Effect of Cryoanalgesia on Post-Thoracotomy Pain

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Abstract- We prepared this study to determine the effect of cryoanalgesia on post-thoracotomy pain. In this double-blinded randomized clinical trial, 60 patients who underwent thoracotomy were divided into two groups (control and cryoanalgesia). Visual Analogue Scale (VAS, 0-10) was used for the measurement of severity of post-thoracotomy pain. It was classified into three categories: 0-1 (mild), 2-3 (moderate), and 4-10 (severe). Pethidine (0.5-1 mg/kg) was administered in case of need for both groups. Patients were visited at the hospital a week later, and were contacted by phone at the first, second, and third months post-operatively. Intensity of pain in the control group was higher than the cryoanalgesia group in all visits the follow-up period. On the second day, the frequencies of severe pain (4-10) were 33.3% and 0 in the control and cryoanalgesia groups, respectively. The mild pain on the seventh day was 13.3% and 83.3% in the control and cryoanalgesia groups, respectively ($P < 0.01$). Pethidine consumption was 151.6 ± 27 mg in the control group and 87.5 ±48 mg in the cryoanalgesia group on the first day post-operation ($P < 0.001$). Cryoanalgesia is a useful technique with not serious side effects in order to alleviate post-thoracotomy pain and reduce the need for opiate consumption.

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Introduction

In spite of recent progressive achievements in anesthesiology, postoperative pain management and treatment in patients is still one of the most complicated problems among anesthesiologists. Thoracotomy is one of the most painful surgical incisions currently used (1-2). Inadequate control of post-thoracotomy pain is associated with increased postoperative morbidity (3). This association causes a significant relationship between effective postoperative analgesia and the rate of postoperative pulmonary complications such as atelectasis, infections, etc after thoracotomies (4). The true incidence of post-thoracotomy pain is difficult to determine, with a reported range from 5% to 80% (5-8). Chronic post-thoracotomy pain consists of different types of pain, both myofascial and neuropathic pain (6,9).

Along with persistent characteristic, post-thoracotomy pain has cardiopulmonary complications as well as psychological adverse effects. Based on previous studies, pain relief in patients undergoing thoracotomy operation is a debatable issue among anesthesiologists (10-11). There are different methods of pain management in these patients (1,12). It has been reported that the local analgesia is one of the most efficient ways of pain relief (13). Of these, the cryoanalgesia is a local pain controlling method that is progressively applied because of the ease of handling, low cost and accessibility. Cryoanalgesia (the use of cold to provide anesthesia or analgesia) is an old analgesic method but still is in current clinical use (14). Its intraoperative use in providing postoperative analgesia for acute thoracic pain problems via an open thoracotomy is well described (15). However, there are controversies about the use of this method in post-

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thoracotomy pain (13,16). As a result, we decided to determine the effect of cryoanalgesia on post-thoracotomy pain.

Materials and Methods

This double blind randomized clinical trial included 60 patients with the age range of 19-51 years and ASA (American Society of Anesthesiologists) classes I-III for whom thoracotomy via posterolateral incisions were required. The exclusion criteria were consisted of: opioids or any other illegal drug addicts and diabetics who were suffering from the disease for more than 10 years. Midazolam (2 mg/kg BW) and fentanyl (3 mg/kg BW) were administered, as pre-medications for patients in the operation room. The monitoring was performed by pulse oximeter, ECG (Electrocardiography), end tidal carbon dioxide (CO_2), arterial blood gas analysis (ABG), and invasive blood pressure. The patients were preoxygenated using 100% oxygen for three minutes. Anesthesia was induced by thiopental (5 mg/kg BW) and atracurium (0.5 mg/kg BW) with a bolus dose which continued in 20-minute intervals. Three minutes later, intubation was done and then thoracotomy by postero-lateral incision was performed. The techniques of thoracotomy and suture materials were the same in all patients.

Before the operation, the patients were randomly divided by simple randomization by random table into two groups: control and cryoanalgesia. In cryoanalgesia group, before closure of the thorax, the intercostal nerves (one at the level of the incision, one cranial, and one caudal) were identified and exposed to peeling off the parietal pleura. The Kooland cryoanalgesiaprobe (administering CO_2 as the cooling agent, JP- 1, Kooland, China) was placed on each nerve, under direct vision. Each nerve received a 90-second application of cold (-70^{o} C). Patients received halothane 1 minimum alveolar concentration (MAC), oxygen and nitrous oxide (N_2O), 50% of each, and atracurium (0.2 mg/kg) as maintenance drugs. Anesthesia was maintained with fentanyl (2 µg/kg; every half an hour) during the operation. Neuromuscular blockade was reversed by atropine (1.25 mg) and neostigmine (2.5 mg). Pethidine (0.5-1 mg/kg) was administered by a nurse in the case of need in both the control and cryoanalgesia groups.

A visual analogue scale (VAS, on a scale of 0-10) was used in order to measure pain after thoracotomy. The VAS was classified into three groups as follows: 0-1 (no pain to mild), 2-3 (moderate), 4-10 (severe) (18). The VAS recording was done at different postoperative times: 0 (start of the recovery period), 0-24 hr (every two hours), 24-48 hr (every four hours) and the third to 7th day (every morning and evening) following surgery by a trained nurse. Both the nurse and the patients were unaware of patient group assignments.

Patients were visited at the hospital one week after discharge and were contacted by telephone at the first, second, and third month post-operatively. Information about the side effects including dysesthesia, allodynia and hypoesthesia were recorded as well.

Descriptive indices including frequency, percentage, mean ± SD were used to express data. The Chi-Square or Fischer's exact tests were used to compare qualitative variables between the control and cryoanalgesia groups.

All analyses were performed using SPSS software for Windows (Ver. 13.0) (SPSS Inc., Chicago, IL).

Results

Sixty patients were randomized into two equal groups (n=30 each of them). There was no significant difference between the two groups in terms of age, ASA class, and the operation site (Table 1). As shown in Table 1, the male population in the cryoanalgesia group (83.3%) was significantly higher than the control group (50%), $P < 0.01$.

Table 1. Comparison of basic characteristics between the two studied groups

	Control (N = 30)	Cryoanalgesia (N = 30)	*P* value
Age, mean ± SD	41.3 ± 15	41.9 ± 16	NS
Gender			
Male	15 (50.0%)	25 (83.3%)	<0.01
Female	15 (50.0%)	5 (16.7%)	
Weight, mean ± SD	64.7 ±10.6	64.1 ± 12.1	NS
Site of thoracotomy			
Right	22 (73.3%)	19 (63.3%)	NS
Left	8 (26.7%)	11 (36.7%)	
ASA class			
I	4 (13.3%)	3 (10.0%)	NS
II	25 (83.4%)	27 (90.0%)	
III	1 (3.3%)	0	

Abbreviations: SD = standard deviation; NS = not significant; ASA = American Society of Anesthesiologists

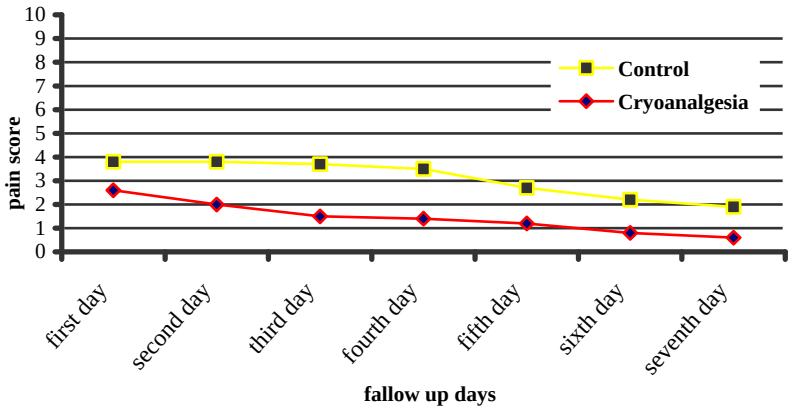

Figure 1. Mean score of patient pain in both groups during the follow-up period

Postoperative pain scores, in both control and cryoanalgesia groups, are presented in Figure 1. As depicted, the intensity of pain in the control group was higher than the cryoanalgesia group throughout the follow-up period. On the second day after the operation, the frequencies of severe pain score were 33.3% and 0 in the control and cryoanalgesia groups, respectively. Subsequently, the "no to mild pain" category on the seventh day was observed in 13.3% and 83.3% of the control and cryoanalgesia groups, respectively. In general, the pain intensity was significantly higher in the control group compared to the cryoanalgesia group ($P< 0.001$). Table 2 presents the severity of pain according to VAS categories between the two studied groups from days one to six.

Mean amount of pethidine administration during the study period is presented in Figure 2. Mean ± SD administration of pethidine was significantly higher in the control group than the cryoanalgesia patients on day one post-operatively (151.6 ± 27 mg vs. 87 ± 48 mg; $P < 0.001$). The usage of pethidine in the cryoanalgesia group was ended on the forth day after operation; however the control group subjects required pethidine until the seventh day post-operatively.

The percentage of sensory dysfunction in the patients who underwent cryoanalgesia surgery showed that the hypoesthesia occurrence was in the following pattern: 90% at the end of the first postoperative week, 76.7% at the end of the first month, and 16.6% at the end of the second month. No hypoesthesia was recorded at the end of the third month. In addition, both allodynia and dysesthesia were diminished to 10% at the end of the first month and no further one was observed at the end of the second month.

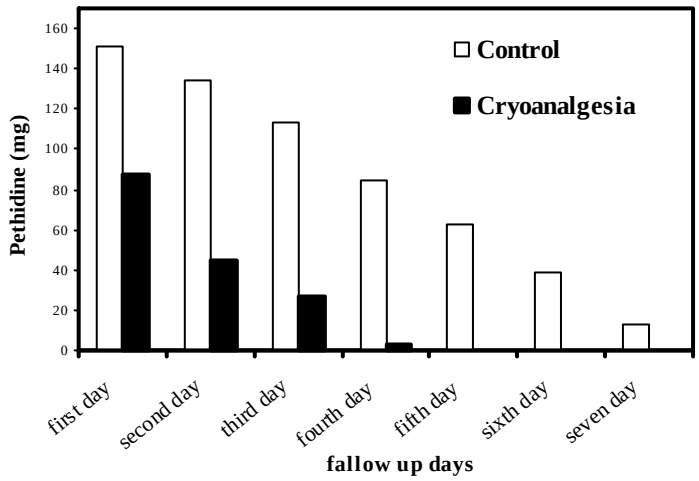

Figure 2. Mean of patient consumption (mg) in both groups during the follow-up period

Discussion

This is the first study, as to our knowledge, to evaluate the clinical efficacy of cryoanalgesia in controlling the post-operative pain of a group of Iranian patients who underwent thoracotomy. The present results demonstrate that the severity of thoracotomy-induced pain was better controlled using cryoanalgesia method. This finding is in affirmity with previous reports about the application of cryoanalgesia in thoracotomy patients. In Maiwand et al. study (18) the successful effect of cryoanalgesia on pain management after thoracotomy has been reported. They also noted that the consumption of opiates was diminished after using cryoanalgesia. It has been shown that efficacy of cryoanalgesia on postoperative pain relief as well as improvement in pulmonary function in patients underwent the cryoanalgesia was more prominent in comparison to intravenous opiates received patients (19, 17). There are some controversial evidences on effectiveness of cryoanalgesia; in other words, in some previous investigations (20), the analgesic efficacy of cryoanalgesia has been reported with less effect on pain relief and long-term postoperative side effects. These controversies might be because of lack of appropriate cryoanalgesia probe and insufficient nerve freezing, nerve freezing at a point distal to the branches, long freezing time, and nerve freezing with a blind technique and with an unsuitable nerve locator. Although the mechanism of cryoanalgesia in pain relief is still unknown, it is likely that when cryoanalgesia probe contacts with peripheral nerves, it causes a second-grade nerve lesion (Axonotmesis). The effects of cryoanalgesia are directly related to the formation of intra- and extracellular ice crystals, which result in microvascular changes and alteration of cellular osmolality and permeability, causing cell damage and disruption of nerve conduction, and consequently cause analgesia.

The obtained results about the need for pethidine administration are in agreement with data reported by Orr et al. (19) and Pastor et al. (17) which showed that the opiate (pethidine) consumption in the control group was higher than the patients with cryoanalgesia surgery. It is likely concerning the disruption of the axonal function and conduction, the pain perception and sensation is being reduced in the patients; therefore, fewer opiates will be demanded. Another considerable finding of the present study is the significant decrease in the incidence of dysesthesia, hypoesthesia and allodynia during the follow-up period in patients who received cyoanalgesia. Hypoesthesia was gradually disappeared at the end of the third month as well as dysesthesia and allodynia which were significantly reduced at the end of the second month. In case of allodynia and dysesthesia it could be questioned whether these abnormalities are related to surgery-induced trauma or to the cryoanalgesiagenic outcomes? One of the limitations in the current investigation was that the incidence rate of these abnormalities was not measured in the control group. In previous studies, all kinds of abovementioned side effects have been observed in the thoracotomy patients without cryoanalgesia. So, we suggest that comparative analyses of postoperative side effects in cryoanalgesia-group versus non-cryoanalgesia-group should not be underestimated in the future hypotheses. It is suggested that comparative interaction of pain relief due to narcotic analgesia and cryoanalgesia should be considered in the upcoming studies. The current findings propose that the effect of cryoanalgesia on the pain alleviation of other kinds of surgical operations collaborating with the moderate to sever neuropathic pain should be explored.

In conclusion, cryoanalgesia is an advantageous technique in order to relieve post-thoracotomy pain and reduce the opiate consumption. Additionally, cryoanalgesia-induced sensory abnormalities disappeared during the time. In the current research, the cryoanalgesia is recommended to thoracic surgeons and anesthesiologists in order to relieve post-thoracotomy pain.

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