

## Original Article

# Efficacy of Cryoanalgesia versus Bupivacaine as Two Methods of Intercostal Nerve Blockade on Post-Thoracotomy Pain Relief: A Human Prospective Randomized Clinical Trial

Sh.Fazely MD\*, A. Amini Harandi MD\*\*, A. Tabatabaei MD\*, M. Hashemi MD\*

## ABSTRACT

**Background:** Pain following posterolateral thoracotomy, is recognized as a major cause of morbidity and mortality. Various methods have been used for the treatment of post-thoracotomy pain, however, the treatment of post-thoracotomy pain remains controversial. The aim of this study was to compare the efficacy of Bupivacaine versus Cryoanalgesia for local intercostal nerve blockade on post-thoracotomy pain relief.

**Methods:** In a randomized clinical trial, eighty patients who were scheduled to undergo posterolateral thoracotomy were selected and classified, randomly, into two groups. Group A underwent intercostal nerve blockade with Bupivacaine every 8 hours after surgery for three days. In group B, two nerves upper and lower of incision level was frozen by Cryoprobe. Postoperative pain was assessed by 0-10 cm visual Analogue Scale (VAS) every 8 hours and then, after one hour, both groups were received intravenous morphine according to their needs.

**Results:** Mean and standard deviation (Mean  $\pm$  SD) of pain level were  $4.70 \pm 2.38$  in group A and  $4.87 \pm 2.25$  in group B. The t-test showed no statistically significant differences between two groups ( $t = 1.08$ ,  $p = 0.28$ ). Morphine consumption was  $5.35 \pm 3.17$  mg in group A and  $5.30 \pm 3.20$  mg in group B; Also there were no statistically significant differences between two groups ( $t = 1.25$ ,  $p = 0.21$ ).

**Conclusion:** Cryoanalgesia and Bupivacaine showed equivalent analgesic effect on posterolateral thoracotomy pain reduction. We suggest cryoanalgesia as an easy-to-use technique, but for routine application, further studies with long-term follow up and more cases are recommended.

**Key Words:** cryoanalgesia, bupivacaine, blockade, postoperation pain, thoracotomy, posterolateral, intercostal nerves, nerve block, analgesia.

Pain following posterolateral thoracotomy is recognized as a major cause of morbidity and mortality<sup>1, 2</sup>. Incision of skin, muscles, and plurae, retraction of muscles, ligaments and intercostal nerves, plural irritation by chest tubes, and fractured ribs all can contribute to cause severe pain in this setting<sup>3</sup>. If pain doesn't adequately be controlled, it can cause restriction of chest wall motion and this leads to shallow breathing and cough suppression. This alteration in respiratory function can lead to atelectasis, ventilation-perfusion mismatches, mucous plugging, hypoxia, and pneumonia<sup>4</sup>. The end results

can be prolonged intensive care unit (ICU) and hospital stay or even respiratory failure and death. Various methods have been used for the treatment of post-thoracotomy pain but the key point in these methods is achievement to balance between adequate analgesia and potential side effects<sup>5</sup>. Systemic opioid analgesics are used commonly for pain relief but they are potential causes of ventilatory depression<sup>6</sup>. Non steroid anti-inflammatory drugs may cause gastrointestinal and renal complications and other adverse effects<sup>7</sup>. Because of these factors, other methods of post-operative pain control have

\* Department of surgery, Isfahan University of Medical Sciences, Isfahan, Iran.

\*\* Medical student, Isfahan Medical Students Research Center (IMSRC), Isfahan University of Medical Sciences, Isfahan, Iran.

Correspondence to: Dr. Shahram Fazely, Department of surgery, Alzahra hospital, Isfahan University of Medical Sciences, Isfahan, Iran.

been sought.

Regional anesthesia by means of intermittent percutaneous intercostal nerve block with long-acting local anesthetics such as Bupivacaine has been shown to be effective in reducing pain and dosage of narcotic required, and improving pulmonary function<sup>8, 9</sup>. However, this method requires multiple sites of injection, frequent dosing, and in addition, repeated blocks may be needed<sup>10, 11</sup>. Cryoanalgesia which is localized freezing of intercostal nerve is another method. It is able to offer both short and long term analgesia. It is based on the application of Cryoprobe, which can induce localized freezing changes. The use of cold as a form of analgesia has been around for many years<sup>12</sup>. However, it was Lloyd in 1976, who first introduced the concept of Cryoanalgesia<sup>13</sup>. This technique was further described by Maiwand in the control of post-thoracotomy pain<sup>14</sup>. Despite of these advantages and some demonstrated benefit in these methods, however, the relief of post-thoracotomy pain remains controversial<sup>15</sup> and they show variable effectiveness. Roberts et al<sup>16</sup> and Pastor<sup>17</sup> advocated the use of Cryoanalgesia since it significantly reduced pain as well as the doses of acquired analgesia. But Cryoanalgesia was not recommended by other such as Muller<sup>18</sup> and Shafei et al<sup>19</sup> and they found no advantages in this method rather than conventional analgesic for postthoracotomy pain relief.

The aim of this study was to compare the efficacy of two latter methods (Bupivacaine versus Cryoanalgesia) of local intercostal nerve blockade. We tried to find the mean of measured pain and Morphine consumption after posterolateral thoracotomy in two groups.

## Materials and Methods

After institutional approval and informed patient consult, we designed our study as a randomized clinical trial. Eighty patients who were scheduled to undergo posterolateral thoracotomy at the surgery ward of Alzahra university hospital in Isfahan, Iran, from September 2002 to November 2003, were classified, randomly, into two groups using a list produced by random number table. Group A (n = 40) received 0.5% Bupivacaine and group B (n = 40) received Cryoanalgesia for intercostal nerve blockade.

Pregnancy, cardiovascular diseases, drug history of sensitivity to Morphine or Bupivacaine, substance or drug addiction, patient's inability to response verbally to question about his/her pain, and age less than 12 years old considered as exclusion criteria.

We used posterolateral incisions whose size were from anterior axillary to paraspinal line and longer or shorter incisions were excluded from project. Indications for these thoracotomy operations contained: mediastinal tumors, Heller myotomy, lung lobectomy, and Hydatid cyst.

Group A underwent intercostal nerve blockade with Bupivacaine. We blocked two nerves upper and lower than borders of incision at the end of operation through the incision of thoracotomy (intra-thoracic) and then, this was repeated every 8 hours, after surgery (extrathoracic) for three days according to patients need to pain reduction.

In group B two nerves upper and lower of incision level was frozen by Cryoprobe with CO<sub>2</sub> as cooling agent twice (0 and 60s) after operation. Cryoprobe was applied during 60s with approximately -60° C for each nerve<sup>15</sup>.

Postoperative pain was assessed by 0-10 cm VAS every 8 hours after operation and then, after one hour, both groups were received intravenous morphine (0.05-0.2mg/kg) according to their needs. Both pain assessment and morphine prescription was done by an intern.

Collected data about pain scores, morphine consumption, and age analyzed with t-test and we used Chi-Square (K<sup>2</sup>) test for sex. Analysis was performed using SPSS version 11 statistical package.

## Results

There were 47 males (58.7%) and 33 females (41.2%) in all 80 patients. There were 22 males and 18 females in the group A and 25 males and 15 females in group B. The gender of two groups analyzed with chi-square and there was no significant difference (P=0.37). Mean and standard deviation (Mean ± SD) of age was 49.3 ± 9.1 and they were in range of 21-72 years old. It was 47.1±9.3 in group B and 51.5±8.0 for group A. Due to significant difference in t-test for age (P=0.026), we deleted a 70 years old male from Cryoanalgesia group and also a 21 years old male from Bupivacaine group. This led the P-value to be more than 0.05 (P=0.074). Then

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we repeated pain and morphine analysis again, but we found same results like as before.

Frequency distribution of operation types in two groups are listed in table 1.

Mean and standard deviation (Mean  $\pm$  SD) of pain during the first to third postoperation days were  $4.70 \pm 2.38$  in group A and  $4.87 \pm 2.25$  in group B. We compared these two group with t-test and there was no statistical significant difference between two groups ( $t = 1.08$ ,  $P = 0.28$ ). Mean and standard deviation (Mean  $\pm$  SD) of dose of prescribed

morphine in each time was  $5.35 \pm 3.17$  mg in group A and  $5.30 \pm 3.20$  in group B. According to t-test results there were no statistical significant differences between two groups ( $t = 1.25$ ,  $P = 0.21$ ). Also, mean and standard deviation (Mean  $\pm$  SD) of dose of prescribed morphine and pain scores in first, second, and third 24 hours after thoracotomy was evaluated. There were no significant differences between two groups in each day ( $P > 0.05$ ) (table 2).

**Table 1.** Frequency distribution and percentage of operation types in two groups.

groups	percent				
	lung lubectomy	mediastinal tumors	Hydatic cyst	Heller myotomy	total
Cryoanalgesia	16(20%)	12(15%)	9(11%)	3(3.7%)	40(50%)
Bupivacaine	18(22.5%)	15(18.7%)	6(7.5%)	1(1.3%)	40(50%)
total	34(42.5%)	27(33.7%)	15(18.7%)	4(5%)	80(100%)

**Table 2.** Mean and standard deviation (Mean  $\pm$  SD) of dose of prescribed morphine (mg) and pain scores in first, second, and third day after thoracotomy. These date compared with t-test.

	group	n	Mean $\pm$ SD & p value			
			Morphine		Pain	
1 <sup>st</sup> 24h	B	40	6.3 $\pm$ 3.1	(P=0.50)	5.5 $\pm$ 2.3	(P=0.12)
	A	40	6.6 $\pm$ 3.9		4.8 $\pm$ 2.2	
2 <sup>nd</sup> 24h	B	40	5.1 $\pm$ 3.7	(P=0.41)	4.8 $\pm$ 1.2	(P=0.28)
	A	40	5.5 $\pm$ 3.7		5.1 $\pm$ 2.3	
3 <sup>rd</sup> 24h	B	40	3.6 $\pm$ 2.7	(P=0.36)	4.2 $\pm$ 2.2	(P=0.58)
	A	40	3.9 $\pm$ 2.9		4.0 $\pm$ 1.9	

Group A: Bupivacaine, Group B: Cryoanalgesia

## Discussion

According to the results, there was no significant difference in pain reduction scores between two groups. The same results have been obtained for morphine consumption in two groups. Our results support other studies that found Cryoanalgesia with the same efficacy rather than other analgesics, such as Bupivacaine<sup>18,19</sup>. It seems that choice of treatment is case and situation dependent. Unfortunately, because of complex multifactorial condition of post-thoracotomy pain, the choice of analgesia, however, remains under debate. Cost benefit, lower rate of complications<sup>15</sup>, and equivalent analgesic effect of Cryoanalgesia comparing with Bupivacaine should be considered in decision making. Applying of

bupivacaine has some disadvantages, for example, accidental intravenous administration of Bupivacaine has been associated with severe myocardial suppression and prolonged asystole. Because of its long half-life, Bupivacaine is slowly cleared when toxic serum levels do occur, even after cessation of the medication<sup>20</sup>, and its application requires multiple sites for injection<sup>21</sup>.

Cryoanalgesia is based on the application of Cryoprobe, which employs the Joule-Thomson effect, whereby carbon dioxide or nitrous oxide is released at high pressure (4000-6000 kPa) and allowed to expand rapidly within the bulb of the Cryoprobe<sup>22</sup>. This causes of the probe tip to be cool

to temperatures of approximately  $-50$  to  $-70^{\circ}\text{C}$ . When applied to peripheral nerves, localized freezing induces consistent changes with a second-degree nerve lesion (axonotemesis)<sup>23-25</sup>. The effects of this method are directly related to the formation of intra and extracellular ice crystals, which result in microvascular changes and alteration of cellular osmolarity and permeability. These lead to cell damage and disruption of nerve conduction<sup>26</sup>. But these cutaneous sensory changes are resolved with complete restoration of function<sup>15</sup>.

The use of these local anesthetic methods is an effective way of decreasing pain and narcotic requirements. Despite these advantages, local analgesic methods such as Cryoanalgesia, however, is not able to provide complete post-thoracotomy pain relief. Stretching of the dorsal spinal ligaments generate considerable amount of pain. Pain signals also transmitted via the phrenic, vagi, and sympathetic

nevers, hence, are not affected by these methods<sup>15</sup>. Unfortunately, our study design has some deficiency. We hadn't control group for comparison between two intervention groups and we couldn't blind our study. Although we divided the cases to two groups randomly, but size and site of incision are very important factors in pain severity. Pulmonary function was not evaluated as a variable, too. Also these practical methods are influenced by experience and technique of surgeon and completely, these can not be generalized to other patients, especially when the sample size is small.

We suggest Cryoanalgesia as an easy-to-use technique with equivalent effect on post-thoracotomy pain control in comparison with Bupivacaine, but for routine application, further studies with long-term follow up and more cases is recommended.

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