Role of Sexual Intercourse after Shockwave Lithotripsy for Distal Ureteral Stones: A Randomized Controlled Trial

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Purpose: To explore whether sexual intercourse is beneficial to the clinical outcome of SWL for ureteral calculi of 7-15 mm in the distal ureter.

Materials and Methods: Between March 2016 and January 2017, 225 patents with a stone (7-15 mm) in distal ureter were randomly divided into three groups after SWL: Group 1 was asked to have sexual intercourse at least three times a week, Group 2 was administered tamsulosin 0.4 mg/d and Group 3 was received standard therapy alone and served as the controls. Stone free rate, time to stone expulsion, pain score at admission, number of hospital visits for pain and steinstrasse were recorded in 2 weeks.

Results: 70 patients in Group 1, 71 patients in Group 2 and 68 patients in Group 3 were enrolled to the study. At the end of the first week and the second week, the stone free rates for Group 1 (68.6%, 80.0%) and Group 2 (69.0%, 81.7%) were approximately the same, but were significantly higher than Group 3 (50.0%, 63.2%) (P = .031, P = .022). The VAS scores of Groups 1 and 2 were slightly higher than those of Group 3 (P = .233). The number of patients in Group 3 who visited the emergency room for pain was significantly higher than in the other two groups (P = .015). At the end of the second week, the incidence of steinstrasse in Groups 1 and 2 was significantly lower (2.9%, 2.8% vs 11.8%) (P = .034).

Conclusion: At least three sexual intercourses per week after SWL can effectively improve the stone free rate, reduce the formation of steinstrasse and relieve renal colic. It provides a choice for urologists in the SWL treatment of lower ureteral calculi.

Keywords: shockwave lithotripsy; sexual intercourse; tamsulosin; ureteral stone; pain

INTRODUCTION

Ureteral calculi are one of the most common diseases of the urinary system[(1)]. The treatment of ureteral stones includes conservative treatment, medical expulsive therapy (MET), shock wave lithotripsy (SWL), ureteroscopy (URS), and other invasive and non-invasive methods [(2)]. Since the 1980s, SWL has gradually become one of the preferred treatment methods for ureteral stones. Management of residual fragment after SWL is still a major concern as it may eventually cause pain and require reintervention. Elimination of residual fragments depends on various parameters, such as stone size, number, location in the urinary tract, patient's anatomy, and ureteral peristaltic capability[(3-6)]. Medical expulsive therapy for urolithiasis has gained increasing attention in the last decade. Various agents have been investigated including calcium channel blockers, alpha-adrenergic antagonists, corticosteroids and phosphodiesterase type 5 inhibitors (PDE5i)[(7-12)]. The goal of medical therapy is to enhance stone expulsion with a parallel decrease in the associated pain after SWL.

Recent studies found that sexual intercourse can effectively promote the expulsion of lower ureteral stones [(13-15)]. However, whether it is also effective for the expulsion of stones after SWL for lower ureteral calculi has not been reported. Therefore, we designed a randomized, prospective study to explore whether sexual intercourse is beneficial to the clinical outcome of SWL for ureteral calculi of 7-15 mm in the distal ureter.

PATIENTS AND METHODS

Study population

This prospective, randomized, controlled study included 225 male patients presented to our institution with renal colic in the period between March 2016 and January 2017. Patients were enrolled in the study by research nurse after a routine preoperative evaluation. Inclusion criteria were presence of distal ureteric or intramural stone from 7 to 15 mm in diameter detected by plain X-ray film and low-dose noncontrast enhanced computed tomography (NCCT) scan for radiolucent stones. Their age ranged from 21 to 50 years. Exclusion criteria were patients with abnormal kidney anatomy and function, body weight over 100 kg, previous administration of drugs that may induce stones, history of urologic surgery, hydronephrosis higher than level 1, coagulation dysfunction, urinary system infection, tamsulosin allergy, serum creatinine greater than 2 mg/dL, multiple ureteral calculi, fever, or hypotension, as well as pain that was difficult to control by analgesics, bladder ureteral

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Table 1. Demographic and clinical characteristics of patients.

	Group1: sexual intercourse(N=70)	Group2: tamsulosin(N=71)	Group3: control(N=68)	*P*- values
Age, year; mean ± SD [a]	35.1 ± 8.3	35.3 ± 8.1	34.1 ± 8.4	0.668
BMI, kg/m2; mean ± SD [a]	24.2 ± 15.8	23.9 ± 8.9	24.0 ± 8.8	0.813
mean HU, HU; mean ± SD [a]	828.2 ± 349.7	880.9 ± 357.2	834.8 ± 362.0	0.633
Left sided stone, N (%) [b]	28 (40.0)	39 (54.9)	32 (47.1)	0.206
Stone diameter, mm; mean ± SD [a]	11.1 ± 2.4	10.6 ± 1.9	11. 9 ± 2.3	0.306

Abbreviations: BMI, Body Mass Index; HU, Hounsfield Unit.
[a] Non-normal distribution variables were compared by Kruskal–Wallis test
[b] Categorical variables were compared by x^2 test

reflux, neurogenic bladder, or erectile dysfunction. The nature of the study was explained to each patient and informed consent was obtained. The protocol of this study was approved by the institutional ethics committee of the Ninth People's Hospital Affiliated to Shanghai Jiao Tong University (No.192). Patients' enrollment algorithm has been illustrated in **Figure 1**.

A complete medical history along with anthropometric parameters was routinely collected. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Blood samples were taken and tested for blood count and serum creatinine. Urinalysis and urine culture were also performed before SWL. In patients with negative urine culture, no antibiotics was administered before SWL. Stone number, size, location and Hounsfield unit (HU) were assessed preoperatively by means of a low-dose NCCT scan, the accurate imaging modality to define stone size and location.

Study design

This study was a prospective single center, parallel-group randomized clinical trial with balanced randomization [1:1:1] by using block randomization method.

Sample size was calculated based on the assumption of an increase in the stone-free rate from 50% to 75% per person in both treatment arms[16]. To detect such a difference with 80% power using a two-tailed test at 5% significance level, it was estimated that 58 evaluable patients per group were needed. To consider possible dropout, 75 patients per group were planned (www.dsssresearch.com).

Block randomization was used to allocate subjects into three equally sized groups. Eligible patients were randomly assigned to one of the three groups according to a computer-based block randomization list generated by the Sealed Envelope. The block sizes were six.

Procedures

All patients underwent SWL within 24 hours after diagnosis. A standard SWL treatment of 3,000 shocks/session transabdominal at a prone position was planned in each patient under adequate sedation and analgesia. All SWL procedures were performed by a single urologist who was blinded to the group allocation. However, the stone was observed to have completely fragmented during the procedure in some patients, and the SWL treatment was terminated earlier. The procedure was performed at a frequency of 90 shocks per minute, by gradually increasing the therapeutic power from 15 kV to 20 kV during the first 500 shocks, using the Dornier HM3 Lithotripter (Dornier MedTech, Germany)

After SWL, it was recommended that all patients take fluids and produce more than 2000 ml of urine per day. In addition, for patients in Group 1 (the sexual intercourse group), it was recommended they have sexual intercourse at least three times per week. The patients in Group 2 (the tamsulosin group) received 0.4 mg tamsulosin daily. The patients in Group 3 received standard therapy (take enough fluids alone) and served as the controls. The patients in Groups 2 and 3 were asked to avoid sexual intercourse and masturbation for two weeks. No patients taking PDE5 inhibitors for any reason which includes on demand consumption in a normal person in any group. The trial will be terminated immediately if the patient has special symptoms such as fever, unrelieved pain, renal function impairment, et al. The patient will be provided with appropriate treatment by the specialist.

Evaluations

The primary outcome was the difference among intervention groups with respect to the stone free rates at the end of the first week and the second week after SWL. All patients underwent a low-dose NCCT scan by a senior radiologist blinded to the group of the study objectives and protocols at that time. Patients were considered stone free if residual stones were ≤ 3 mm. Even though a few patients passed fragments of stone during the treatment period, NCCT was still performed in all the patients to confirm complete clearance of stones.

The secondary outcomes were the differences among intervention groups with respect to pain score at admission, number of hospital visits for pain and steinstrasse in 2 weeks after SWL. After SWL, patients were informed regarding how to complete a visual analogue scale (VAS) (0: no pain, 1–4: mild, 5–6: moderate, and 7–10: severe) and provided with one paper copy, so that they could mark the intensity of pain when the most pain happening in 2 weeks. If the pain was not relieved, further treatment was given in the emergency room of the hospital, and the number of patients in such a situation was recorded for each group. Steinstrasse is a well-recognized complication of SWL and defined as the presence of more than one ipsilateral ureteral stone simultaneously[17].

Statistical Analysis

Statistical analysis was performed using SPSS 12.0 software. Kolmogorov-Smirnov test was used to verify the normality of the distribution of continuous variables. Evaluation of data distribution showed a non-normal distribution of the study data set. Differences between groups of patients in medians for quantitative variables and differences in distributions for categorical variables were tested with Kruskal–Wallis test and x^2 test respectively. A value of 5% was considered as threshold for significance.

Table 2. Therapeutic effect and pain after ESWL in each group.

	Group1: sexual intercourse(N=70)	Group2: tamsulosin(N=71)	Group3: control(N=68)	P values(1-2-3, 1-2, 1-3, 2-3)
SFR after 1 weeks, free/failure(%)[a]	48/22 (68.6%)	49/22(69.0%)	34/34(50%)	0.031 0.955 0.026 0.022
SFR after 2 weeks, free/failure(%)[a]	56/14(80.0%)	58/13(81.7%)	43/25(63.2)	0.022 0.799 0.029 0.015
VAS; mean ± SD [b]	5.76±1.74	5.58±1.69	6.04±1.40	0.233 0.510 0.299 0.091
Need for relieve pain emergency yes/no(%)[a]	6/64(8.6%)	4/66(5.7%)	14/54(19.1%)	0.015 0.512 0.045 0.009
Steinstrasse yes/no(%)[a]	2/68(2.9%)	2/69(2.8%)	8/60(11.8%)	0.034 0.989 0.044 0.041

Abbreviations: VAS, Visual Analogue Scale.
[a] Categorical variables were compared by x^2 test
[b] Non-normal distribution variables were compared by Kruskal–Wallis test

RESULTS

Of 225 patients, 209 met the inclusion criteria, which were randomly assigned into 3 groups. There was a dropout of 5 patients in Groups 1, 1 in Group 2, and 4 patients in Group 3 for wrong contact. In addition, 3 patients in Group 2 and 3 patients in Group 3 were excluded from the study due to having sexual intercourse and masturbating more than once weekly. No patients withdrew from the study for other reasons, such as emergency surgery or patient request. No statistically significant differences were observed regarding patient's age, BMI, stone size laterality, and mean Hounsfield units. Patient's demographic characteristics has been outlines in **Table 1**.

At the end of week 1, the stones free rate was 48 (68.6%) of the 70 patients in the sexual intercourse group, 49 (69.0%) of the 71 patients in the tamsulosin group, and 34 (50.0%) of the 68 patients in the control group. Group 1 and Group 2 showed a significantly higher stone free rate compared with Group 3 ($P = .031$, and .022, respectively). Group 2 had a slightly higher stone free rate than group 1 but was not statistically significant ($P = .955$). At the end of the second week of the study, similar results were observed ($P = .022$). Additionally, the VAS scores of Groups 1 and 2 were slightly higher than those of Group 3, but there was not a significant difference among the three groups ($P = .233$). However, the number of patients in Group 3 who visited the emergency room due to severe acute pain was significantly higher than in the other two groups ($P = .015$). At the end of the second week, the incidence of steinstrasse in Groups 1 and 2 was significantly lower ($P = .034$) (**Table 2**).

DISCUSSION

Due to its characteristics of a high success rate, no anesthesia needed, and outpatient treatment, SWL is becoming a non-invasive important method for the treatment of ureteral calculi since its introduction in the 1980s [(18)]. However, compared with ureteroscopic lithotomy, SWL still requires expulsion of the stone fragments from the long ureter after the operation. Therefore, there remain a series of postoperative complications, including renal colic, steinstrasse formation, bladder irritation, and urinary tract infection [(19)]. The size of the stones, comminution degree of the stones, and patency of the ureter are important factors affecting the success rate of stone expulsion. The expulsion of stones may cause ureteral smooth muscle spasms, mucosal edema and pain which may hinder expulsion. Local inflammation and even infection caused by stones may further aggravate the ureteral smooth muscle spasms and mucosal edema [(20-22)]. Therefore, the proper conservative treatment after SWL to relieve ureteral smooth muscle spasms, reduce mucosal edema, and relieve pain will be conducive to reducing the occurrence of complications and increasing the success rate of stone expulsion.

To increase the stone free rate after SWL, many scholars have conducted research in regard to changing the ureteral factors affecting stone expulsion. The use of α-receptor blocking agents, calcium antagonists, and steroid hormones after SWL can effectively increase the stone free rate[(7,8)]. Our results are in agreement with those of previous scholars. In our study, the stone clearance rate was significantly higher in the tamsulosin group compared with the control group, at 81.7% and 63.2%, respectively ($P = .029$).

Renal blood flow (RBF) and glomerular filtration rate improvement also can facilitate stone passage except for ameliorating ureteral factors. Ziaee et al. found that the percent of stone-free patients was higher in the group of patients who slept ipsilaterally relative to the kidney stone compared with patients who slept on the contralateral side by increasing RBF[(23)]. However, this study did not collect patients sleep position data after SWL.

The smooth muscle of the distal ureter and uretero-vesical junction is regulated by the autonomic nervous system, including noradrenergic, cholinergic, and non-adrenergic non-cholinergic nerves. Neurotransmitter nitric oxide (NO), released by male penis erections, regulates

peristalsis and tension in the distal ureter[24]. Many studies have shown that the nitric oxide/guanosine monophosphate (NO/cGMP) pathway in human and rat ureteral tissue plays a significant role in ureteral tension regulation[12]. In males, sexual activity releases a large amount of NO from the nerve endings to act on the lower part of the ureter, which can reduce the tension of the ureteral wall, enhance the urine transport capacity, and accordingly increase the pressure above the stone while weakening ureteral peristalsis and reducing the distal resistance of the stone, thereby forming a powerful pressure gradient to promote stone expulsion. The study by Doluoglu and Abdel-Kader found that having sexual intercourse three or four times per week can significantly increase the rate of stone expulsion in the lower ureter and shorten the expulsion time[13,14]. In a prospective, randomized controlled study, Bayraktar et al. used tamsulosin and sexual intercourse as interventions to treat patients with lower ureteral stones (5-10 mm), and the results showed that both tamsulosin and sexual intercourse could increase the expulsion rate of distal ureteral stones of 5-10 mm in size. Having sexual intercourse at least three times per week had the same effect as oral tamsulosin, which is inferred to be related to increasing NO levels during erection[15]. In this study, sexual intercourse was used as an adjuvant treatment option after SWL for ureteral calculi for the first time, and whether it could prevent the formation of steinstrasse was explored. The results showed that the stone free rate of the sexual intercourse group in the first and the second week after SWL (68.6% and 80.0%, respectively) was higher than that of the control group (50.0% and 63.2%; $P = .026$ and $P = .029$, respectively). The formation rate of steinstrasse in the sexual intercourse group (2.9%) was also much lower than that in the control group (11.8%; $P = .044$). The results of the sexual intercourse group were similar to those of the tamsulosin group, indicating that sexual intercourse could effectively increase the rate of stone expulsion after SWL and prevent the formation of steinstrasse. After SWL for ureteral calculi, expulsion of the stone debris from the ureter often causes severe pain. In our study, the average VAS pain scores of the sexual intercourse group and the tamsulosin group (5.76 ± 1.74 and 5.58 ± 1.69, respectively) were slightly lower than that of the control group (6.04 ± 1.40; $P = .233$). Although there was no significant difference between them, the number of patients in the control group who received pain relief treatment in the emergency room was significantly greater than in the sexual intercourse and tamsulosin groups ($P = .015$), and the number of such patients in the sexual intercourse group and the tamsulosin group was similar ($P = .512$). It suggests that the stone fragments have more chance to discharge after severe pain in the sexual intercourse group and the tamsulosin group than the control group. Patients in the control group can only visited the emergency room due to severe persistent pain caused by the stone fragment. But no such measurement was performed in this study. Further studies may be useful to focus on this issue.

One study confirmed that the use of α-receptor blocking agents can relieve the patient's pain by selectively acting on the α-1D receptors in the lower ureter, reduce the frequency of colic attacks, and reduce the pain score, thus reducing the need for analgesics[25]. In our study, post-SWL sexual intercourse could also effectively relieve pain and achieve the same effect as oral tamsulosin. Recent studies showed that sexual intercourse can significantly reduce the frequency of renal colic and analgesic demand in patients with lower ureteral calculi, which is considered to be related to the elevated level of endogenous NO[13,14]. Suresh et al. found that PDE5i, such as tadalafil, can reduce the onset of ureteral colic and the required amount of analgesia through the NO/cGMP pathway, thereby improving the patient's painful experience in the treatment of ureteral calculi [26]. Therefore, the analgesic effect of sexual intercourse after SWL may also be related to the elevated NO level during erection.

However, the most important limitation of our study is the lack of double-blind design and the intercourse treatment standardization include the frequency, body position, intensity and duration of sexual intercourse. The effects of sexual intercourse, masturbation, relaxations on the smooth muscles of the lower ureter still should be examined in the future. Whether or not moderate sexual intercourse is equally effective in female patients, patients with upper urinary stones in other sites after SWL, or patients undergoing ureteroscopic holmium laser lithotripsy will also be our future research direction.

CONCLUSIONS

In summary, having sexual intercourse more than three times per week after SWL can effectively improve the stone free rate, shorten the stone expulsion time, reduce the formation of steinstrasse, and relieve renal colic. To some extent, it makes up for the shortcomings of a single SWL treatment and provides a choice for urologists in the SWL treatment of lower ureteral calculi.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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