

Original Article

The efficacy of preventive parasternal single injection of bupivacaine on intubation time, blood gas parameters, narcotic requirement, and pain relief after open heart surgery: A randomized clinical trial study

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Abstract

BACKGROUND: Postsurgical pain usually results in some complications in the patients. This study has tried to investigate the effects of parasternal single injection of bupivacaine on postoperative pulmonary and pain consequences in patients after open heart surgery.

METHODS: In a prospective double blind clinical study, 100 consenting patients undergoing elective open heart surgery were randomized into two groups. In case group, bupivacaine was injected at both sides of sternum, immediately before sternal closure. In the control group, no intervention was performed. Then, the patients were investigated regarding intubation period, length of ICU stay, arterial blood gas (ABG) parameters, morphine requirement, and their severity of postoperative pain using a visual analogue scale (VAS) device.

RESULTS: No differences were found between the two groups regarding to age, sex, pump time, operation time, and body mass index and preoperative cardiac ejection fraction. Mean intubation length in case group was much shorter than that in control group. Mean PaO₂ in case group was lower in different checking times in postoperative period. The patients in the case group needed less morphine compared to those in the control group during the 24-hour observation period in the ICU. Finally, mean VAS scores of pain in case group were significantly lower than those in control group at 6, 12, and 24 hours postoperatively.

CONCLUSIONS: Patients' pain relief by parasternal single injection of bupivacaine in early postoperative period can facilitate earlier ventilator weaning and tracheal extubation after open heart surgery as well as achieving lower pain scores and narcotic requirements.

KEYWORDS: Bupivacaine, Cardiac surgical procedures, Pain, Postoperative, Analgesia.

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Early tracheal extubation after cardiac surgery has become more popular and it can be safe and result in decreased cost and improved outcome.¹ Anesthetic techniques have been adopted to achieve this goal such as using small opioid doses, but these strategies may not provide adequate analgesia in the immediate postoperative period.² Intrathecal and epidural analgesia may be used for this purpose but the risk of potential epidural he-

matoma may offset the benefits.³ Also, epidural analgesia may not be protective against hypoxemia with opioids.²

Intravenous (IV) opioids are most often used for postoperative analgesia in these patients. Median sternotomy incision and the mediastinal tube insertion site are main sources of pain in cardiac surgical patients.⁴ Therefore, infiltration of local anesthetic agents near the sternotomy wound is a possible way

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of diminishing early postoperative pain.⁵ This method may reduce opioid requirements, and subsequent opioid induced side effects such as sedation and respiratory depression.

This was a prospective blind controlled study to examine whether a parasternal block with a long acting local anesthetic agent at the sites of the sternotomy wound and tube insertion can provide early postoperative analgesia and fewer requirements to morphine and lesser pain in patients undergoing median sternotomy for cardiac surgery.

Methods

In a double blind, randomized clinical trial study, from Sep 2006 to Nov 2007, after obtaining approval from the Institutional Research Committee and informed consent from patients, 100 patients, undergoing either single valve replacement or CABG (coronary artery bypass grafting) with CPB (cardiopulmonary bypass) were enrolled. Inclusion criteria were non-smoking status, age between 19 and 72, non-diabetic status, no opium addiction, lack of history of significant respiratory disease and also an acceptable preoperative pulmonary function test (PFT). Patients with emergency surgery, previous cardiac surgery, poor left ventricular function (EF < 40%), preoperative use of inotropic drugs or intra-aortic balloon pump, pre-existing neuromuscular disease, patients with allergy to local anesthetics or morphine were not included in the study. Exclusion criteria were prolonged CPB time (CPB time > 120 minutes), tracheal extubation after 24 hours past from the end of surgery, intraaortic balloon pump (IABP) requirement during surgery, and emergency re-sternotomy. Based on a computer generated randomization table and before the end of surgery, the participants were allocated to one of the two study groups, case group (50 patients) and control group (50 patients). Six patients excluded from the study in case group, 3 patients because of prolonged CPB time and 3 patients because of postoperative bleeding and need for re-sternotomy. Finally, 94 patients entered to our study analysis (Figure 1).

Patients were instructed about the visual analogue scale (VAS) device before surgery. They were all intramuscularly premedicated with morphine (0.1 mg/kg) and promethazine (0.3 mg/kg) about 30 to 60 minutes before admission to operating room. All operations were performed by the same surgery team and with similar method of surgery and anesthesia. Monitoring included an arterial catheter and a CVP (central venous pressure) line. For anesthetic induction, patients were given fentanyl (10 µg/kg), sodium thiopental (5 mg/kg), lidocaine (1.5 mg/kg) and pancuronium (0.1 mg/kg). Anesthesia was subsequently maintained by administrating isoflurane (0.5-1.5 MAC), 100% oxygen, and morphine (0.1 mg/kg). During the cardiopulmonary bypass (CPB), propofol (50-100 µg/kg/min after a bolus of 1 mg/kg) was prescribed. For CPB system, a membrane oxygenator (Affinity, Medtronic, USA) and crystalloid prime solution (including 1 L of ringer lactate, 500 mL of hemaxel and 60 g of mannitol) were used. During bypass, the hematocrit was maintained between 20% and 25%. In managing arterial blood gas (ABG), \square -stat protocol was adopted.

The components of the parasternal block included infiltration of bupivacaine near the intercostal nerves via transpleural injection, close to the sternal borders, and the deep subcutaneous layers around the chest tube sites. To achieve this, the surgeon performed the parasternal block in a standardized fashion just before sternal wire placement. Patients in the case group received 20 mL of 0.5% bupivacaine and the control group received no injection of drug or placebo.

In the case group, bupivacaine was infiltrated directly just lateral to LIMA (left internal mammary artery) harvesting site in CABG patients at left side and via transcutaneous injection blindly just aside the right border of sternum at right side. Finally, 2.5 mL of bupivacaine was infiltrated deeply around the mediastinal tube sites and then, the sternum was closed.

After termination of surgical operation, neuromuscular block was not antagonized and the

patients were admitted to ICU and underwent mechanical ventilation and the mediastinal tubes were connected to low power suction. All data in ICU were recorded by a blinded investigator, who was not involved in operating room and ICU care. The criteria for tracheal extubation included the patient's alertness to follow instructions and a steady hemodynamic state (systolic blood pressure > 90 mmHg), stable cardiac rhythm, no active bleeding, SaO₂ > 95% (arterial saturation from oxygen) on 0.5 fraction of inspired oxygen, a respiratory rate between 10 to 30 breaths/ min, and PH > 7.30. Sedation with IV midazolam (2 to 4 mg) was permitted until 30 min before extubation. All of the subjects were NPO for 6 hours after extubation. VAS was assessed when the patient was awake enough to respond (Ramsay Sedation Scale of 2 or less). Postoperative pain was managed with intravenous morphine, 2 to 4 mg boluses if patients asked for analgesics or experienced pain with a VAS pain score of more than 3. The total amount of morphine given was recorded. Other end points measured included VAS scores (scale 0-10) of pain, vital signs, time to tracheal extubation and ABG analysis results. ABG parameters consisted of PaO₂ (arterial partial pressure of oxygen), PaCO₂ (arterial partial pressure of carbon dioxide) and PH. These measurements were taken at 0, 6, 12 and 24 hours after arrival of patients in ICU. VAS scores of pain were evaluated after tracheal

extubation, when the patient was awake enough to respond and indicate the level of pain on the VAS. All data were recorded by a blinded investigator, who was not involved in surgery procedure.

For sample size calculation, it was estimated that with 40 patients per group, a difference of 30% in clinical efficacy between groups could be found with a statistical power of 80% and a cutoff point for significance of 0.05. Statistical analysis was performed using the unpaired t-test, Mann-Whitney and χ^2 tests to compare parameters between the two groups. Fisher exact test was used to compare categorical values between groups. Statistical significance was defined as $P < 0.05$. The results have been presented as mean \pm standard deviation.

Results

The basic and demographic specifications of the two groups before intervention are summarized in Table 1. There were no significant statistical difference between the two groups according to age, sex, pump time, operation time and body mass index, systolic, diastolic and mean intra-operative blood pressure and heart rate, and preoperative cardiac ejection fraction (EF) ($p > 0.05$).

During 24 hours after admission to ICU, both groups had mean PaCO₂ levels close to each other ($p > 0.05$). The mean PaO₂ level, up to 24 hours in the ICU, was lower in the control group, compared with the case group ($p < 0.001$).

Table 1. Demographic and morphometric factors and clinical data.

Variable	Case group (n=44)	Control group (n=50)	P Value*
Gender (M/F)	28/16	32/18	NS
Age (yr)	54.2 \pm 11.4	49.8 \pm 13.2	NS
BMI	26.1 \pm 3.9	25.1 \pm 4.3	NS
Type of surgery (CABG/valve)	36/8	41/9	NS
Duration of surgery (hr)	4.35 \pm 0.49	4.44 \pm 0.76	NS
Bypass time (min)	86 \pm 21	85 \pm 24	NS
Preoperative EF (%)	52.4 \pm 12.7	51.3 \pm 14.6	NS

Data are presented as number or means \pm SD or number.

* Chi-squared test was used for comparing gender and type of surgery and t-test was applied for other variables.

Abbreviations: NS, not significant; BMI, body mass index; CABG, coronary artery bypass graft; EF, ejection fraction

The overall morphine requirement, up to 24 hours in the ICU, was greater in the control group compared with the case group ($p < 0.001$). In other words, mean morphine necessity of patients in the case group was half of that in the control group.

There were significant statistical differences between the two groups according to mean VAS scores of pain at 6, 12 and 24 hours after admission to ICU (Table 2) ($p < 0.0001$).

Like wise, mean intubation time was obviously less in the case group compared with the control group ($p < 0.001$). In other words, the case subjects were extubated about two times more quickly than the control group. There was no difference according to the length of ICU stay between the two groups ($p > 0.05$). The mean systolic blood pressure and mean heart rate were significantly higher in control group compared with the case group during the first 24 hours in ICU ($p < 0.01$) (table 2).

Discussion

One of the most important points in the post-operative period of cardiac surgery patients is rapid weaning of them from mechanical ventilator as soon as possible.¹ It is clear that prolonged intubation time can lead to many complications especially pulmonary disturbances. In this way, one of the important factors in rapid weaning of such patients from ventilator is reduction of postoperative pain.^{6,7}

We found a significant opioid-sparing effect in patients receiving bupivacaine compared with control group. Patients' pain relief by parasternal single injection of bupivacaine in early postoperative period can facilitate earlier ventilator weaning and tracheal extubation after open heart surgery patients as well as achieving lower pain scores and narcotics requirements.

In one study, Egan and coworkers explained that in early post-laparotomy period,

Table 2. Data relating the stay in the intensive care unit.

Variable	Case group (n=44)	Control group (n=50)	P Value
Duration of ventilation (hr)	4.3 ± 1.9	9 ± 3.8	0.001*
Time to extubation (hr)	4.8 ± 2.6	9.5 ± 4.8	0.001*
Total midazolam consumption (mg) before tracheal extubation	3.8 ± 2.1	4.1 ± 1.9	NS
Total morphine consumption (mg)	5.6 ± 4.9	12.7 ± 4.6	0.001*
Patients needed for rescue analgesics	22(50%)	45(90%)	0.001*
Mean PaCO ₂ (mmHg)	42 ± 5.4	40 ± 5.4	NS
Mean PaO ₂ (mmHg)	115 ± 26	90 ± 44	0.001*
Mean systolic blood pressure (mmHg)	121 ± 45	135 ± 52	0.01*
Mean diastolic blood pressure (mmHg)	78 ± 22	81 ± 34	NS
Mean heart rate (beat/min)	83 ± 22	94 ± 32	0.01*
Severity of pain (case/control)			
VAS-6 hr (44/5) [#]	3.5 ± 1.1	5.8 ± 1.1	0.001*
VAS-12 hr (44/40) [#]	2.6 ± 1.2	5.1 ± 1	0.001*
VAS-24 hr (44/50) [#]	1.7 ± 1.3	5.3 ± 1.4	0.001*
Satisfaction of patients for pain relief at 24 hr [†]	1.6 ± 0.5	5.8 ± 2.3	0.001*

Data are presented as means ± SD or number (%). All data are calculated for the first 24 hours in ICU.

*A significant difference was found between the case and the control groups.

[#]Numbers in parenthesis are as case/control frequencies.

[†]Answers were graded from 1 (very satisfied) to 5 (not satisfied at all).

P value for quantitative parameters calculated by chi-squared test; the severity of pain (VAS) scores calculated by Mann-Whitney test.

Abbreviations: NS, not significant; VAS, visual analogue scale; PaCO₂, partial pressure of arterial CO₂; PaO₂, partial pressure of arterial O₂.

the patients needed equal doses of narcotic analgesic agents after injection of bupivacaine in laparotomy incision site, comparing with control group, although the time to first analgesic was considerably longer in the case group (2.2 vs. 1.3 hours, $p < 0.055$).⁸ In this manner, Berisford infiltrated bupivacaine in thoracotomy incision site with a catheter in continuous method up to 24 hours postoperatively. That resulted in reduction of narcotic analgesic requirements and visual pain scores and also rapid recovery of pulmonary function and minimizing the lung disturbances ($p < 0.01$).⁹ So, the results of the latter study similar to the results of our study showed that reduction of postoperative pain can result in a trend to weaning of patients from ventilator sooner.

In contrary to above studies, Magnano and coworkers showed that presternal bupivacaine wound infiltration (bupivacaine 0.5%; 10 ml, followed by continuous infusion of 10 mg/24 H), compared with control group, did not reduce postoperative pain or shorten assisted ventilation time (189.0 ± 56.4 vs. 147.7 ± 35.8 minutes, $p < 0.05$). ABG parameters and VAS value in both case and control groups were similar.¹⁰ In that study, the catheter used for continuous infusion had a few holes only at the tip. Furthermore the sites of mediastinal drains were not infiltrated and the bupivacaine dose was less than that in our study.

In one study that is very similar to our study, McDonald and coworkers showed that infiltration of bupivacaine in area of sternotomy incision site can make significant reduction of morphine demand (20.8 ± 6.2 mg versus 33.2 ± 10.9 mg in the placebo group, $p < 0.013$) and intubation time (36.4 ± 26.1 versus 38.1 ± 24.1 min, $p = 0.9$) and improvement of pulmonary condition.⁵ Of course, they used 54 mL of 0.25% levobupivacaine with 1:400,000 epinephrine. The total amount of morphine given was much higher than that in our study. The reason seems to be that their narcotic administration was based on patient controlled analgesia (PCA) demands and not the protocol we used. Another difference is that in McDonald's study, the neuromuscular blockade was reversed, and the

patients were allowed to breathe spontaneously once the sternum was closed.

In a recent study, Olivier has presented a technique of bilateral single-shot paravertebral blocks (BSS-PVB) (bilateral blocks of 3 mL bupivacaine 0.5% each, T1-7) for cardiac surgery via median sternotomy.⁷ He compared this technique and its efficacy versus high thoracic epidural analgesia (TEA). Both groups of patients received general anesthesia. There were no complications related to epidural catheter usage or BSS-PVB. After both techniques, instant extubation following cardiac surgery was possible. But, TEA provided better pain relief after cardiac surgery than BSS-PVB (immediately at 2.4 ± 2.2 versus 3.7 ± 2.6 , at 6 hours at 1.1 ± 1.5 versus 2.4 ± 1.8 , and at 24 hours at 1.0 ± 1.4 versus 2.3 ± 1.6 ; 0 = no pain, and 10 = maximum pain). Despite our study, they have not infiltrated the sites of mediastinal drains. Also, that study performed a paravertebral and not a parasternal technique. In their study, patients underwent off-pump coronary artery bypass grafting, on-pump and mitral valve replacements.

Likewise, Barr and colleagues have demonstrated that parasternal intercostal block with ropivacaine can cause reduction of postoperative pain after cardiac surgery.¹¹ This regional anesthetic technique with parasternal single injection of bupivacaine is simple, relatively noninvasive, and rapidly performed, and unlike neuraxial blocks, it can be performed in patients who are anticoagulated perioperatively. However, the safety of this technique, as with any regional anesthetic block, depends on careful application.

Although our study was a prospective, randomized and double-blind, there were some limitations. The smaller analgesic requirements in the case group did not indicate earlier ICU discharge. Although earlier tracheal extubation and better oxygenation parameters may translate into better pulmonary function, a larger study with the primary aim of studying outcome variables (such as long term pulmonary infections) is now needed. Although length of stay in the ICU and hospital is imperative, it

remains very subjective (depending to discharging protocols), and hence differences (if any) are not easy to identify. White and colleagues also did not find any decrease in duration of the intensive care unit stay following a continuous infusion of bupivacaine 0.25% or 0.5%, at the median sternotomy site, for 48 h after cardiac surgery.¹²

Another limitation of the present study was that the patients received morphine according to their complaints of pain to the nurse. It would be better if patient controlled analgesia (PCA) had been adopted for rescue treatment of pain in ICU.

One point in our study may be that only a selected group of cardiac surgical patients (i.e., only those with good ventricular function undergoing cardiac surgery for the first time and with no serious comorbidity) were included. More complicated cases may benefit with greater degree from this method of preventive

pain management.

Conclusion

Results of this study showed that one of the most important parameters in rapid weaning of cardiac surgery patients from ventilator is control and reduction of pain in early postoperative period. Reduction of pain can lead to reduction of intubation time and narcotic requirements and improvement of ABG parameters in early postoperative period. Patients who were enrolled were not from a selected group of cardiac surgical population. So the results may be applicable to all of these procedures.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

MS carried out the design and coordinated the study, participated in all of the experiments and prepared the manuscript. OA provided assistance in the design of the study, coordinated and carried out all the experiments and participated in manuscript preparation. MMS provided assistance for most experiments. MM carried out the design and coordinated the study. All authors have read and approved the content of the manuscript.

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