Original Article

Controlling Post-Thoracotomy Pains With Local Injection Of Bupivacaine Before Surgery: A Randomized Controlled Study

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Abstract

Objective: Controlling thoracotomy pain prevents post-op complications, including hypoxia, atelectasis, and pneumonia by improving respiratory condition**.** Thus, it is highly important to introduce the best pain-control method. This study aims to assess local injection of bupivacaine before surgery as a means of thoracotomy pain control.

Methods: Patients were compared in a two independent groups of 40 in a double-blind randomized clinical trial conducted between February 2014 and January 2015. After anesthesia and before incision, the intervention group received subcutaneous injection of 2 mg/kg of bupivacaine 0.5% diluted with 5cc distilled water all around the incision line. The control group received normal saline in a similar way. Pain was assessed using numerical analogue scale (NAS) at 2, 4, 8, and 24 hours after surgery, and hemodynamic monitoring was performed before anesthesia, before injection (drug or placebo), and 5 minutes after incision.

Results: In the intervention group, mean (± standard deviation) pain based on NAS at 2, 4, 8, and 24 hours after surgery was 5.5±5.75, 5.5±5, 2±3.5, and 5±5.5, and in the control group, 7±4.5, 8±5.25, 6±5.5, and 5.5±4, with no significant difference between the two groups (P>0.05). The two groups were not significantly different in terms of hemodynamic signs, either (P>0.05).

Conclusion: No relationship was found between injection of bupivacaine at incision site and reduced thoracotomy pain or use of morphine and diclofenac. Moreover, no improvement was observed in vital signs the first time analgesic was needed.

Keywords: Thoracotomy, Post-op pain, Bupivacaine.

INTRODUCTION

Post-thoracotomy pain is one of the severest post-op pains, leading to pulmonary complications (1, 2). It can prevent proper coughing and deep breathing, and can cause patient's non-cooperation in physiotherapy, retention of pulmonary secretions, and complications such as pulmonary atelectasis, pneumonia, and respiratory failure (3). The source of pain is probably the intercostal nerve damage, which can cause chronic pain syndrome as in other neuralgias, thus preventing normal daily activities (4). Post-thoracotomy pain may be caused by various factors, such as surgery technique, post-operative cares, and factors associated with the patient, including physical fitness, pain threshold, and choice of anesthesia methods (5).

Various post-thoracotomy pain relief methods used include local anesthesia (intercostal nerve block, intercostal catheters, and intrapleural catheters), regional blocks (epidural, intrathecal, paravertebral) and cryotherapy (1, 6). Currently, the standard post-thoracotomy pain control technique is thoracic epidural block (7-9); although several studies have recently highlighted its cardiovascular complications such as cardiac arrest and myocardial infarction (10, 11). In addition, epidural anesthesia is time-consuming, costly, effective for a short period (4-6 hours), requiring an experienced operator, and cannot be performed in all centers; it is also impracticable for patients receiving oral anticoagulant and venous infusion of heparin due to the risk of spinal hematoma and pressure on spinal cord (11, 12). Furthermore, epidural anesthesia is often accompanied by postoperative hypotension, paralytic ileus and nausea (13). Thus, recently attentions have been drawn to alternative methods to epidural anesthesia, including infusion of various amounts of local anesthetics using a variety of methods. But, there is no consensus on

the type of anesthetic, local method, or their response level. Bupivacaine was first discovered by Ekenstam-Egner in 1957 (14), and its clinical application began in 1964 in infiltration, nerve block, and epidural and intrathecal anesthesia, and its postoperative pain-relief effect can last up to 20 hours (15). This drug is metabolized in the liver, with about 6% excreted in urine (16). Cardiotoxicity is its most important side-effect, which has not yet been reported with subcutaneous infiltrations (17, 18). In addition to prolonged local anesthetic effects; this drug also relieves pain, and is referred to as residual anesthesia, which can reduce postoperative pain and post-anesthesia patient care (19-21). In this study, patients' post-thoracotomy pain was measured following administration of bupivacaine as local anesthetic.

Materials and Methods

After approval from the Ethics Committee of Semnan University Medical Sciences (No A22-521), 80 consecutive patients were considered who underwent thoracotomy between February 2014 and July 2015. All recruited patients provided informed and written consent to the study. Our inclusion criteria was Age>18 or <80 y, American Society of Anesthesiology Classification < IV, Forced expiratory volume in 1 second ≥ 50% predicted, and normal liver enzymes. Exclusion criteria were previous chest surgery, central and peripheral neuropathies and sepsis over the incision of thoracic and systemic sepsis, allergy to the amide type of local anesthetics, patients on long-term opioid therapy, patients receiving Beta-blockers and coagulopathy, psychiatric diseases, past acute myocardial infarction and pregnancy.

In the operating room, an intravenous catheter, a radial artery catheter, and a central venous catheter were inserted. All surgical procedures were performed with a posterolateral thoracotomy in the fourth or fifth intercostal space.

General anesthesia was typically induced with intravenous 2 μm/kg fentanyl, 0.6 mg/kg of atracurium and 1.5–2 mg/kg propofol and paralytic agent as needed. Anesthesia was maintained using desflurane, nitrous oxide and oxygen. Both groups had similar access to rescue analgesia via acetaminophen, ketorolac and pregabalin, if needed, during the postoperative period.

All patients had mechanical ventilation that maintains pCO2 between 35 mm Hg and 40 mm Hg and had continuous cardiopulmonary monitoring for the duration of their hospitalization. The same chest tube policy was used in both groups. A single chest tube with size of 32 French was placed at the end of the operation in the seventh or eighth intercostal space. For patients undergoing pneumonectomy, this chest tube was removed in the operating room.

Patients were allocated randomly to the bupivacaine group or the normal saline group (n = 20 per group) using a computer-generated sequence.

In bupivacaine group after induction of general anesthesia, patients were positioned and before incision of thorax, 2mg/kg of bupivacaine 0.5%, diluted in 5 cc distilled water subcutaneously was injected in the surgical incision line so that was infiltrated in incision length. In normal saline group, injected 5 cc normal saline. Both groups had similar method and site of injection. Incision line began from anterior axillae, passed 2 cm below inferior scapula, and continued between the inner edge of scapula and spinal cord. Saline-diluted marcaine (2 mg/body weight and 1.5 cc to 2 cc for each space) was used for intercostal block. In addition, two incisions were made above and below, and also in and around chest tube intercostal space. Care was taken not to egress into the pleural space and disrupts the parietal pleura. Injection was done by the surgeon. Protocol of postoperative analgesia and the protocol used to give extra painkiller were same between two groups.

Pain level was measured using a numerical analogue scale (NAS), where 0 (no pain) and 10 (severe pain), at 2, 4, 8 and 24 hours after surgery. An assigned ward nurse that not informed of study assessed patients' pain, by patients were asked to rate their pain on scale.

Vital signs recorded before general anesthesia, before incision of thorax and 5 min after incision by pulse oximetry and monitoring setting that was connected to the patients.

All documented demographic data, duration of surgery, durations of the anesthetic procedures, summation of prescribed Morphine, time to first request for analgesic and total number of prescribed Diclofenac Na suppositories during the patient's hospitalization was recorded.

Statistical analysis was performed using SPSS (V.22, IBM.Chicago, IL, USA). Normally distributed results were compared by Student t test analysis and no normally distributed results were compared by Mann-Whitney analysis.

Results

In this study, surgery was performed on 41 patients using Z method (bupivacaine group), and 40 patients using Y method (normal saline group). The most frequent underlying causes requiring thoracotomy were surgery and biopsy of tumors and pulmonary masses including metastatic or primary pulmonary malignancies (26 patients), hydatid cyst (24 patients), empyema (12 patients),

and pneumothorax (4 patients). Other cases included schwannomas (3 patients), pericardial cyst (3 patents), bronchiectasis (2 patients), esophageal cancer (2 patients), achalasia (2 patients), esophageal diverticulum, and mesothelioma (one patient each). Distribution of underlying causes requiring thoracotomy was not significantly deferent between two groups (p= 0.851).

Mean and standard deviation of patients' age in two groups were 46.14±16.09 years and 49.42±17.76 years, with no significant difference between them (P=0.539). Similarly, no significant difference was observed in patients' weights between the two groups (67.71±14.57 against 65.45±17.76, P=0.645). Of all patients, 53 (66.2%) were undergoing surgery for the first time. Table 1 presents distribution of patients in terms of gender, smoking, and history of previous surgery.

According to table 1, no significant difference is observed between the two groups in terms of gender, smoking and history of previous surgery (P>0.05).

Table 2 shows mean and standard deviation of duration of surgery and anesthesia, as well as patients' vital signs including blood pressure (systolic and diastolic), heart rate, and oxygen-saturated blood on three occasions: before anesthesia, before injection of drug (or placebo), and 5 minutes after incision.

According to Table 2, no significant difference can be observed between the two groups in terms of duration of surgery and anesthesia, as well as patients' blood pressure (systolic and diastolic), heart rate, and oxygen-saturated blood in each of the occasions: before anesthesia, before injection of drug (or placebo), and 5 minutes after incision (P>0.05).

During patients' follow-up in terms of pain, one of the patients (with esophageal cancer) in group Z could not be evaluated due to persistent intubation and death after surgery, and hence exclusion from study. Table 3 shows level of postoperative pain in the remaining patients in intervention and comparison groups based on the follow-up 24 hours after surgery and the need for analgesics.

Table 3 shows that although patients in Y group scored worse in terms of pain, no significant difference was reported between the two groups (P>0.05).

DISCUSSION

Thoracic epidural analgesia has become the gold standard for analgesia after thoracotomy but this technic has several limitation such as adverse effect, require closing monitoring of vital signs, highly operator dependent, short half-life and contraindication for patients taking anticoagulant or antiplatelet drugs, that For these reasons, other simpler forms of pain management after thoracic surgery have been investigated. In this study we found that subcutaneously injection of bupivacaine 0.5% in the surgical incision line provided better pain score and was accompanied by lower morphine requirement and Diclofenac Na suppositories, although difference between bupivacaine group and NS group was not significant.

This study was double-blind, controlled clinical trial with full respect of the principles that controlled any bias and duration and times of follow-up of patients were considered to get the best results. We based our assessment of analgesia on the pain scores and hemodynamic parameters that the method of recording was similar between both groups.

Study on skin infiltration of bupivacaine was started in the late 80s. It has been shown to provide effective analgesia with skin infiltration of bupivacaine after craniotomy and various surgeries but there are no published reports of use in thoracic surgery. Only in a study by Strichartz et al (2015), bupivacaine-releasing microspheres were subcutaneously injected 2 hours preoperatively near the thoracotomy incision in male Sprague-Dawley rats. This study showed that locally injection of bupivacaine suppresses postoperative mechanical hypersensitivity for ≥4 weeks after experimental thoracotomy, while systemic bupivacaine from this treatment had no effect on hypersensitivity (22). However, Strichartz et al (2015) compare local and systemic methods of injection in rats; this study supports effects of subcutaneously injection of bupivacaine and results which we observed. Anyway, a clinical trial aimed to compare local and systemic injection of bupivacaine before surgery for controlling post-thoracotomy pains should be done.

Our results study was same with Nesioonpour. et al (2013) study that survey local infiltration of bupivacaine in patients undergoing inguinal hernia repair, the patients in the intervention group received 10 cc of 0.5 % bupivacaine and the control group received 10 cc of normal saline in the operation site before surgical incision that the pain scores analgesic request after operation was lower in case group while time of first analgesic request was longer in treatment group (23).

Saringcarinkul, et al (2008) in Thailand, determined the effect of scalp infiltration on postoperative craniotomy pain with 0.5% bupivacaine before skin closure comparing normal saline, that pain score was lower in the bupivacaine group in the first 12 hours but differences between two groups were not statistically significant, So that first administration of tramadol was longer in the bupivacaine group (24).

Infiltration of bupivacaine was performed after scalp skin closure by Law-Koune. et al (2005) that There was no difference in the visual analogue scale scores among the bupivacaine group and placebo group (normal saline) but Scalp infiltration with

bupivacaine had a statistically significant effect on morphine consumption during the first 2 postoperative hours (25).

Bloomfield. et al (1998) studied scalp infiltration with bupivacaine during craniotomy aimed reducing postoperative pain and hypertension. Adult patients receive scalp infiltration with either bupivacaine (0.25%) or epinephrine (1:200,000) or saline/ epinephrine (1:200,000), MAP was significantly greater and HR was significantly faster in the saline group and the bupivacaine group reported significantly less pain than the saline group in 1hr after craniotomy (26).

LIMITATION

Following thoracic surgery, post thoracotomy pain decrease approximately 40% the baseline values of FEV1, forced vital capacity, and functional residual capacity that can lead to atelectasis and pneumonia. With recovering ventilation perfusion relationship due to relief of pain can prevent these complications. Other limitation in this study was the probably physiological changes in patients included serum levels of catecholamines and cortisol following pain control in two groups that not investigated.

CONCLUSION

In our study, although effect of bupivacaine in form of subcutaneous injection before surgery incision on pain, vital signs, consumption of morphin and diclofenac and first request for analgesic was not significantly less than NS but further study with larger sample size is needed in future.

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COMPETING INTERESTS

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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Table 1: Distribution of patients in intervention and comparison groups in terms of gender, smoking, and history of previous surgery

characteristic		**Count (%)**		**P**
		Bupivacaine Group	**NS Group**	
sex	female	15(37.5)	14(35.0)	0.837
	male	25(62.5)	26(65.0)	
smoking	yes	8(20.0)	9(22.5)	0.731
	no	32(80.0)	31(77.5)	
Previous history of surgery	yes	13(32.5)[a]	14(35.0)[b]	0.910
	no	27(67.5)	26(65.0)	
a: limb 7, abdomen 6; b: limb 7, abdomen 7				

Table 2: Duration of surgery and vital signs before anesthesia, before injection, and 5 minutes after incision in intervention and comparison groups

Vital signs	**Measuring time**	**Mean ± SD**		**P***
		Bupivacaine Group	**NS Group**	
Duration of surgery(min)		103.06±71.92	124.50±55.66	0.295
Duration of anesthesia(min)		138.80±80.52	172.25±65.10	0.153
Systolic blood pressure (mmhg)	Before anesthesia	133.42±24.32	126.15±21.72	0.319
	Before injection	118.69±21.69	118.25±25.35	0.960
	After incision	121.42±23.94	115.45±18.79	0.381
Diastolic blood pressure (mmhg)	Before anesthesia	82.85±15.63	79.00±13.34	0.402
	Before injection	74.23±19.23	75.90±18.71	0.781
	After incision	73.52±15.36	72.75±15.40	0.873
Heart rate (beat/min)	Before anesthesia	96.76±20.73	86.40±15.94	0.114
	Before injection	88.80±12.90	83.95±18.76	0.338
	After incision	88.66±13.06	83.25±13.33	0.197
O2 saturation (%)	Before anesthesia	95.66±3.56	95.75±2.91	0.935
	Before injection	98.09±2.02	97.90±2.10	0.763
	After incision	98.19±1.86	98.20±1.76	0.987
SD: Standard Deviation; *T-test				

Table 3: Level of pain in patients in intervention and comparison groups based on the follow-up 24 hours after surgery in terms of NAS score and the need for analgesics

Pain status	**Median (IQR)**		**P***
	Bupivacaine Group (n=40)	**NS Group (n=40)**	
Pain after 2 hours	5.5(5.75)	7(4.5)	0.403
Pain after 4 hours	5.5(5)	8(5.25)	0.374
Pain after 8 hours	5.5(3.5)	6(5.5)	0.946
Pain after 24 hours	5(2)	5.5(4)	0.881
Time to first request for analgesic (hour)	4.5(5.25)	3(2.38)	0.161
Summation of prescribed Morphine (mg)	10(13.75)	17.5(6.88)	0.131
Total number of prescribed Diclofenac Na suppositories	2(0.5)	3(2)	0.056
IQR: Inter Quartile Range; *Mann-Whitney U test			

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