

Original Article

**A comparison between subpleural patient-controlled analgesia by bupivacaine and intermittent analgesia in post-operative thoracotomy: A double-blind randomized clinical trial\***

*Vahid Goharian<sup>1</sup>, Sayyed Abbas Tabatabaee<sup>2</sup>, Sayyed MozafarHashemi<sup>3</sup>, Gholamreza Mohajery<sup>3</sup>, Mohammad Arash Ramezani<sup>4</sup>, Fatemeh Shabani<sup>5</sup>, Zahra MotevalliEmami<sup>6</sup>*

**Abstract**

**BACKGROUND:** The efficacy of subpleural analgesia to reduce postoperative pain intensity in patients after lateral thoracotomy is controversial. In this study, we demonstrated the efficacy of two types of subpleural analgesia.

**METHODS:** This prospective, controlled, randomized, double-blind trial was performed in Department of Thoracic Surgery of Alzahra Hospital associated with Isfahan University of Medical Sciences from June 2009 until August 2010. After posterolateral thoracotomy and admission to the ICU, patients were randomly assigned into two groups of subpleural patient-controlled analgesia (SPCA) (0.02 cc/kg/h of 0.5% bupivacaine) and subpleural intermittent analgesia (SIA) (0.1cc/kg/6h of 0.5% bupivacaine). The data regarding age, sex, visual analog scale (VAS) (at 8, 16 and 24 hours after initiation of analgesia), morphine consumption, systemic adverse effects, length of ICU and hospital stay, complications, public health service (PHS) criteria, and cost was recorded. Data was analyzed by Mann-Whitney U-test, repeated measured test, chi-square test and the Fisher's exact test. A  $p < 0.05$  was considered significant.

**RESULTS:** The study population consisted of 90 patients. There were no significant differences in sex, age, weight, intraoperative analgesics, duration of one-lung ventilation, and adverse effects between the SPCA and SIA groups. Although pain scores were significantly reduced at 16 hours after the first subpleural instillation of bupivacaine 0.5% with patient-controlled analgesia, comparison between mean pain scores in the two groups at 8 and 24 hours after the first subpleural instillation of bupivacaine 0.5% revealed no significant difference. In addition, no significant difference was found in VAS scores at the three evaluated times ( $p < 0.05$ ).

**CONCLUSIONS:** Optimal use of SPCA bupivacaine for postoperative pain treatment is more effective in pain reduction than SIA bupivacaine. The consumption rate of opioid and bupivacaine was also decreased in SPCA group.

**KEYWORDS:** Analgesia, Patient-Controlled, Postoperative, Bupivacaine, Thoracotomy.

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Postoperative pain after thoracic surgery is the most important factor responsible for ineffective ventilation, ineffective cough, and impaired ability to sigh and breathe deeply. This may contribute to pulmonary atelectasis leading to ventilation/perfu-

sion abnormalities and hypoxemia, as well as infection, after thoracotomy. Although analgesia has the potential to reduce pulmonary morbidity, most analgesic techniques carry the risk of concomitant complications associated with systemic drug administration or place-

1- General Thoracic Surgeon, Department of Surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

2- Associate Professor, Department of Surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

3- Assistant Professor, Department of Surgery, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

4- MD, MPH, Department of Cancer Control and Prevention, Isfahan University of Medical Sciences, Isfahan, Iran.

5- BSc in Microbiology, Institute of Novin Tahlilgaran-e-Nesfe-Jahan, Isfahan, Iran.

6- Obstetrician, Institute of Novin Tahlilgaran-e-Nesfe-Jahan, Isfahan, Iran.

Corresponding Author: Vahid Goharian

E-mail: goharian@resident.mui.ac.ir

ment of catheters (e.g., epidural catheterization). Therefore, the choice of pain therapy in thoracotomized patients is complex and controversial.<sup>1, 2, 3</sup>

Subpleural (SP) analgesia is induced by placing local anesthetic into the SP space which lies between the parietal pleurae and costal department. subpleural analgesia can produce regional analgesia of the chest wall and is used for pain therapy of different indications which include breast, renal, gall bladder and thoracic surgery, and chronic pain like intrapleural analgesia.<sup>4</sup> In patients undergoing lateral thoracotomy, this technique has the advantage of intraoperative catheter placement under direct vision with a low risk for complications caused by catheterization. However, there is a controversy about its efficacy for pain relief after thoracotomy for pulmonary surgery.<sup>5-7</sup>

We compared subpleurally patient-controlled analgesia (SPCA) bupivacaine for postoperative pain treatment with subpleurally intermittent analgesia (SIA). Our objective was to determine whether SPCA bupivacaine affects postoperative pain relief, morbidity, and hospital stay. Furthermore, we analyzed the effects of sex and anterolateral or posterolateral approaches on postoperative pain.

## Methods

This study was a double blind randomized clinical trial which approved by the institutional review board of the Isfahan University of Medical Science.

Sampling method was done by two mean comparison sample size formula with type I error  $\alpha < 0.05$  and power 80% (Type II error  $\beta < 20\%$ ). Ninety Patients were included whom had indication for thoracic surgery. Patients with an allergy to bupivacaine, with postoperative air leak through the chest tubes, undergoing pleurectomy, having repeat thoracotomy, having full rib resection, or unable to cooperate were excluded from the study.

Written, informed consent for participation was obtained.

After premedication with midazolam, anes-

thesia was induced IV with 3  $\mu\text{g}/\text{kg}$  fentanyl, 5 mg/kg thiopental and muscle relaxation with 0.5 mg/kg atracurium. The tracheas of all patients were intubated with a double-lumen endobronchial tube. Anesthesia was maintained with 50% nitrous oxide in oxygen and isoflurane supplementation as required. During one-lung ventilation, inspired oxygen concentration was increased to 100%. Intraoperative systemic analgesia was limited to fentanyl in unrestricted doses. Pulmonary operations were performed at the fifth or sixth intercostal space through a standard posterolateral thoracotomy, respectively. Posterolateral thoracotomy extended from the anterior axillary line to a point midway between the vertebral spines and the vertebral border of the scapula.<sup>8</sup> At the end of the surgical procedure, just before chest closure, the surgeon released parietal pleural from the chest wall interval between the second intercostal space and the ninth intercostal space and posteriorly on the paravertebral line and inserted an SP catheter percutaneously in this space. Then the margin of parietal pleurae was sutured to chest wall to close this space.

After surgery, patients were ventilated with pressure support; all patients were tracheally extubated after rewarming, during the first 4 h after admission to the intensive care unit (ICU). After admission to the ICU, every participants had a code and based of this code, they were allocated to two groups randomly.. Just after, arrival patients in the SPCA group received 0.02 cc/kg/h of 0.5% bupivacaine subpleurally patient-controlled analgesia, whereas patients in the SIA group received 0.1 cc/kg/6h 0.5% bupivacaine subpleurally intermittent analgesia in 60 seconds. In the SPCA group, bupivacaine was administered via a patient-controlled analgesia (PCA) device (model 1000 Korea). The PCA device was programmed to provide a bolus of 0.005 cc/kg bupivacaine; the lockout time was 15 min. The contents of the syringes were prepared immediately before injection by a nurse who was not further involved in this investigation. Patients were kept in a supine position before injection

of the study solution into the SP catheter. When the patients were awake, they were encouraged to take supplementary doses of morphine as much as the patient needed and the surgeon postulated. In both groups 2cc bupivacaine was subpleurally administered at the end of operation. Data collection was commenced at 8, 16 and 24h after initiation of analgesia. They were asked to assess the intensity of the chest pain, at rest and when coughing, using a visual analog scale (VAS) (0–100 mm; 0 = complete pain relief and 100 = unbearable pain). At the same time, the morphine demand within the elapsed 8 h was recorded. During the study period, patients were evaluated for systemic adverse effects (i.e., drowsiness, confusion, dizziness, nausea, vomiting, hallucinations and drug sensitivity). We further recorded length of ICU and hospital stay, complications, such as pneumonia and atelectasis. All evaluations was done by different investigator which could perform blindness. It was a double-blind study.

Statistical analysis: Data were analyzed by SPSS 15 software (SPSS Chicago, IL). The VAS scores of each patient were summarized as

three VAS mean scores: Mean VAS at 8,16 and 24h after first injection of the study solution and mean of all. The dose of analgesics administered was compared between two groups, male and female patients using the Mann-Whitney *U*-test. Differences in the mean VAS scores within the groups after the administration of bupivacaine at 8, 16 and 24h after first injection of the study solution, were evaluated by using repeated measure of ANOVA. Differences between the groups for sex and post-operative complications were calculated by using the chi square test and the Fisher's exact test. Differences in numeric demographic data (e.g., age, and body weight), ICU and hospital stay were analyzed by using the Mann-Whitney *U*-test. A  $P < 0.05$  was considered significant.

## Results

90 patients participated in the study. There were no differences in sex, age, weight, intra-operative analgesics, and duration of one-lung ventilation between SPCA and SIA groups (Table 1).

**Table 1.** Patient Characteristics, Operation Data, and Postoperative Complications

	Group SPCA	Group SIA
N	45	45
Sex (F/M)	18/27	14/31
Age (yr)	45± 13	40 ± 17
Weight (kg)	72 ± 15	71 ± 13
<b>Surgery</b>		
Lobectomy or bilobectomy	34	29
Wedge resection	6	9
Partial rib resection	3	1
Operation side (right/left)	21/24	20/25
Duration of one-lung ventilation (min)	85 (30–120)	82 (35–140)
Time to extubation after ICU admission (h)	1.5 (0.5–2.7)	1.9 (0.8–2.9)
<b>Postoperative complications</b>		
Dizziness, confusion	0	0
Pneumonia	8	6
Atelectasis (radiograph)	12	17
Bronchoscopic intervention	2	3
Reintubation	1	1
ICU stay (h)	35 (18–72)	39 (24–85)
Hospital stay (d)	6 (3–24)	12 (3–27)

Data are given as mean ± sd, mean (range), or *n*. There were no statistically significant differences between the groups.

With regard to the outcome data, there were no significant differences between the SP-treatment groups comparing the incidence of adverse effects, such as pneumonia, atelectasis, bronchoscopic interventions, reintubations, hypersensitivity and postoperative ICU and hospital stay (Table 1)

Reintubation of two patients (Table 1) was necessary after the study was terminated. One patient was reintubated in the SPCA group, with suspected pulmonary embolism, and one patient with pneumonia was reintubated in the SIA group.

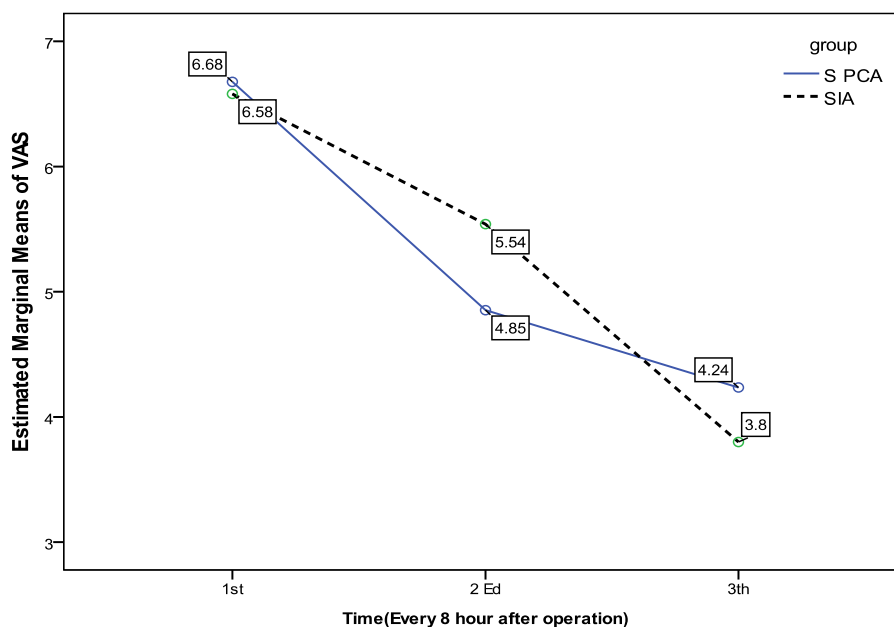
Mean pain scores were significantly reduced at 16 h after the first SP instillation of bupivacaine 0.5% with patient-controlled analgesia. However, there was no difference between the groups when comparing mean pain scores at 8 and 24h the first SP instillation of bupivacaine 0.5% (Figure 1). When VAS scores were analyzed duration 24h, there were also no differences between the groups. There weren't any differences between sex and VAS scores at three times. ( $p < 0.05$ )

Treatment significantly reduced mean pain scores in both groups, however, no differences in pain scores were observed between Groups SPCA and SIA duration 24h. VAS mean score at 16 h after the first SP instillation of bupivacaine 0.5% in SPCA group was significantly reduced to SIA group.

Supplemental opioid demand, PHS criteria and bupivacaine consumption were statistically significant, as, rate of IV opioid consumption, PHS criteria and bupivacaine consumption in SPCA group was significantly lower than in SIA group. (Table 2).

## Discussion

The aim of postoperative pain management is to provide good subjective comfort and to contribute to early recovery and a good outcome after surgery. After thoracotomy, pain therapy with systemic opioids has the potential for a good pain relief at rest with a lack of effective pain reduction when coughing or breathing deeply. However, effective coughing is necessary for a sufficient bronchial clearance to



**Figure 1.** Visual analog scale (VAS) mean scores at 8, 16 and 24 h after the first SP instillation of bupivacaine 0.5% as patient-controlled analgesia (SPCA group) and intermittent analgesia (SIA group) respectively.

**Table 2.** Morphine consumption, initial consumption, PHS criteria, cost and bupivacaine consumption in two groups

	SPCA group	SIA group	p value
Morphine consumption(mg)	11.45 ± 4.25	16.5 ± 6.65	0.04
initial consumption(hours)	4.59 ± 2.02	4.6 ± 2.20	0.65
PHS criteria	1.61 ± 0.95	1.92 ± 1.2	0.04
Cost (dollar)	8543.45 ± 2454.85	9657.76 ± 4467.85	0.2
bupivacaine consumption	12.35 ± 2.45	18.45 ± 3.76	0.03

Data are given as mean ± sd. Morphine consumption, bupivacaine consumption and PHS criteria were significantly lower in SPCA group than SIA group. initial consumption and cost were not different in two groups

prevent atelectasis and bronchopulmonary infection. Therefore, many attempts have been made to combine systemic drug administration with different kinds of regional anesthesia to improve postthoracotomy pain control.<sup>9,10</sup> Intrapleural analgesia has studied more than subpleural analgesia but Silomon suggested that Interpleural analgesia does not influence postthoracotomy pain.<sup>11</sup> Subpleural analgesia use has increased follow publication of its excellent effect on postthoracotomy pain.<sup>9, 12</sup> The mechanism of action appears to be through a multilevel intercostal nerve blockade.<sup>12</sup> If the catheter is placed intraoperatively under direct vision, this technique is safe and easy. Despite its wide use, systemic absorption and toxicity from local anesthetics have not been substantiated in clinical studies that assayed plasma levels, even when using larger amounts of bupivacaine than we administered.<sup>13</sup> in comparison to intrapleurally use that may lead to blood levels in the toxic range.<sup>2</sup> Furthermore, Richardson et al.<sup>14</sup> suggested a chest tube loss of bupivacaine after intrapleural(IP) administration, and IP local anesthetics may actively induce diaphragmatic and abdominal muscle weakness and cause impairment of respiratory function.<sup>14,15</sup> There are two methods for installation of drug subpleurally, subpleurally patient-controlled analgesia (SPCA) and subpleurally intermittent analgesia (SIA).we compare these two methods about their effects. The current study indicated a significant pain reduction 16 hours after subpleural injection of bupivacaine 0.5% in SPCA method in comparison to SIA method. Furthermore, we could not show any difference in mean VAS scores after

8 and 24 hours.VAS scoring was shown to be a valid measure of pain in the early postoperative period.<sup>16</sup> Chung showed that Subpleural block with 20 ml 0.5% bupivacaine can be an alternative approach of regional anesthesia in patients with multiple rib fractures.<sup>4</sup> Koehler recommended that continuous administration of local anesthetics directly in the subpleural plane, posterior to the intercostal incision, provides excellent pain control.<sup>17</sup> The cause of various effects of analgesia in SPCA group possibility related to various dose of bupivacaine that use by patients. Since interval 8h until 16 h after the first SP instillation of bupivacaine, the patients used bupivacaine optimal and duration first 8h and after 16h because of incompletely consciousness and sleeping they didn't use bupivacaine optimal. We showed that bupivacaine consumption was significantly lower in SPCA than SIA group. Furthermore, supplemental analgesia was significantly reduced in SPCA group and patients received opioid lower than SIA group at their request. Like other study, there are a few studies that support effectiveness of the postoperative pain management via SP analgesia after thoracotomy. A dilution of the local anesthetics by pleural exudation doesn't appear to play a subordinate role in SP analgesia that seen in IP analgesia.<sup>14</sup> In the current study the posterolateral thoracotomy was shown to be the more painful approach that may be explained by greater damage to the latissimus dorsi muscle<sup>18</sup> and more stress on the costovertebral joints, with wide rib retraction near the spinal column. These anatomical factors may contribute to the pain intensity at rest; however, they ap-

pear to have less influence during the dynamic process of coughing.

The effect of sex on postoperative pain intensity was opposite to recent studies showing sex to be an important variable in recovery from general anesthesia.<sup>19</sup>The possible mechanisms leading to higher pain scores after surgery in women as shown are not fully understood.<sup>20</sup> Because pain during coughing and therefore, the ability to cough, was not influenced by sex, a clinical relevance of sex differences appears to be questionable. This conclusion is supported by the outcome data showing no differences between male and female patients. However, further studies dealing with postoperative pain measurement should pay special attention to the distribution of sex within subsamples.

Many studies have shown post-thoracotomy pain relief enhanced quality of

life of patients and reduced morbidities.<sup>21-23</sup> Patient-control analgesia after thoracic surgery has been considered because of safety, patients' satisfaction.<sup>24, 25</sup> It has been shown that Bupivacaine and the similar drugs are appropriate for postoperative analgesia. In our study we could find that subpleural patient-control analgesia was better clinically not statistically in patients with post-thoracotomy pain relief. Other studies have supported our result approximately.<sup>21, 26-28</sup> Additionally we can reduce the consumption of morphine in SPCA method. Thus we can run SPCA as a safe method in our clinical practices.

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### Conflict of Interests

Authors have no conflict of interests.

### Authors' Contributions

VG designed the study and drafted this manuscript, SAT, SMH, GRM Carried out the study and drafted the manuscript, MAR, ZME, FSH, helped in Statistical analysis, revising the manuscript procedures.

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