



Can Sexual Intercourse or Masturbation be a New Therapy for Distal Ureteric Stones: An Updated Meta-Analysis

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Abstract

Purpose: To explore if sexual intercourse or masturbation could be a new therapy for distal ureteric stones.

Method: PubMed, Embase, Cochrane Library was used to search for Randomized Control Trials (RCT) about sexual intercourse or masturbation for distal ureteric stones.

Result: 6 RCTs were included in this meta-analysis. Between Tamsulosin group and sexual intercourse or masturbation group, no significant difference exists in stones expulsion rate at the second week (OR: 1.54, 95% CI: 0.80 to 2.96, P=0.20, I²=57%) and at the fourth week (OR: 1.43, 95% CI: 0.79 to 2.61, P=0.24, I²=2%), stone expulsion time (Mean Difference [MD]: - 2.54, 95% Confidence Intervals [CI]: - 5.18 to 0.11, P=0.06, I²=76%), and number of needed analgesic injections (MD:- 0.38, 95% CI: - 0.85 to 0.10, P=0.12, I²=90%). Between sexual intercourse or masturbation group and symptomatic treatment group, there were significant difference in stones expulsion rate at the second week (OR: 4.33, 95% CI: 2.90 to 6.47, P<0.01, I²=18%) and at the fourth week (OR: 4.54, 95% CI: 2.70 to 7.63, P<0.01, I²=0%), stone expulsion time (MD: - 3.64, 95% CI: - 6.76 to - 0.52, P=0.02, I²=84%), and number of needed analgesic injections (MD: - 0.52, 95% CI: 0- .94 to - 0.11, P=0.01, I²=88%).

Conclusion: Sexual intercourse or masturbation could be a new therapy for distal ureteric stones.

Keywords: Sexual intercourse; Masturbation; Distal ureteral stone; Heterogeneity; Meta-analysis

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Received Date: 28 Feb 2022

Accepted Date: 07 Apr 2022

Published Date: 20 Apr 2022

Citation:

Wu Q, Liang R, Huang Y, Tan C, Tang T. Can Sexual Intercourse or Masturbation be a New Therapy for Distal Ureteric Stones: An Updated Meta-Analysis. *Clin Surg*. 2022; 7: 3490.

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Introduction

Urolithiasis is a common disease in urological practice. Urolithiasis is reported in 5% to 10% of the world's population, and the ratio of males to females is 2:1 [1-3]. Ureteral stones account for 20% of urinary calculi; however, 70% of ureteral calculi are located in distal ureter [4]. A study showed that the likelihood of spontaneously expelling calculi less than 5 mm was 68% and that of calculi 6 mm to 10 mm was 47% [5]. According to the location and size of stones, there are diverse options for the treatment of ureteral calculi, such as conservative therapy, observation or spontaneous passage, Medical Expulsive Therapy (MET), extracorporeal shock wave lithotripsy, and ureterorenoscopy lithotripsy. MET is recommended for stone size 5 mm to 10 mm [6]. The essential drug in MET is α adrenergic receptor blockage. There are abundant α -1 adrenergic receptors in the distal ureter. Studies have shown that α -1 adrenergic blockers can reduce the ureteral peristaltic frequency and basal ureteral tone, resulting in ureteral relaxation [7]. Tamsulosin is one of the most commonly used α blockers [8-10]. Studies performed 20 years ago demonstrated that there are abundant nitrergic fibers in both porcine and human intravesical ureters [11,12]. Nitric Oxide (NO) is a neurotransmitter of nitrergic fibers. Both endogenous and exogenous NO can relax the porcine intravesical ureter [12,13]. The main neurotransmitters of penis erectile and clitoral engorgement are NO, which is released by nerve endings when sexual stimulation and arousal occurred [14]. Doluoglu speculated that relaxation of the distal ureter during penile erection and sexual intercourse would facilitate the expulsion of the stones [10]. Based on this speculation, several studies about sexual intercourse for treating distal ureteral calculi have been performed [10,15-18]. A previous meta-analysis, which included only three original studies, involved only male patients, and only compared sex intercourse with placebo, indicated that sexual intercourse was effective for the treatment of distal ureteral calculi [19]. More articles have been updated about sexual intercourse treating distal

Table 1: Characteristics of studies included in this meta-analysis.

Study	Publish year	Design	Age (years)	Gender	Stone size (mm)	Sample size			Follow-up time
						Tamsulosin	Masturbation or Sexual intercourse	Symptomatic therapy	
Doluoglu	2015	RCT	35.9	Male	4.85	21	31	23	4 weeks
Abdel-Kader	2016	RCT	36.9	Male	6.86	28	28	-	4 weeks
Bayraktar	2017	RCT	36.7	Male	7.07	60	66	64	4 weeks
Li	2019	RCT	34.8	Male	11.19	71	70	68	2 weeks
Turgut	2020	RCT	36.8	Female	6.84	-	35	35	4 weeks
Turgut	2020	RCT	37.7	Male	6.96	41	43	44	4 weeks

ureteral calculi [20]. In addition, a study has reported the treatment of distal ureteral calculi by masturbation [21]. The purpose of this meta-analysis was to compare sex intercourse or masturbation with symptomatic therapy and tamsulosin, respectively, and was further to explore the effectiveness of sexual intercourse or masturbation treating distal ureteral calculi in men and women.

Methods

Search strategy

We have registered this meta-analysis in the International Platform of Registered Systematic Review and Meta-analysis Protocols (Registration number: 202130066). PubMed, EMBASE, and Cochrane Library (by November 2020) were used to search related articles. The P. I. C. O search tool was applied as follows: P: Patients with distal ureteral stones; I: Patients with distal ureteral stones treated with sexual intercourse or masturbation; C: patients with distal ureteral stones treated with tamsulosin or symptomatic therapy; O: Stone expulsion rate at the second week and at the fourth week, number of needed analgesic injections, and stone expulsion time. The search terms were as follows: Sexual intercourse, masturbation, ureteral stones, ureteral calculi, ureteric calculi, distal ureteral calculi, and randomized controlled trials. To avoid missing the related literature, reference lists were searched to select related literature that evaluated the effectiveness of sexual intercourse or masturbation treating distal ureteral calculi.

Trial selection

Inclusion criteria: (1) Studies that evaluated the effectiveness of sexual intercourse or masturbation for management of distal ureteral calculi, (2) studies that offered direct data or indirect data that could be calculated, including mean expulsion time of distal ureteric calculi, number of required analgesic injections, and expulsion rate of distal ureteric calculi, (3) studies that the full text was available. The flow diagram of the screening process was demonstrated in Figure 1.

Data extraction

Two reviewers (Qiao Wu and Rui Liang) independently evaluated and extracted the data from each article. If any disagreement exists between the two reviewers, the third reviewer (Yi Huang) was invited to resolve the problem. No authors of the original were contacted to gain the missed data. The data needed to extract were as follows: the last name of the first author, study design, publication year, sample size, time of follow-up, age, stone size, the number of patients in the Tamsulosin group, sexual intercourse or masturbation group, and symptomatic therapy group, stones expulsion rate at the second week, stones expulsion rate at the fourth week, number of required analgesic injections, stone expulsion time.

Quality evaluation

The quality of included RCTs was evaluated by using the revised

Jadad Scale. The quality of each included study was determined by sequence generation, concealment of allocation, blinding method, number of cases lost to follow-up.

Statistical analysis

RevMan version 5.3 was used to analyze the data. The Mean Difference (MD) for continuous variables was evaluated by Mantel-Haenszel method and DerSimonian and Laird method and the Odds Ratio (OR) was used to measure dichotomous variables results that pooled across studies, with corresponding 95% Confidence Intervals (CIs). If there is conspicuous heterogeneity, the random effects model is used; if there is no significant heterogeneity, the fixed effects model is used. Heterogeneity was assessed by the chi-squared tests. $P < 0.05$ was considered to be significantly different.

Result

Characteristics of each included studies

According to the inclusion criteria and exclusion criteria developed and after rigorous screening, 6 RCTs were included in this study, including 600 patients. The basic information for each article is shown in Table 1.

Quality of each included study

The research method of each included study was randomized, and randomization processes were described in detail in the methods section. The quality of each included article was assessed by the revised Jadad Scale. As shown in Table 2, the score of each study was more than or equal to 4, which was considered as high quality.

Expulsion rate of distal ureteral stones

Six RCTs with a total of 728 patients (221 patients in the tamsulosin group, 273 patients in the sexual intercourse or masturbation group, and 234 patients in the symptomatic therapy group) were included in this meta-analysis. As shown in Figure 2, compared with the symptomatic therapy group, a conspicuously higher stones expulsion rate was discovered at the second week in the sexual intercourse or masturbation group (OR: 4.33, 95% CI: 2.94 to 6.47, $p < 0.01$, $I^2 = 18\%$); furthermore, a significantly higher stones expulsion rate was found at the fourth week in sexual intercourse or masturbation group (OR:

Table 2: Quality assessment of each included study.

Study	Sequence generation	Allocation concealment	Blinding	Exit and lost to follow up
Abdel-Kader	2	2	0	1
Bayraktar	1	1	1	1
Doluoglu	2	2	1	1
Li	2	1	1	1
Turgut	1	1	1	1
Turgut	2	1	1	1

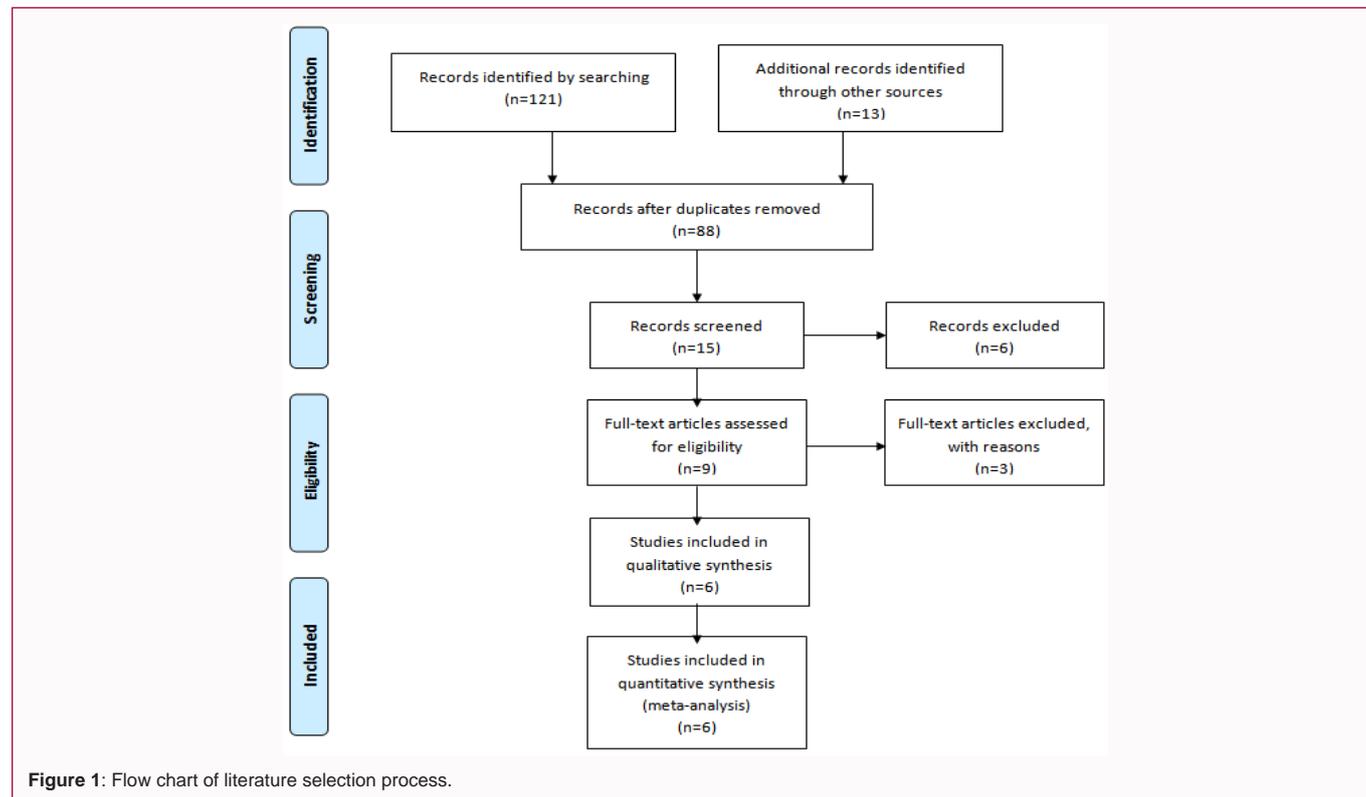


Figure 1: Flow chart of literature selection process.

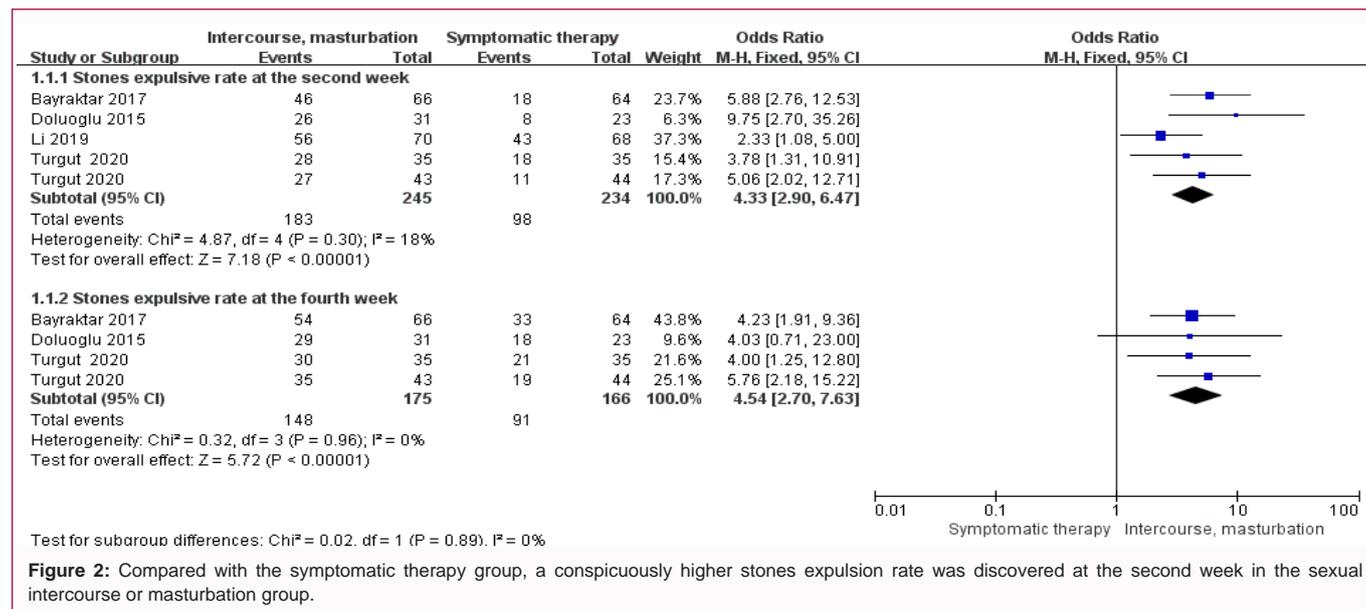


Figure 2: Compared with the symptomatic therapy group, a conspicuously higher stones expulsion rate was discovered at the second week in the sexual intercourse or masturbation group.

4.54, 95% CI: 2.70 to 7.63, $p < 0.01$, $I^2 = 0\%$). As shown in Figure 3, there was no significant difference in the stones expulsive rate at the second week (OR: 1.54, 95% CI: 0.80 to 2.96, $P = 0.20$, $I^2 = 57\%$) and the stones expulsion rate at the fourth week (OR: 1.43, 95% CI: 0.79 to 2.61, $P = 0.24$, $I^2 = 2\%$) between tamsulosin group and sexual intercourse or masturbation group.

Number of required analgesic injections

In the study, if necessary, non-steroidal anti-inflammatory drug injections (e.g., diclofenac) were used. Pain control is measured by the number of analgesic injections. As shown in Figure 4, compared with the symptomatic therapy group, there was a marked reduction

in the number of analgesic injections needed by patients in the sexual intercourse or masturbation group (MD= - 0.52, 95% CI: - 0.94 to - 0.11, $p = 0.01$, $I^2 = 88\%$). As shown in Figure 5, there was no conspicuous reduction in the number of analgesic injections required by patients between the sexual intercourse group or masturbation group and tamsulosin group (MD= - 0.38, 95% CI: - 0.85 to 0.10, $p = 0.12$, $I^2 = 90\%$).

Expulsion time of distal ureteral stones

As shown in Figure 6, compared with the symptomatic therapy group, the expulsion time of stones was shortened in the sexual intercourse or masturbation group (MD= - 3.64, 95% CI: - 6.76 to -

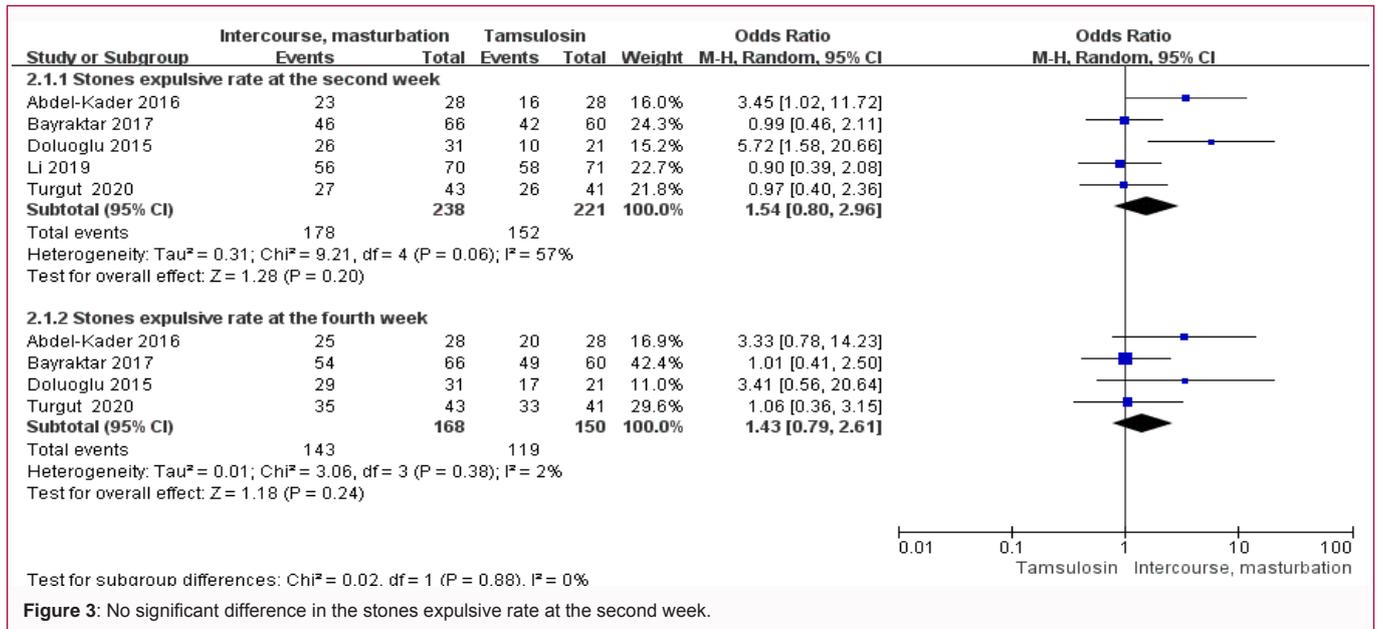


Figure 3: No significant difference in the stones expulsive rate at the second week.

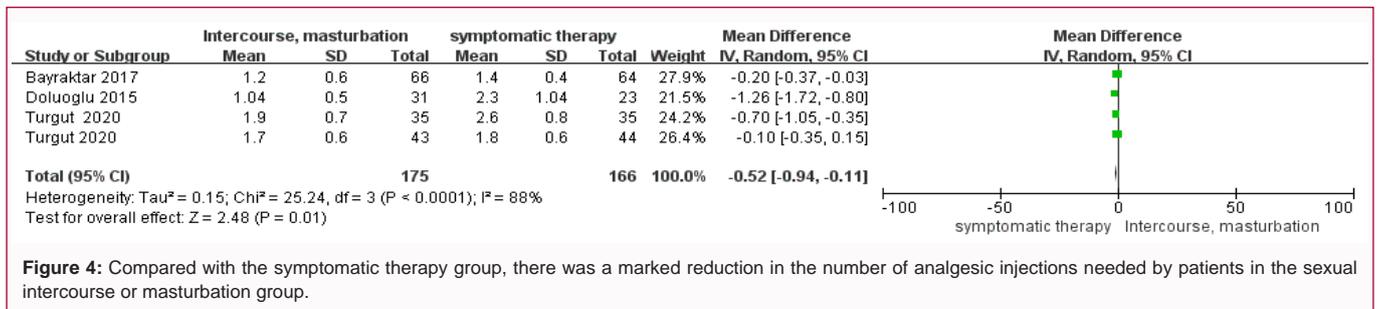


Figure 4: Compared with the symptomatic therapy group, there was a marked reduction in the number of analgesic injections needed by patients in the sexual intercourse or masturbation group.

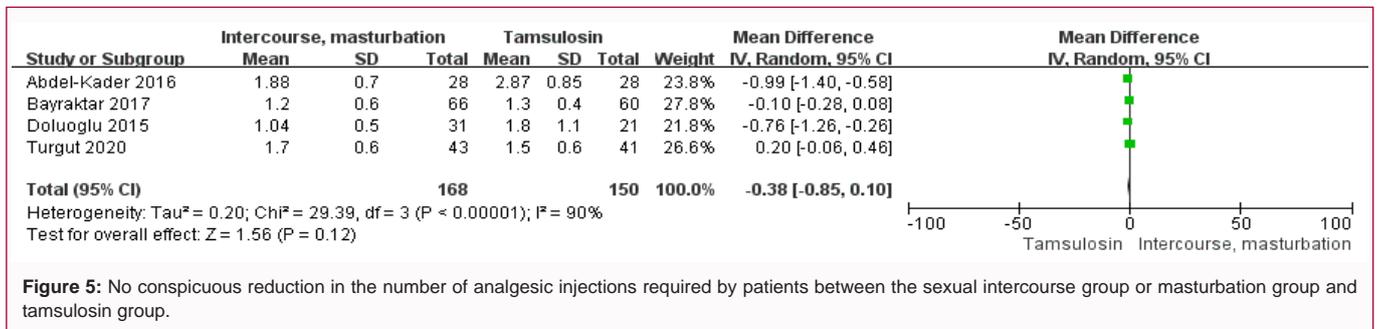


Figure 5: No conspicuous reduction in the number of analgesic injections required by patients between the sexual intercourse group or masturbation group and tamsulosin group.

0.52, p=0.02, I²=84%). As shown in Figure 7, there was no significant difference in the expulsion time of stones between the tamsulosin group and sexual intercourse or masturbation group (MD= - 2.54, 95% CI: - 5.18 to 0.11, p=0.06, I²=72%).

Discussion

Today, MET is recognized as a non-invasive treatment for ureteral calculi, although there is no consensus on the stone size in MET use. EAU guidelines recommend MET for all ureteral calculi, while AUA guidelines recommend MET for distal ureteral calculi less than or equal to 10 mm. One study has shown that MET increases the probability of expulsion of ureteral stones by 5 mm to 10 mm [22]. Another meta-analysis showed that MET increased the likelihood of passing stones equal to or greater than 5 mm [23]. Regardless of how controversial the use of MET may be regarding stone size, the basic principle of the use of MET remains the same: ureters are rich

in alpha receptors, and alpha-receptor blockers can relax the ureter and facilitate stone expulsion [7]. Some studies demonstrated that nitrergic fibers exist in both porcine and human intravesical ureters [11,12]. NO is the neurotransmitter of nitrergic nerve fibers. Studies have confirmed the presence of nitrogenous fibers in the distal ureter segment, which can produce NO and thus relax the ureteral smooth muscle [11,24]. Some studies have shown that both endogenous and exogenous NO could cause smooth muscle relaxation of porcine intravesical ureters [25,26]. The main neurotransmitters of penis erectile and clitoral engorgement are NO, which is released by nerve endings when sexual stimulation and arousal occurred [14]. NO levels rise in both men and women during sexual intercourse or masturbation, which promotes the relaxation of the ureter, limits the use of analgesic injections, and accelerates the expulsion of stones. Doluoglu is the first to demonstrate that performing sexual intercourse 3 to 4 times per week is effective in the treatment of distal

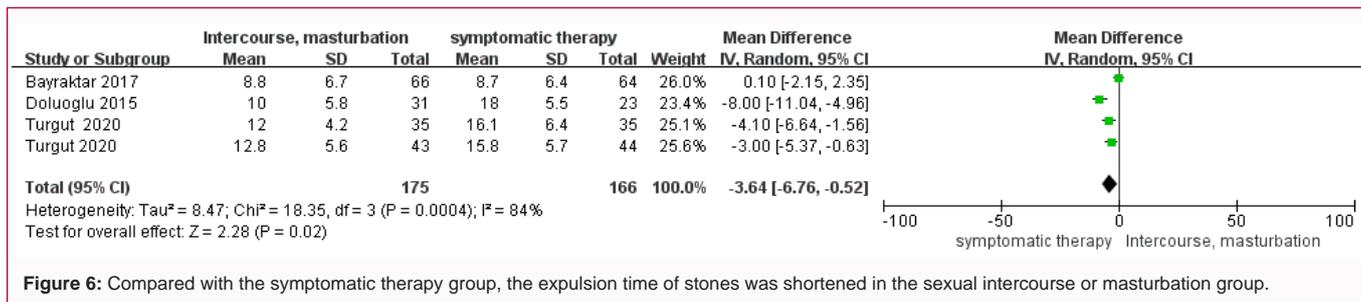


Figure 6: Compared with the symptomatic therapy group, the expulsion time of stones was shortened in the sexual intercourse or masturbation group.

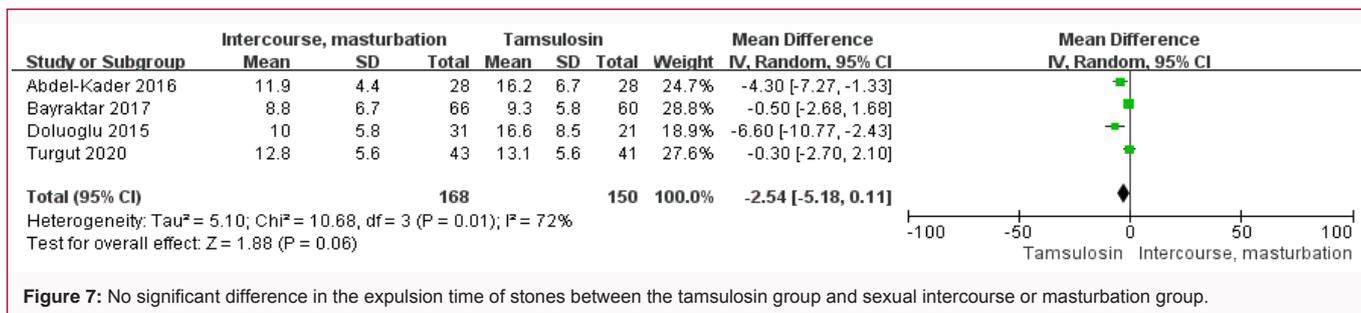


Figure 7: No significant difference in the expulsion time of stones between the tamsulosin group and sexual intercourse or masturbation group.

ureteral calculi, increasing the rate of calculi expulsion, reducing the use of analgesic drugs, and shortening the time of calculi expulsion [10]. A meta-analysis that comprised three RCTs about sexual intercourse for the treatment of distal ureteric calculi demonstrated that performing sexual intercourse 3 to 4 times per week could relieve pain and accelerate the expulsion of stones [19]. However, the study only looked at male patients, and the number of original literature included in the study was small, which may lead to bias. Furthermore, the previous meta-analysis only compared sexual intercourse with a placebo. We compared the treatment of sexual intercourse or masturbation with symptomatic treatment and tamsulosin treatment, respectively, to provide a better reference for the actual therapeutic effect of sexual intercourse or masturbation on distal ureteral calculi. As shown in Figure 3, there was no significant difference in stone expulsion rate at the second week (OR: 1.54, 95% CI: 0.80 to 2.96, P=0.20, I²=57%) and the fourth week (OR: 1.43, 95% CI: 0.79 to 2.61, P=0.24, I²=2%) between sexual intercourse or masturbation group and tamsulosin group. As shown in Figure 5, 7, there was no significant difference in the stone expulsion time (- 2.54, 95% CI: - 5.18 to 0.11, P=0.06, I²=72%) and the number of needed analgesic injections (MD: - 0.38, 95% CI: - 0.85 to 0.10, P=0.12, I²=90%) between tamsulosin group and sexual intercourse or masturbation group. These results suggest that sexual intercourse or masturbation may be an alternative to MET in the treatment of distal ureteral calculi. In this study, the heterogeneity of results was relatively high, which may be related to the small number of included studies and the inconsistency in the basic characteristics of patients. Based on the above results, we believe that sexual intercourse or masturbation may be a new treatment for distal ureteral calculi. We might even venture to speculate that sexual intercourse or masturbation combined with MET might be more effective in treating distal ureteral calculi, but this would require more research to provide sufficient evidence. The novelty of this study is as follows: our meta-analysis is the first study to compare sexual intercourse or masturbation with tamsulosin and symptomatic treatment, is the largest sample size study so far, and is the first meta-analysis involving male and female patients. But there are some limitations. Firstly, the small number of original studies included may lead to bias in the results. Secondly, the heterogeneity of

the results was high. A RCT with large sample size and crosses centers are needed to determine further the efficacy of sexual intercourse or masturbation treating distal ureteral calculi.

Conclusion

Sexual intercourse or masturbation could be an alternative option for patients with distal ureteral calculi. Sexual intercourse or masturbation increases the likelihood of expelling calculi and shortens the time of expelling calculi as well as relieves pain.

Funding

This study was supported by grants from the Science and Technology Strategic Cooperation Project of Nanchong and North Sichuan Medical College (19SXHZ0185).

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