

Efficacy of cold application on pain during chest tube removal: a randomized controlled trial A CONSORT-compliant article

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Abstract

Background: Use of analgesics is the most common method to alleviate the pain induced by chest tube removal (CTR), but patient response to medication can vary and may not be achieved complete relaxation. This study was to determine the effectiveness of cold application in combination with standard analgesic administration before CTR on CTR-induced pain.

Methods: A prospective, randomized, single-blind, sham-controlled study was conducted. In addition to the same routine care, subjects in the experimental group (n=30) received cold application of 600-g ice packs 15 minutes before CTR, whereas subjects in the sham group (n=30) received tap water packs. Numerical rating scale was used to measure pain intensity before, immediately after, and 10 minutes after CTR.

Results: The generalized linear estimating equation (GEE) model, adjusted for other factors, both the groups demonstrated a trend toward decreased pain during CTR over time (P < .001), but no significant differences between the 2 groups (P = .65), even stratifying by gender. If we fixed experimental group, women significant reduced pain score of 2.7 on immediately after CTR compared with before CTR (P < .0001) and reduced pain score of 2.05 on 10 minutes after CTR compared with before CTR (P < .0001). The sham group had no similar performance as the experimental group. In the male subgroup, both experimental and sham groups, men significantly reduced pain score on immediately after CTR and 10 minutes after CTR compared with before CTR (P < .0001).

Conclusion: The results indicate that cold application is not more effective than sham treatment in decreasing pain during CTR, even among gender. Although statistically non-significant, clinically important differences of decreased pain score were observed with cold application among women (Clinical Trial Registration: clinicaltrials.gov identifier NCT03307239).

Abbreviations: CTR = chest tube removal, GEE = generalized linear estimating equation, NRS = numerical rating scale, NSAIDs = non-steroidal anti-inflammatory drugs, VAS = visual analog scale, VATS = video-assisted thoracoscopic surgery.

Keywords: chest tubes, cryotherapy, pain management

1. Introduction

During the process of chest tube removal (CTR), separating the chest tube from attached and adhered tissues causes pain in patients.^[1] CTR is described as one of the worst experience for patients.^[2] Use of analgesics is the most common method to alleviate the pain induced by CTR, but patient response to medication can vary and may not achieve complete relaxation. Combination of pharmacological and non-pharmacological

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approaches is reported to achieve the highest level of pain control.^[3] Cold application has been clinically used as an effective alternative therapy to alleviate pain. Previous studies have shown that the mechanisms by which cold therapy might elevate pain threshold include a decrease in nerve conduction, reduction in muscle spasms, and prevention of edema after injury.^[4] The analgesic effect of cold application can be explained by the gate control theory proposed by Melzack and Wall in 1965 that cold application activates descending inhibitory neurons that prevent the ascending nociceptive neurons from sending pain signals to the brain.^[5] This thereby "closes the gate" to pain, and our brain will not interpret the impulse as painful.^[6] With regard to the duration of cold application, 10-minute cold application, which decreases the skin temperature to 13.6°C, can have an effective analgesic effect.^[7] The other report demonstrated that a 10- to 20-minute cold application can potentially decrease the skin temperature to 10°C to 15°C and have a local analgesic and swelling-reducing effect.^[8]

Few studies reported the use of cold application to alleviate the pain induced by CTR.^[6,9–12] A study in 2002 reported the alleviating effect of 10-minute cold application on CTR-induced pain (immediately after and 10 minutes after CTR) was not significantly different from that of placebo treatment.^[9] However, recent studies all demonstrated that cold application could clinically be used as an effective alternative therapy to alleviate pain.^[6,10–12] Ertuğ and Ulker found that patients with single pleural chest tube who received cold application had significantly decreased pain indices immediately after and 5 minutes after

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CTR.^[10] Gorji et al showed that pain reduction was significantly better in the cold application than in the standard care group in the patients undergoing coronary artery bypass graft surgery.^[11] In addition, Payami et al showed that the pain index immediately after CTR was significantly lower in the group that received cold application than in the one that received placebo.^[12] However, there were no related studies reported in East Asia population.

In the other hand, recent years research regarding sex differences in pain have substantially increased.^[13] Experimental studies demonstrate gender differences in pain sensitivity with women indicating lower pain thresholds and tolerances for a variety of noxious stimuli in the laboratory.^[14,15] Women tend to more readily detect pain and to attenuate it less than men. A recent clinical study showed that women have a distinctly different pain experience than men after thoracic surgery.^[16] There are likely differences in pain responses between men and women with CTR.

The procedure of cold application in alleviating CTR-induced pain remains unclear and the weight of ice packs used was not considered yet. The study by Janwantanakul indicates that an ice pack containing 600g of ice leads to a greater magnitude of cooling, whereas the size of the contact area has no significant effect on the degree of cooling.^[17] Therefore, this is also the first study to identify the weight of ice packs using 600-g ice packs for cold treatment.

The primary purpose of this study was to determine if cold application by 600-g ice packs combined with regular analgesics could decrease the pain induced by CTR in patients who underwent video-assisted thoracoscopic surgery (VATS). The secondary purpose was to investigate the effectiveness of cold application between female and male. We hypothesized that cold application would be more effective than sham treatment in decreasing pain during CTR.

2. Methods

2.1. Participants

This prospective, randomized, single-blind, sham-controlled study enrolled all patients who underwent VATS hospitalized in a surgical ward of the Ditmanson Medical Foundation Chia-Yi Christian Hospital (DMF-CYCH) between September 15, 2014 and September 15, 2015. From a total of 140 patients who underwent VATS during the study period, 73 patients did not meet the inclusion criteria and 7 declined to participate in the study. Finally, 60 subjects were enrolled in the study (Fig. 1). Inclusion criteria were as follows: age >20 years, single chesttube insertion, first-time insertion of the chest tube, ability to verbally report pain, body mass index of <30 kg/m², and normal vital signs. Exclusion criteria were cold urticaria.

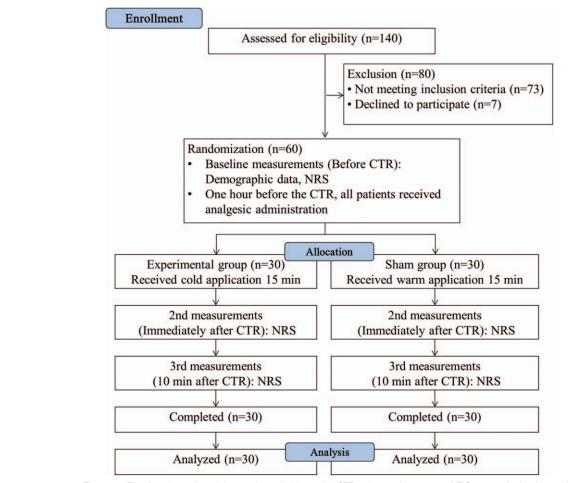


Figure 1. The flowchart of participants through this study. CTR=chest tube remove, NRS=numerical rating scale.

This study was approved by the Institutional Review Board (IRB) of the DMF-CYCH (CYCH IRB No: 103044). Written informed consents were obtained from all participants prior to enrollment. The purpose, study details, and the right to withdrawal from the present study at any time were explained to each participant. Recorded data were stored in an anonymous and confidential manner.

2.2. Research design

The researcher used the SPSS System for Windows (version 21.0; IBM Corporation, Somers, NY) to generate the random allocation sequence using block randomization with block sizes of 4. Once patients agreed to participate in this study, the researcher assigned participants to 1 of the 2 groups: cold application (experimental group) or tap water packs application (sham group) according the random allocation sequence. Participants were blinded to the group assignment during the study to control for placebo effects. Prior to CTR, patients in the experimental group received cold application and those in the sham group received application of body temperature (36°C) tap water packs. Pain was assessed before, immediately after, and 10 minutes after CTR. The flowchart of participants through the present study is shown in Figure 1.

2.3. Sample size

The sample size was calculated on the basis of a similar previous study^[12] with a statistical power of 95% and an alpha level of 0.001 (2-tailed). According to the mean and standard deviation of pain intensity scores immediately after CTR in the experimental and sham groups $(2.67 \pm 0.79 \text{ and } 3.9 \pm 0.76$, respectively), a minimum of 23 subjects were required in each group to detect a significant difference. Assuming an attrition rate of approximately 20%, the sample size in the present study was increased to 30 subjects per group.

2.4. Outcome measures

Data collection instruments included a demographic questionnaire and a numerical rating scale (NRS). Demographic information included age, gender, weight, chest-tube insertion indication, days of chest-tube insertion, and details of postoperative analgesics administered. Pain intensity was evaluated by the NRS ranging from 0 (no pain) to 10 (worst imaginable pain). Li et al^[18] showed that the reliability coefficients of NRS across current, worst, least, and average pain on 7 postoperative days were consistently high (0.67-0.82); in addition, NRS values at each rating were strongly correlated with those of other scales, such as visual analog scale (VAS), a verbal descriptor scale, and the Faces Pain Scale Revised (r=0.71-0.99). Paice and Cohen also found a strong positive correlation between the VAS and the NRS (r=0.847, P<.001).^[19] Because the VAS is widely accepted as a standard tool to measure pain intensity and the NRS is highly correlated with the VAS, these findings confirm the validity, and the reliability in measuring pain intensity is supported.

2.5. Interventions

We manufactured 2 ice packs $(17 \times 12 \text{ cm})$ with a combined weight of 600 g. The ice packs were inserted into adjustable wraps made in our hospital so that they can be fixed next to the skin on each side of the chest tube in patients awaiting CTR. The combined contact area of the ice packs was approximately 25 cm in diameter around the chest tube. Because of the differences in body size, the ice pack wrap was equipped with Velcro so that its length can be adjusted. In addition, there are 2 elastic bands on top of the ice pack so that the wrap could be fixed close to the skin.

For patients of the experimental group, the intensity of pain at the chest tube region was assessed first before cold application (first measurement). Then the patients were asked to lie in bed and maintain their posture while receiving 15-minute cold application. Within 1 to 2 minutes, after completion of cold application, a nurse practitioner removed the patients' chest tubes, and the patients' pain intensity was assessed immediately after (second measurement) and 10 minutes after CTR (third measurement) by one of the researchers. The total procedure duration spend approximately 25 minutes for the participants in the experimental group. Patients in the sham group underwent the same procedure as those in the experimental group; the only difference was that the ice packs were replaced by body temperature (36°C) tap water packs as a sham treatment. Intervention and sham procedures were implemented by 2 nurses who were trained to record NRS values and use cold or sham application. All procedures were supervised by one of the researchers to check the fidelity of the procedures. In addition, a pilot study was conducted before the actual study to assess possible difficulties in recording patient responses.

2.6. Statistical analysis

Descriptive statistics were used to describe patient demographic information in both the groups. The Wilcoxon rank sum test was used for non-normally distributed continuous data between 2 groups. The chi-squared test was used for categorical data. A generalized linear estimating equation (GEE) analysis was performed to estimate the effects of cold application on pain intensity scores between the groups before, immediately after, and 10minutes after CTR adjusting for gender, age, weight, chest-tube insertion indication, days of chest-tube insertion, number of analgesics required before CTR, and the use of opioid drugs. All statistical analyses were using IBM SPSS 21.0 (IBM Corp., Armonk, NY) software program for Windows. We considered a *P* value of .001 to be statistically significant. A total of 2 GEE were used for gender stratification. Thus, the level of significance criterion was $\alpha = .0005$ (.001/2).

3. Results

The present study included 60 patients, 30 each in the experimental and sham groups. No patients withdrew from the study. Participant demographics for both the groups are shown in Table 1. The median age of participant was 56 (interquartile, 43-74) years in the experimental group and 57 (45-66.5) years in the sham group. The majority of patients required 2 types of analgesics before CTR. Fourteen patients (46.7%) in the experimental group and 16 patients (53.3%) in the sham group received opioid drugs. There were no significant differences in age, gender, weight, chest-tube insertion indication, days of chest-tube insertion, or number or type of analgesics required prior to CTR between the groups at baseline.

Figure 2 shows the estimated marginal mean of pain intensity between the groups before, immediately after, and 10 minutes after CTR and demonstrates that pain was decreased in both the groups immediately after CTR and was marginally increased at

Table 1		
Compariso	n of demographic data between 2 grou	ips.

	Experimental	Sham	
Variable	group (n = 30)	group (n = 30)	Р
Age, y	56 (43–74)	57 (45-66.5)	.82
Gender			.43
Male	20 (66.7)	17 (56.7)	
Female	10 (33.3)	13 (43.3)	
Weight, kg	58 (51-71.3)	59.5 (52-67.3)	.88
Chest tube insertion indication			.58
Pleural effusion	19 (63.3)	21 (70.0)	
Pneumo-hemothorax	11 (36.7)	9 (30.0)	
Days of chest tube inserted	4 (3–5)	4 (3-6)	.28
Number of analgesics required before CTR			.96
1	5 (16.7)	5 (16.7)	
2	15 (50.0)	14 (46.7)	
3	10 (33.3)	11 (36.7)	
Analgesics required before CTR			
Opioids			.80
Yes	14 (46.7)	16 (53.3)	
No	16 (53.3)	14 (46.7)	
NSAIDs			1.00
Yes	5 (16.7)	5 (16.7)	
No	25 (83.3)	25 (83.3)	
Non-narcotic analgesics			.61
Yes	27 (90.0)	29 (96.7)	
No	3 (10.0)	1 (3.3)	

CTR = chest tube removal; NSAID = non-steroidal anti-inflammatory drug.

Continuous variables are presented as median (25th to 75th) and analyzed using the Wilcoxon rank sum test; categorical variables are presented as n (%) and analyzed using the chi-squared test.

10 minutes after CTR. Figure 2A shows the pain severity ratings of the 2 groups at the 3 time points. A GEE analysis was performed to measure the efficacy of cold application in decreasing pain during CTR.

The results shown in Table 2 demonstrate no statistically significant difference in pain severity (estimate: 0.18; 95% CI: – 0.54, 0.94; P = .54) between the 2 groups after adjusting for gender, age, weight, chest-tube insertion indication, days of chest-tube insertion, number of analgesics required before CTR, and the use of opioid drugs. A trend toward decreased pain during CTR over time was observed in both the groups. Immediately after and 10 minutes after CTR, patients had significantly lower pain intensity scores than before CTR (estimate: -1.27; 95% CI: -1.97, -0.57; P < .001 and estimate: -1.28; 95% CI: -1.76, -0.81; P < .001, respectively).

The results shown in Table 3 demonstrate that after stratification by gender, the use of cold application in women and men both were associated with lower pain intensity scores immediately after and 10 minutes after CTR. No differences in pain intensity scores were observed between the male and female groups (Fig. 2B and C). There were also no significant interactions between groups and measurement time. Nevertheless, among women, compared with before CTR, experimental group reduced more pain intensity score immediately and 10 minutes after CTR than sham group (estimate: -2.01; 95% CI: -3.36, -0.66; P=.004 and estimate: -1.24; 95% CI: -2.20, -0.29; P=.01, respectively, Fig. 2B). Statistical differences between groups at each observation period are further showed in Supplemental Table 1, http://links.lww.com/MD/B954 according to the stratified gender model (Table 3). In the female subgroup the pain score of experimental group at the timing of before CTR

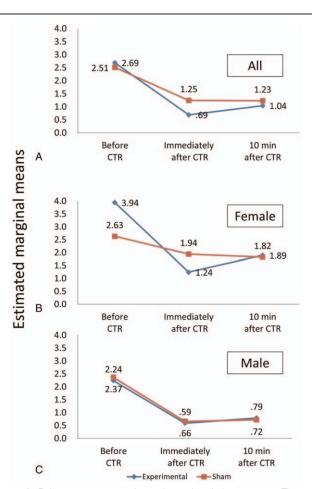


Figure 2. Pain measurements of experimental and sham groups. The pain intensity estimated marginal means (A) of all; (B) of the women; and (C) of the men in 2 groups at the 3 time points. CTR=chest tube removal.

was higher than that of sham group, but not reached the significant criterion ($\alpha = 0.0005$). If we fixed experimental group, women significantly reduced pain score of 2.7 on immediately after CTR compared with before CTR (P < .0001) and reduced pain score of 2.05 on 10 minutes after CTR compared with before CTR (P < .0001). The sham group had no similar performance as the experimental group. In the male subgroup, both experimental and sham groups, men significantly reduced pain score on immediately after CTR and 10 minutes after CTR compared with before CTR (P < .0001). No side effects were observed in any participant.

4. Discussion

Our results showed that pain intensity scores decreased in a timedependent manner immediately after and 10 minutes after CTR in both the experimental and sham groups. Although the mean score in the experimental group was lower than that in the sham group, no significant difference was observed, indicating that cold application is not more effective in alleviating pain than sham treatment. This finding is in agreement with that observed by Sauls,^[9] but different from that observed by others.^[6,10–12] For example, Ertuğ and Ulker found that the pain intensity immediately after and 5 minutes after CTR were significantly lower in the cold application group than those in the placebo group.^[10] Because pain is a subjective feeling, it is not easy to

Table 2				
Changes in	nain	intensity	hv	GEE

Variable	Estimate	SE (95% CI)	Р
Intercept	3.80	0.82 (2.18, 5.41)	<.001
Group			
Experimental	0.18	0.39 (-0.59, 0.94)	.65
Sham	ref		
Time			
Before CTR	ref		
Immediately after CTR	-1.27	0.36 (-1.97, -0.57)	<.001
10 min after CTR	-1.28	0.24 (-1.76, -0.81)	<.001
Interaction*			
Before CTR	ref		
Immediately after CTR	-0.73	0.46 (-1.63, 0.16)	.11
10 min after CTR	-0.37	.32 (996, .26)	.25
Age	0.00	0.01 (-0.02, 0.02)	.80
Weight	-0.01	0.01 (-0.03, 0.004)	.12
Days of chest tube inserted	-0.07	0.06 (-0.17, 0.04)	.23
Gender			
Male	-0.41	0.30 (-1.00, 0.18)	.18
Female	ref		
Chest tube insertion indication			
Pleural effusion	-0.48	0.42 (-1.31, 0.34)	.25
Pneumo-hemothorax	ref		
Number of analgesics required before CTR			
1	0.08	0.46 (-0.81, 0.98)	.86
2	-0.08	0.23 (-0.53, 0.37)	.73
3	ref		
Opioids			
No	0.29	0.26 (-0.22, 0.80)	.26
Yes	ref		

CI=confidence interval, CTR=chest tube removal, GEE=generalized linear estimating equation, SE=standard error.

* Experimental compared with sham group time.

exclude the placebo effect even in the experimental group; therefore, the results can be controversial. Furthermore, Gorji et al found that both cold application and relaxation technique can alleviate the pain induced by CTR. Although the relaxation technique requires no equipment or cost, the patients should be acquainted with the relaxation techniques before surgery and adherence to the process.^[11] The placebo control used by Sauls was tap water pack at 30.5°C to 31.6°C, which is lower than the normal body temperature.^[9] The cool feeling induced by the tap

water pack may contribute to its placebo effect that is not different from the effect of the ice pack. Therefore, the author suggested that tap water pack used in future studies should be kept at body temperature to eliminate this possible error, and the present study was designed based on this suggestion.

All previous studies were conducted in mid-Eastern and Western countries and this is the first study to be conducted in Taiwan. Previous studies reported that the intensity of pain increased from mild to moderate immediately after CTR and

Table 3

Gender effect on the pain associated with CTR by GEE

	Male			Female		
Variable	Estimate	SE (95% CI)	Р	Estimate	SE (95% CI)	Р
Intercept	3.19	1.11 (1.01, 5.36)	.004	4.43	1.88 (0.74, 8.12)	.018
Group						
Experimental	-0.13	0.49 (-1.09, 0.84)	.79	1.31	0.66 (0.02, 2.60)	.046
Sham	Ref			Ref		
Time						
Before CTR	Ref			Ref		
Immediately after CTR	-1.71	0.47 (-2.62, -0.79)	<.001	-0.69	0.51 (-1.70, 0.32)	.18
10 min after CTR	-1.65	0.36 (-2.36, -0.94)	<.001	-0.81	0.23 (-1.27, -0.35)	<.001
Interaction [†]						
Before CTR	Ref			Ref		
Immediately after CTR	0.06	0.57 (-1.06, 1.17)	.92	-2.01	0.69 (-3.36, -0.66)	.004
10 min after CTR	0.20	0.43 (-0.64, 1.03)	.64	-1.24	0.49 (-2.20, -0.29)	.01

CI=confidence interval, CTR=chest tube removal, GEE=generalized linear estimating equation, SE=standard error.

* Adjusted for age, weight, days of chest tube inserted, chest tube insertion indication, pleural effusion, pneumo-hemothorax, number of analgesics required before CTR, and opioids.

significantly decreased to mild pain 10 minutes after CTR.^[6,9–12] However, this pattern is different from the present findings that pain intensity was at its highest before CTR and lowest immediately after CTR and slightly increased 10 minutes after CTR. Because pain is a multidimensional subjective feeling that can be affected by physiologic, sensory, affective, cognitive, behavioral, and sociocultural elements,^[20] the expression for the feeling of pain may well be different between Chinese and Westerners. More future studies should be conducted to fully understand the difference in the expression of the feeling of pain between Chinese and Westerners.

The pain scores obtained in this study were all in the range of light pain, thereby indicating that the patients received superior pain control during CTR in Taiwan. This finding is in agreement with the study conducted by Puntillo and Ley in which the pain scores of 74 cardiac surgery patients, who received proper and timely analgesics, were 1 to 4 during CTR and their pain intensity immediately after and 20 minutes after CTR were lower than those before CTR. Most patients in this study took 2 kinds of analgesics, including opioids (morphine sulfate) and non-narcotic analgesics 1 to 2 hours before CTR. This finding helps confirm that using appropriate and timely analgesic administration can substantially minimize pain during CTR without causing adverse sedative effects.

In addition, previous studies have indicated that responses to pain were different between men and women.^[14-16,22] Various biological and psychosocial mechanisms, including gender hormones, endogenous opioid systems, genotype, pain coping strategies, and stereotypical gender roles, may contribute to gender differences in responses to pharmacological and non-pharmacological pain treatments.^[22] In this study upon further examination on gender difference, we found there were no significant difference of pain score between experimental and sham groups both women and men. Nevertheless, women have different performance compared with men. Compared to before CTR, immediately after, and 10 minutes after the CTR, women using cold application significantly reduced >2 pain intensity scores, whereas women without using cold application had no significant difference. Men in both the applications significantly reduced pain intensity scores. Lund et al used high frequency transcutaneous electrical nerve stimulation to investigate the gender-related pain-alleviating effects of non-pharmacological methods.^[22] Results showed that systematic changes toward increased electrical pain thresholds were only seen in women, while they were unchanged in men. A clinical study showed that women have a distinctly different pain experience than men after thoracic surgery.^[16] Women reported more pain than men during the entire study period. Our result is in agreement with these findings that there is a gender difference in responses to pain treatments. However, recent studies showed that gender has no effect on the pain during CTR for the patients in both the groups.^[10,12] At present, there is no related studies focusing on this aspect, further research is needed to explore these issues.

The major strength of this study was that it is the first experimental study conducted in Taiwan to evaluate a non-pharmacological treatment (cold application) for pain during CTR. Another strength of the study is that we tried to standardize the cold application procedure and used 600-g ice packs to provide the fastest cooling of the skin tissue.^[17]

As for limitations of the study, we did not actually measure the skin temperature during cold application, while earlier studies used infrared thermometer to check the skin temperature and stopped cold application only after skin temperature reached 13°C.^[10,11] Because infrared thermometer is not a popular instrument in our hospital, we used the duration of cold application (15 minutes) instead as our standard practice. This is based on literature review by Greenstein that skin temperature will drop to 10°C to 15°C after 10- to 20-minute cold application.^[8] In addition, there were 3 surgeons working in the surgical ward during this study and each doctor would prescribe different analgesics according to patients' illnesses. Therefore, there were 7 different analgesics used by the 60 study participants. All patients were taking at least 1 analgesic, 2 at most, either orally or intravenously. Thus, it was difficult to quantify and control the dosages of analgesics. We classified the analgesics into opioids, NSAIDs, and non-narcotic analgesics, and recorded the types and number of analgesics patients took. No significant difference was found in the analgesics took by the 2 groups of patients. To achieve a more rigorous experimental design in the future, it is suggested that researchers cooperate with doctors to control the dosage of analgesics taken by patients. And pain is a multidimensional subjective feeling that involves interactions among sensations, perceptions, and cognition, and the result of our study was limited to the subjective pain score and lacked objective data, it suggested that future studies should include data such as vital signs and oxygen saturation. Further studies are required to fully elucidate the characteristics of pain as described by patients, allowing comprehensive evaluations and complete presentations of the pain experience.

5. Conclusion

The study results show that cold application is not more effective than sham treatment in decreasing pain during CTR, even among gender. Although statistically nonsignificant, clinically important differences of decreased pain score were observed with cold application among women. Further studies with more rigorous selection criteria and larger sample sizes are required to confirm the findings of the study.

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