Improvement of Erection Related Incision Pain in Circumcision Patients using Interrupted Rapid Eye Movement Sleep: A Randomized Controlled Study

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Introduction: Postoperative pain from male circumcision (MC) is common especially in the sleep-related erection period. This study aims to explore the effect of interrupted rapid eye movement (IREM) sleep on relieving SRE-related incision pain and the improvement of other clinical outcomes.

Materials and Methods: This simple randomized controlled study was conducted between May and November 2016. Approval was obtained from the local ethical committee on 5 May 2016. Ninety participants who underwent male circumcision were divided into the interrupted rapid eye movement sleep group and the control group. The times and the cumulative time of erection-related moderate and severe pain in minutes at night for 3 days after the operation were observed and compared. We also compared the condition of the incision swelling and healing. Sleep time at night was used to evaluate the safety of interrupted rapid eye movement sleep.

Results: For the first 3 days after the operation, the times of sleep-related erection pain were significantly decreased in the IREM sleep group (P = .010). Five patients reported that there was no pain during night. The cumulative time of erection-related moderate and severe pain was statistically decreased in the interrupted rapid eye movement sleep group (P = .034). After 3 days, there was no moderate and severe pain related to sleep-related erection in the 2 groups. There were no significant differences in incision swelling (P = .768), healing (P = .626), and sleep time (P = .231).

Conclusion: Interrupted rapid eye movement sleep is an effective, simple, and free treatment to relieve incision pain of sleep-related erections.

Keywords: rapid eye movement; interrupt; sleep-related erection; pain; circumcision.

INTRODUCTION

Male circumcision (MC), being usually performed on adults in China[1,2], is one of the most common surgical procedures, whose benefit is a reduction in urinary tract infections and improvement of sexual performance [3,4], especially with regard to sex drive and mental erection confidence[5]. Although regarded as routine and minor, it is a painful procedure which, compounded by general anesthesia, can prove to be a particularly distressing event[6]. The incidences of moderate and severe pain during the first and third day after circumcision were reported as occurring in up to 96% and 78% of patients, respectively, in China[7]. These episodes of pain would be worsened when nocturnal erection caused by increased circulating testosterone occurred[8]. Almost all patients complained of worsened incision pain when they were undergoing nocturnal erections in our hospital. Currently, the main treatment for incision pain resulting from sleep-related erections (SREs) is a hormone-related regimen such as diethylstilbestrol and acetaminophen in China[9]. In addition, a number of analgesic and anesthetic methods such as opioids and dorsal penile nerve block using clonidine and fentanyl have been widely used for male circumcision[10-12], but there can be side effects from using these kinds of pain-relief methods[13]. However, this is not suitable for preventing the pain of MC patients. Hence, it was necessary to explore more reasonable and effective ways of relieving postoperative pain related to MC[13].

Sleep-related erections (SREs) refer to the erections occurring spontaneously during sleep with rapid eye movement (REM)[14].There are 4 to 5 episodes of SREs during one night, each episode lasts 30 to 45 minutes, with a total time of 80 to 180 minutes in healthy men. In a young adult male, the erection begins near the onset of REM sleep, increases quickly to full tumescence, persists throughout the REM sleep episode, and then ends in rapid detumescence at the end[8]. With the extension of sleep time, the frequency and duration of REMS gradually extends. Sleep-related penile erections (SRE) are naturally occurring, physiologically normal, occur several times on any given night, and are stable across time,[15] but in MC patients, SREs could increase the pain and result in bleeding and suture avulsion. Therefore, we aimed to find a reasonable method to relieve this problem.

According to the association between the circadian

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Table 1. Comparison of demographic and clinical characteristics.

Groups	Intervention (N = 33)	Control (N = 42)	t/Z/x^2	*P*
Age (years)	25.52 ± 6.11	26.81 ± 5.94	-0.925a	0.358
Education (years)	15.00 (12.00,16.00)	13.82 (11.75,16.00)	-1.226b	0.220
BMI (kg/m^2)	22.60 ± 2.63	23.95 ± 4.83	-1.439 a	0.154
HR (times/min)	86.37 ± 16.23	87.21 ± 12.97	-0.246 a	0.806
SBp (mmHg)	123.99 ± 24.38	125.52±8.51	-0.380 a	0.705
DBp (mmHg)	74.91 ± 7.99	73.79 ± 6.88	0.647 a	0.519
Other diseases				
Diabetes (Yes)	0 (0%)	1(2.4%)	0.796 c	1.000
Others (Yes)	0 (0%)	1(2.4%)	0.796 c	1.000
Baseline NRS	4.00 (3.00,5.00)	4.00 (3.00,5.00)	-0.050 b	0.960

Abbreviations: BMI, body mass index; HR, heart rate; SBp and DBp, systolic and diastolic blood pressure; NRS, numerical rating scale. Education and Baseline NRS were presented as median (interquartile range). The item of other diseases was presented as count (proportion). Others were presented as mean and standard deviation. a: *t* test; b: Wilcoxon rank-sum test; c: Fisher's exact test.

rhythmicity of sleep and the regular pattern of SRE, we designed the regimen of interrupted rapid eye movement (IREM) sleep for MC patients. The IREM sleep in this study meant that patients who underwent circumcision were awoken a few times a night at the beginning of REM sleep and kept awake for 10-minute intervals, during three nights after the operation. Based on this intervention, we assumed that the total time of sleep-related erections would be decreased by decreasing the time of REMS or interrupting REM sleep. Thus, incision pain and edema would be relieved and wound healing would be accelerated.

MATERIALS AND METHODS

Study Design and Population

This randomized controlled study was approved by the ethics committee of the First Affiliated Hospital of Soochow University (Clinical trial identifier:2016023). From May to November 2016, patients were recruited from the operating room of the outpatient department of the First Affiliated Hospital of Soochow University. Eligible patients were[(1)] scheduled for circumcision,[(2)] aged 14 to 60 years,[(3)] fully conscious,[(4)] able to clearly express their feelings,[(5)] previously having an erection every morning, and[(6)] able to voluntarily participate in the study. Patients were not eligible if they had[(1)] too low a threshold of pain, with numerical rating scale (NRS) > 5 points at preoperative anesthesia,[(2)] a history of chronic insomnia or psychological diseases,[(3)] sexually transmitted diseases or male genitalia inflammation, and[(4)] other chronic diseases or cancers. A power analysis determined that 22 is the least amount of sample (effect size 0.1, alpha 0.05)[(7)]. Finally, we enrolled 45 participants for each group.

Procedures

There were 2 researchers (a physician who performed the circumcisions with stapler for all the participants in this study and a nurse who was responsible for data collection and delivering the intervention). Patients who were willing to participate in this study were informed about the study by the physician and provided signed informed consent when patients visited him first time at clinic. Patients were randomly assigned in to the IREM sleep group or control group by the physician according to the computer-generated random number sequence. The nurse presented the rights of withdrawal and confidentiality to eligible participants when patients were admitted for the operation. Baseline information, including demographics, history of previous morning erections and current clinical data, were collected.

To ensure the participants' full understanding of the meaning of the numbers of the NRS that was used to evaluate incision pain, the nurse provided education concerning the NRS scale to all the participants before the operation. Patients were also educated regarding the evaluation methods for edema, time of sleep, and other irregular conditions which the patients might experience. Then the nurse ordered the participants to take down these data in detail. In addition, patients in the IREM sleep group were given a booklet on IREM sleep and one-on-one education, which took about 15 minutes. All these procedures were conducted in the waiting area of the operating room.

Interventions

The research physician performed the incisions and dressings for all the participants. The participants underwent wound dressing at day 3 and day 7 after the operation.

Control group

The participants in the control group received regular care, including telling them the incision pain during night, how to identify severe bleeding and edema which would require a physician visit, and the scheduled time to attend hospital for wound dressing.

IREM sleep group

Pilot study

First, we examined whether the regimen of IREM sleep schedule was reasonable for 5 patients as follows: sleep for 120 minutes, awake for 10 minutes, for 2 cycles; then sleep 60 for minutes, awake for 10 minutes, for 2~3 cycles. The results indicated that the 120-minute sleep period was too long for 3 patients. Therefore, we modified the schedule of IREM sleep schedule: sleep for 90 minutes, awake for 10 minutes, for 3 cycles; then sleep for 60 minutes, awake for 10 minutes, for 2~3 cycles.

Booklet

A booklet for patients in the IREM sleep group was developed by our research group, including urologists, nurses, and venereological experts. The content of the booklet was as follows:[(1)] Brief description of the male circumcision procedure and the expected discomfort af-

Table 2. Comparison of times of SRE-related MSP and the cumulative time of MSP at night.

Groups (N)	Times of MSP		The cumulative time of MSP(min)
	1d	2-3d	1-3d
Intervention (33)	2.00 ± 1.28	2.00 (1.50,3.50)	28.00 (11.00,50.50)
Control (42)	2.86 ± 1.93	3.47 (2.00,6.25)	55.00 (13.75,220.00)
F/Z	6.944	-2.125	
P	0.010a *	0.034b *	

1d: the first day after operation; 2-3d: the second and third day after operation; 1-3d: first 3 days after operation. The times of SRE-related MSP at 1d was presented as mean and standard deviation (SD), that of 2-3d and the total time of MSP were presented as median (interquartile range). a: repeated measure; b: Wilcoxon rank sum test. *: *P* value < 0.05.

terward,[2] Description of the association between REM sleep and sleep-related erection,[3] Introduction to the evaluation of the NRS with regard to pain and edema, [4] Introduction to the purpose of IREM sleep,[5] Introduction to the IREM sleep method (the alarm was set before sleep). The schedule of IREM sleep was: sleep for 90 minutes, awake for 10 minutes, for 3 cycles; then sleep for 60 minutes, awake for 10 minutes, for 2~3 cycles. If a patient was still troubled by SRE pain, he could shorten the time awake.

Education of IREM sleep

In the one-on-one education session, the nurse and the patient reviewed the booklet together, with emphasis on the knowledge and methods needed for IREM sleep. In the waiting area of the operating room, patients were taught the waking time intervals during the night and the skills to set the phone alarm clock. This education took approximately 15 to 20 minutes.

Data collection

On the next morning after operation, we collected the data of pain, edema and sleep on the first day of the night after the operation, by the participants' self-report using telephone. At day 3 and day 7 post operation, the nurse collected the rest data when the patients came to the hospital for wound dressing.

Measurements

Pain Assessment

Pain was assessed with the NRS[16]. The scores ranged from 0 to 10; 0 indicated no pain, and 10 indicated the most intense pain. The pain classification was as follows: 4-6 and 7-10 indicated moderate pain and severe pain (MSP), respectively. In further detail, the score with NRS ≥ 4 meant MSP. The total time of MSP was taken as the cumulative time during the night. The times of SRE pain imply the times of MSP related to SRE.

Incision edema and healing

The degrees of edema severity resulting from the penis incision were classified as 3 levels. Level 1 indicated striae-present edema, level 2 indicated striae-absent edema without blister, and level 3 indicated severe edema with blister and high skin temperature[7], respectively counted score 1, 2 or 3. The level of incision healing was evaluated by the physician at 1 week after the incision. The levels of incision healing were classified into 3 levels: level A indicated primary healing of the incision without any adverse reactions, level B indicated poor healing, but the incision did not become infected, and level C indicated that the incision was infected and needed drainage[7].

Duration of sleep

To observe the side effects of IREM sleep, we recorded the duration of sleep at night. In this study, the duration of sleep means the cumulative time of night time sleep that was observed.

Outcomes

The primary outcomes were the times of SRE-related MSP and the cumulative time of MSP at night during first 3 days after operation. The secondary outcomes were the levels of swelling and condition of incision healing during the second and third day. The cumulative times of sleep at night during first 3 days were safety indicator.

Statistical Analysis

All analyses were performed with SPSS 16.0 (SPSS, Inc., Chicago, Illinois). Continuous variables are presented as mean and standard deviation (SD) when normally distributed on visual inspection of their histograms and as median (interquartile range) when not normally distributed. Categorical variables are summarized as count (proportion). Data from the participants who withdrew from the study were not included in these analyses. The baseline characteristics were compared using t test, Wilcoxon rank sum test, repeated measure and Fisher's exact test. The level of statistical significance was 0.05.

Table 3. Comparison of levels of swelling and condition of incision healing.

Groups (N)	Level of swelling(2-3d)		Level of incision healing (7d)
	Level A	Level B	
Intervention(33)	2.00 (1.00,2.00)	32 (97.0%)	1(3.0%)
Control (42)	2.00 (1.75,2.00)	39 (92.6%)	3 (7.4%)
Z/x^2	-0.295	0.619	
P	0.768a	0.626b	

Level of swelling (2-3d) was presented as median (interquartile range) and Level of incision healing at 7d was presented as count (proportion). 2-3d: the second and third day after operation; 7d:the seventh day after operation. a: Wilcoxon rank sum test; b: Fisher's exact test.

Table 4. Comparison of cumulative time of sleep at night (h) (± s)

Groups (N)	1d	2d	3d
Intervention (33)	6.50 ± 1.51	6.39 ± 1.57	6.69 ± 1.22
Control (42)	5.72 ± 2.05	6.11 ± 1.81	6.21 ± 1.79
F		1.456	
P		0.231	

1d, 2d and 3d: the first night, the second night and the third night after operation, respectively. *P* values were derived from repeated measure.

RESULTS

Baseline Characteristics

Ninety MC patients were recruited to this study, of whom 45 were randomly allocated to the IREM sleep group and 45 to the control group (Figure 1). Twelve participants in the IREM sleep group and 3 in the control group withdrew during the study, leaving 33 in the intervention group and 42 in the control group. There were several different reasons to withdraw from this study in the IREM sleep group, 4 participants did not like to influence another family member's sleep, 6 forgot to set the alarm clock, 1 was unwillingly to answer the phone, and 1 was excluded due to a sustained erection. In the control group, 1 was wound re-suturing and 2 did not answer the phone. Demographic parameters were similar between both groups (**Table 1**). The pain scores between two groups were not significantly different at baseline (**Table 1**).

Times, the cumulative time, and incidences of SRE-related MSP at night

During the first 3 days after the operation, the times of SRE-related MSP in the IREM sleep group were significantly fewer than the control group (P = .010). Five patients reported that there was no pain during the night. The cumulative time of SRE-related MSP was significantly decreased in the IREM sleep group (P = .034) (**Table 2**). At day 1 after the operation, the incidences of SRE-related MSP in the IREM sleep group was 66.7%, while in the control group, it was 81.6%.

Incision swelling and healing

There were no statistical differences in incision swelling (P = .768) and healing (P = 0.626) after the operation between the 2 groups (**Table 3**).

The cumulative time of sleep at night

We recorded the cumulative time of sleep at night for 3 days after the operation. The results indicated that there was a little longer sleep time in the IREM sleep group than in the control group. But this was not significantly different (P = .231) (**Table 4**).

DISCUSSION

In this study, we found that the incidence of incision MSP was 81.6%, which was lower than that reported by Xiao-mei et al, who found the incidence of MSP was 96%[7]. The reason might be that we only collected the data of MSP related to SRE, while Xiao-mei et al. included all the patients' pain data. In addition, we found that MC patients in the nonintervention group experienced about 3 times the incidence of SRE-related MSP, with the total time of MSP lasting for about 1 hour, and even up to 13 hours. The results above indicated that the postoperative pain status of patients with MC is not well noticed. Although there have been related studies that reported the association between IREM sleep and erection[17], we have not found existing reports using IREM sleep for SRE-pain intervention in MC patients. From our pilot study, we first designed the regimen of IREM sleep, and then tested the effect of this method. We found that IREM sleep improved SRE-related MSP for MC patients. We also found the times of sleep-related erection were noticeably fewer, and thus, the occur-

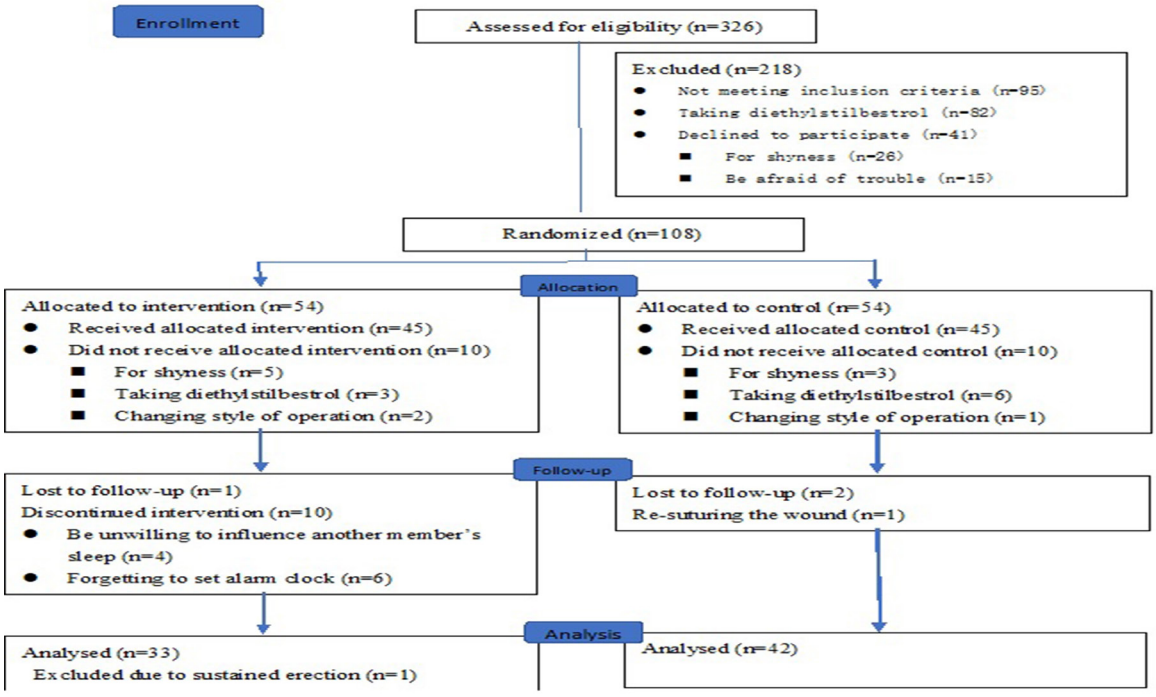

Figure 1. Patients' flow diagram.

rence of MSP was improved. The beneficial effects of IREM sleep on relieving SRE-incision pain could also be observed on the third postoperative day. As the times of SRE-related MSP decreased, the cumulative time of MSP decreased. Some patients even reported that there was no pain at night after the operation. This phenomenon indicated that IREM sleep effectively interrupted the occurrence of REM sleep in MC patients, leading to decrease times of erection, and therefore, the incision pain was effectively improved.

Although this method was good, the adherence to the IREM sleep schedule was a problem. We understand that some patients had not paid the attention to the likelihood of SRE-related pain; hence, we should increase the educational time and improve its effectiveness in the future. Some other patients had a shorter sleep cycle, while the human normal sleep cycle lasts from 80 minutes to120 minutes[14], which resulted in the IREM sleep intervention being invalid. The reasons might be associated with limited time of education (about 20 to 30minutes), as well as the sub-optimal time at which the education program was performed (just before the operation). At that time, the patients were anxious, and they paid more attention to the operation than the IREM sleep intervention education; hence, the adherence of patients to the education might be affected. In addition, we did not pay attention to patients' caring to interrupt their family members' sleep, which resulted in four patients' noncompliance. In further studies, we should modify the regimen of IREM sleep according to the patients' condition, arrange reasonable educational time and consider risk factors to affect the compliance.

Some patients in the control group kept themselves awake all night to avoid sleep-related incision pain, after they once experienced severe erection-related pain. Hence, they had less sleep time. In this study, we recorded the cumulative time of sleep during the first 3 days. The results found that there were shorter sleep times in the control group than that of IREM sleep group, although the result was not significantly different. Therefore, IREM sleep is one of the safe and effective methods for relieving SRE pain.

Incision healing is another indicator of the advantages and disadvantages of circumcision [10]. The occurrence of SRE after MC usually exacerbates incision swelling, which then delays the time of healing. Xu et al found that the incidence of moderate and severe incision swelling was up to 44% at the third day after the operation, which could affect patient outcomes. Hence, we explored the effect of IREM sleep on improving incision swelling and healing.[7] However, we did not find that IREM sleep could improve these indicators. The reason might be that SREs provided adequate engorgement of the corpora cavernosa, which then led to increased tissue oxygenation[18], and thus promoted incision healing.

The interrupted rapid eye movement sleep is an effective, safe, and free method of treatment to relieve incision pain of sleep-related erections.

Limitations: In this study, we did not perform blinded measurements, and the erection-related MSP using NRS and the time of sleep was by patients' self-report; therefore, these measurements were somewhat subjective, and a measuring bias might exist. We did not perform the intentionality analysis, and therefore a selection bias might exist. There was limited education time which might result in poor adherence to our intervention program. The limited sample was given in this study. In a further study, we could perform an individualized regimen of IREM sleep, which may bring more benefits to the MC patients.

CONCLUSIONS

We proposed the method of interrupted rapid eye movement sleep, then explored the effect of pain-relieving on male circumcision. We found that the interrupted rapid eye movement sleep is an effective, simple, and free treatment to relieve incision pain of sleep-related erections.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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