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Original Article

Effects of ethyl chloride spray on early recovery after total knee arthroplasty: A prospective study

Wang Rui ^{b,1}, Gong Long ^{a,*}, Geng Li ^a, Yu Yang ^a, Li Hengjin ^{b,**}, Wang Zhenhu ^{a,***}^a Department of Orthopedics, Chinese PLA 252 Hospital, 071000, No. 991 Baihua Dong Road, Baoding, Hebei, China^b Department of Dermatology, The General Hospital of Chinese PLA, 100853, Fuxing Road, Beijing, China

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ABSTRACT

Background: Ethyl chloride spray as a common cooling modality has been widely used in acute sports injuries and joint injection procedures. Several clinical studies reported that use of ethyl chloride has positive effects on swelling, pain reduction and recovery from sports injuries. The main aim of present study was to analyze whether postoperative use of ethyl chloride spray benefits results after primary total knee arthroplasty (TKA).

Methods: Between April 1, 2014 and October 21, 2015, 306 subjects undergoing primary TKA used ethyl chloride spray for improving recovery from the damage from surgery. After exclusion of 31 subjects due to adverse events including periprosthetic joint infection (PJI), deep venous thrombosis (DVT), acute myocardial infarction, finally 275 subjects' data regarding pain score, knee range of motion (ROM), knee girth, time of being able to reach 90° knee flexion and analgesic consumption were analyzed.

Results: Significant differences in pain score, knee ROM at each time point and knee girth at on 21st and 28th postoperatively were detected without increased incidence of adverse events. Besides, time of being able to reach 90° knee flexion and analgesic consumption in the treatment group were significantly decreased in comparison to the control group.

Conclusion: Use of ethyl chloride spray can help patients recovery from the damage from TKA safely.

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1. Introduction

Pain, edema, muscle spasm, hemorrhage and inflammation in the peri-operative tissues are common problems in the immediate postoperative phase of total knee arthroplasty (TKA) [1]. These factors interfere with postoperative functional rehabilitation and thus influence ultimate results after surgery [1]. Cryotherapy is a common treatment modality to reduce pain and enhance recovery after arthroscopic and TKA procedures [2,3]. The beneficial effects of cold therapy have been clearly confirmed [2–4]. Studies have indicated that cold application helps decrease enzymatic function in inflammatory reaction and produce vasoconstriction [3–5]. Reduction in blood flow contributes to decreasing local inflammatory response and edema formation [4,5]. Besides, local cooling is regarded as slowing pain signal transmission, inhibiting the stretch

reflex and reducing muscle spasm [5,6]. However, current techniques of cryotherapy mainly including ice packs, cryocuff and continuous temperature-controlled cryotherapy system are limited by their lack of convenience respectively [1,7–9].

Ethyl chloride spray as a common cooling modality has been widely used in acute sports injuries and joint injection procedures [10–12]. Several clinical studies reported that use of ethyl chloride has positive effects on swelling, pain reduction and recovery from sports injuries [11–13]. To our best knowledge, however, we found no study investigating the effect of ethyl chloride spray on patients' recovery from the damage from TKA. Therefore, the main aim of present study was to analyze whether postoperative use of ethyl chloride spray benefits results after TKA. We hypothesized that ethyl chloride application would reduce pain, swelling and result in better active range of motion (ROM).

2. Patients and methods

Between April 1, 2014 and October 21, 2015, in the hospital of Chinese PLA 252 Hospital and general hospital of Chinese PLA, 306 consecutive participants accepting unilateral TKA were randomized into the treatment or control group. Participants in the treatment

* Corresponding author. Fax: +86 03122058085.

** Corresponding author. Fax: +86 03122058085.

*** Corresponding author. Fax: +86 03122058085.

E-mail addresses: Gonglong301@163.com (G. Long), wzh_0312@sina.com (W. Zhenhu).¹ Wang Rui and Gong Long contributed equally to this work.² Li Hengjin and Wang Zhenhu contributed equally to this work.

group accepted the use of ethyl chloride spray (Baiyun Shan Co. Limited, Guangzhou) for four weeks while participants in the control group did not. The research coordinator who was blinded to the process of this study created a random list of numbers sealed with envelopes. The blind numbers were unconcealed when patients were admitted. The uneven and even number respectively represents the use of cold spray or not. This study has been approved by the research ethics committees of hospital of Chinese PLA 252 Hospital and the general hospital of Chinese PLA, and in accordance with the declaration of Helsinki. All the participants gave their written informed consent to the research.

2.1. Participants

Patients were eligible for inclusion if they were between the ages of 50 and 80 with a diagnosis of severe osteoarthritis and accepted a unilateral TKA under epidural anesthesia. Participant was excluded if he or she (1) was allergic to ethyl chloride, (2) was unable to complete our assessments and other patient-reported questionnaire, (3) had neuromuscular or neurodegenerative diseases. Flow chart of this study is seen in Fig. 1. Patient demographics and surgical time are detailed in Table 1.

2.2. Interventions

In comparison to their controls, participants in the treatment group received ethyl chloride spray when they performed

functional exercise for the first four weeks after surgery. We required patients to exercise 3 times in each day unless severe complication occurred. Specific time points were 9:00 am, 15:00 pm and 20:00 pm respectively. Ethyl chloride spray was applied during exercise based on our experience which summarized from patients' feedback and their subjective feelings for about 40 s at a distance of about 10 cm from the incision (including popliteal fossa, lower 1/3 region of the thigh and higher 1/3 region of the calf). In addition, patients use the cold spray to relief any pain area which possible trouble them and their exercise such as the other region of lower 1/3 region of the thigh.

We routinely administered patients with prophylactic antibiotics (vancomycin or cefotaxime) before the skin incision and then every 8 h after surgery for 48 h. All procedures in this study were performed by the same surgical team under epidural anesthesia. All knees were approached through a mid-line anterior incision. Cemented cruciate-retaining prosthesis (Gemini MK-II, Link, Germany) with patellar resurfacing was used for all patients in this study. Total knee arthroplasty was performed with a tourniquet (300 mm Hg) applied for 21 min (18.5–22.5 min). It was used merely from beginning of preparing femoral bone bed to the end of fixing prosthetic components. The drainage tube was promptly removed at postoperative 24 h. Patients were equipped with patient-controlled analgesic (PCA) pump during postoperative 48 h. For relieving postoperative pain, all patients received routinely diclofenac sodium (50 mg, tid) orally during hospital stay and tramadol (100 mg, tid) if necessary after discharge. Preventive

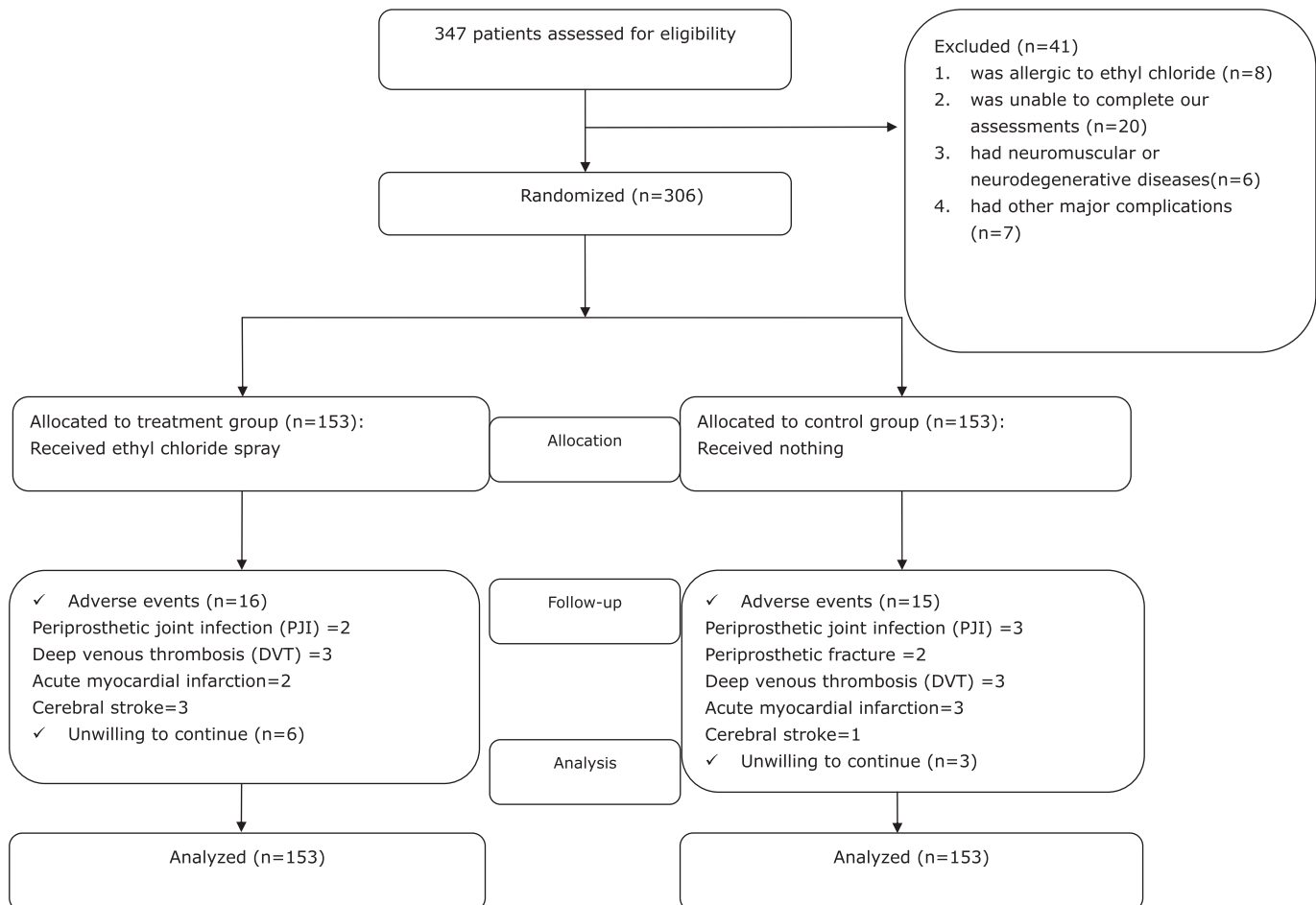


Fig. 1. Flowchart of enrolled participants.

Table 1
Demographic characteristics and baseline information.

Variables	Treatment group (n = 153)	Controlled group (n = 153)	p value
<i>Patient characteristics</i>			
Age (years)	62.8 ± 4.3	63.5 ± 4.0	0.16
Sex (male/female)	35/102	42/96	0.44
BMI (kg/m ²)	29.3 ± 1.8	29.0 ± 1.9	0.18
<i>Preoperative data</i>			
ROM	109.6 ± 15.2	108.5 ± 14.8	0.54
Knee girth (cm)	35.0 ± 3.8	35.7 ± 3.6	0.12
VAS pain scores	3.9 ± 1.1	3.8 ± 1.3	0.49
Duration of surgery (min)	63.2 ± 9.6	62.2 ± 8.9	0.37
Duration of femoral tourniquet (min)	28.6 ± 5.5	29.6 ± 5.9	0.15

BMI Body Mass Index, ROM range of motion, VAS Visual Analogue Scale.

anticoagulant therapy (10mg rivaroxaban every day or [10 mg rivaroxaban every day or 2850 international units (IU) low-molecular-weight heparin (LMWH) (body weight <90 kg) or 5700 IU (body weight >90 kg)] began within 12 h after surgery and continued for 35 days.

2.3. Outcome measures

Patients' outcome were evaluated by one experienced physical therapist who was blinded to this research before surgery and then at 3, 7, 14, 21 and 28 days postoperatively. Primary outcome measure was active range of motion of the operated knee. Active ROM was measured using a standard hand-held goniometer with the patient in a supine position. The goniometer was placed over the joint space with one arm aligned with the fibular head and lateral malleolus and the other in line with the greater trochanter. The knee was flexed maximally at patient's best. Then the angle was measured in degree. Secondary outcome measures included visual analogue scale (VAS) pain scores rated on a scale of 0–10 from no pain to severe pain, knee girth, time of being able to reach 90° knee flexion and analgesic consumption. Knee girth at the superior patellar border (suprapatellar girth), was examined to investigate whether ethyl chloride spray influences knee swelling after surgery. The suprapatellar girth was recognized as the index of the intra-articular swelling. Measurements were performed preoperatively and at postoperative day 3, 7, 14, 21 and 28. Analgesic consumption was referred to total doses of opioid analgesic (mg) that is the doses of the tramadol and did not include the dose of opioid used in PCA during the first 28 days after surgery. It was obtained by patient's report. Doppler ultrasonography was performed in all patients to confirm the presence or absence of DVT after surgery.

2.4. Statistical analysis

The student t-test and chi-square test were used to compare continuous and categorical variables respectively. It was assumed that all these statistics was normally distributed. All differences

were considered significant when the p value was <0.05. Continuous variables and categorical variables were presented as the form of mean ± SD and percentage respectively. Statistics analysis was performed using SAS 9.2 by SAS Institute Inc., Cary, NC, USA and Excel 2003, version 11 by Microsoft, Redmond, Washington. All analyses were performed on the basis of intention-to-treat (ITT).

3. Results

3.1. Knee ROM, VAS pain score and knee girth

Mean ROM at all time points after surgery was significantly greater in the treatment group than that in the control group (Table 2). VAS pain score was significantly lower at all time points after surgery in the treatment group (Table 2). In comparison with the control group knee girth was significantly less at postoperative day (POD) 21 and POD 28 in the treatment group in comparison with the control group, as no significant differences were detected POD 3, POD 7, POD 14, and before surgery between groups (Table 2).

3.2. Time of being able to reach 90° knee flexion and total analgesic consumption

Time of being able to reach 90° knee flexion was significantly shorter in the treatment group than that in the control group (Table 3). A significant group effect was observed for total analgesic consumption during the first four weeks postoperatively (Table 3).

3.3. Complications

There were no significant differences in incision complication (9 vs. 11, $p = 0.83$), DVT (2 vs. 3, $p = 0.69$), periprosthetic joint infection (PJI) (3 vs. 2, $p = 0.69$) and other severe complications (Fig. 1) between groups.

4. Discussion

This prospective observation was scheduled at multiple time points post-operatively to assess effects of ethyl chloride spray on early recovery from damage from TKA. Our results revealed that patients in the treatment group after TKA showed better active ROM than patients in the control group. Also, with four weeks application of ethyl chloride spray, patients consumed significantly less narcotics and experienced less pain feeling. The decrease in total opioid consumption can translate to a clinical benefit of fewer side effects, such as constipation, nausea, dizziness. Therefore, patients may have a more pleasant recovery and feel less medicated [1]. Due to a statistically significant difference in knee girth POD21 and POD28 between groups, there seemed to be less clinically benefit on postoperative swelling.

Many studies showed that cold can control pain and prevent edema effectively for patients accepting orthopedic surgery [1,3–5,14]. It helps inhibit pain and swelling which surgical trauma

Table 2
ROM, VAS pain score and knee girth between groups.

Variables	Active ROM(°)			VAS pain score			Knee girth (CM)		
	TG	CG	p value	TG	CG	p value	TG	CG	p value
POD 3	58.0 ± 12.4	53.8 ± 11.2	$p < 0.001^*$	4.3 ± 1.1	5.1 ± 0.9	$p < 0.001^*$	38.2 ± 3.6	38.3 ± 4.0	$p = 0.66$
POD 7	98.0 ± 8.4	89.4 ± 8.2	$p < 0.001^*$	3.1 ± 1.1	3.7 ± 1.4	$p < 0.001^*$	37.4 ± 4.2	37.6 ± 4.0	$p = 0.42$
POD 14	107.2 ± 9.5	94.8 ± 10.3	$p < 0.001^*$	2.5 ± 1.5	3.1 ± 1.9	$p < 0.001^*$	36.5 ± 3.9	37.4 ± 4.1	$p = 0.14$
POD 21	115.2 ± 8.6	103.9 ± 9.4	$p < 0.001^*$	1.7 ± 0.9	2.3 ± 1.0	$p < 0.001^*$	36.2 ± 3.4	37.2 ± 3.7	$p = 0.01^*$
POD 28	119.8 ± 9.0	106.2 ± 8.9	$p < 0.001^*$	1.5 ± 0.6	2.3 ± 0.9	$p < 0.001^*$	35.5 ± 3.1	36.7 ± 3.5	$p < 0.01^*$

ROM range of motion; VAS Visual Analogue Scale; TG treatment group; CG control group; POD postoperative day, *represents significant difference between groups.

Table 3
Time of reaching 90° knee flexion and Analgesic consumption.

Variables	TG (n = 153)	CG (n = 153)	p value
Time of reaching 90° knee flexion (days)	6.6 ± 1.3	8.6 ± 1.4	p < 0.001*
Total analgesic consumption (mg)	1190.5 ± 238.2	1356.2 ± 288.0	p < 0.001*

TG treatment group; CG control group; *represents significant difference between groups.

leads to [11,14]. Present cryotherapy mainly includes cold compressive dressing, ice packs, and other cooling device [1,3–5,14]. However, inconvenience of these methods results in limited clinical application, especially for patients after discharge. Orthopedists try to explore a portable, economical, and easily controlling method for patients after surgery. One inexpensive, readily available, and effective option is topical refrigerant ethyl chloride [15,16]. To our best knowledge, no study on effect of ethyl chloride spray on the recovery from the damage from TKA was found. However, it has been applied and proved to be effective in the venipuncture, minor surgical procedures, sports injuries and intra-articular injections for years [11–13,15,16]. Our results demonstrate use of ethyl chloride spray can benefit patients' recovery from the damage from TKA as well. Previous studies have reported the addition of cold to compression increases the rate, magnitude and depth of temperature reduction as well as the speed of lymph evacuation. This is a more effective way to reduce tissue temperature and swelling than the use of cold spray. However, our observation revealed the use of cold spray alone prompted far better recovery after TKA over the control group which mainly refer to better pain relief and active ROM at each time point and later stage reduced swelling at the 21 and 28 day postoperatively. Therefore, main advantages of cold spray comes from less pain and improved active ROM. Possible explanations are mainly lied in that our cryotherapy was easily as well as quickly shiftable application when patients performed painful flexion and extension exercise. In addition, patients use the cold spray to relief any pain area which possible trouble their exercise such as the other region of lower 1/3 region of the thigh. From our patients' feedback, one of reasons for their unwillingness to exercise is from painful lower calf, inner or lateral thigh. Being less painful, our patients achieved improved active ROM, less time of reaching 90° knee flexion and analgesic consumption. By contrast, it is relatively difficult for most present cryotherapies to be used as TKA patients do the exercise. Fortunately, insignificant difference in complications such as wound problem and DVT were detected. Polishchuk's study has been performed to evaluate the effect of ethyl chloride spray on the sterility of the skin during injection or aspiration procedures involving the knee and shoulder. And this study demonstrated this spray did not alter the sterility of the skin at the injection site [17]. To avoid potential risk of wound problem, in the first 2 weeks patients were required to applicated this spray in the area which keeps 1 cm and above away from the incision [17]. Thus, ethyl chloride spray was a safe method to relieve pain. However, we found that it seemed to exert less effect on postoperative swelling. Significant difference in knee girth between groups failed to be found at POD3, 7, and 14. We assumed that it was due to intermittent use of this spray (tid) and best effects of cold are difficult to show. Improvement in swelling at POD21 and 28 may be explained by the results of better pain relief and active ROM. Better functional exercise with less pain contribute to anti-swelling.

Many studies that include meta-analysis and review showed advantages of postoperative cold therapy after TKA in regard to blood loss, knee ROM, narcotic needs and pain relief [1–5,7–11].

The present study concurs with the results these studies reported. In addition to cold effect which ethyl chloride spray can produce, this medication also makes patients achieve pain relief by its pharmacological character of anesthetic action. Our results reveal that time of being able to reach 90° knee flexion in the treatment group was advanced nearly 2.1 days in comparison with the control group. Hence, combination of dual property of cold and anesthesia of this spray can lead to less pain and better ROM so that better recovery from the damage from TKA was achieved.

What is the most meaningful aspect of this study lied in the possibility of providing a new selection for application of cryotherapy. This new cooling method is easily and safely used. It did not have negative effects on wound healing. Besides, it needed negligible cost in comparison with other electronic cooling devices. One additional merit of this study is that it is a prospective, randomized, controlled trial. The absence of preoperative difference between groups ensures a well homogeneity. As a result, the significant results after TKA we obtained are of a certain value to its practice.

The main weaknesses of this work include a relative small sample size and a lack of objective data such as real temperature of soft-tissue. This makes our results relatively limited and less persuasive. Another criticism of this study would be less surveillance and information related to details in how patient used ethyl chloride spray, as this treatment was mainly applied at home after discharge. Although necessary information is required at the point of follow-up, it relies on the report by patient. Thus, the degree of reliability is discounted. Last, our results could be false positive as no placebo was given in the control group. Thus, future studies are expected to answer above-mentioned questions.

5. Conclusion

Patients who use ethyl chloride spray after TKA in our hospital had greater knee ROM, less pain, and less time to reach 90° knee flexion in comparison to patients who did not use it. In addition, this application results in a lower less analgesic consumption and less swelling with no adverse effect on wound healing.

Conflict of interest

The authors declare that they have no conflict of interest.

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