to perform or not to perform masturbation or sexual intercourse are difficult to ascertain. Fourthly, due to the small number of included studies, the findings of the study should be treated tentatively until validated by more future studies. Last but not the least, sleep-related erection is hard to control. Further studies should address these concerns.

CONCLUSIONS

Conducting sexual intercourse or masturbation 3 or 4 times a week can achieve better efficacy in the treatment of distal ureteral calculi and better pain controls compared with placebo. However, given the concerns mentioned above, more studies with better study designs are expected.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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