Presternal local analgesia for postoperative pain relief after open heart surgery: a randomized, controlled study

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Infiltration of local anesthetics near the surgical wound has shown to improve early postoperative pain in various surgical procedures, especially after open heart surgery. Inadequate pain control reduces the capacity to cough, mobility, increases the frequency of atelectasis, and prolongs recovery.

Patients and methods

This study is designed to examine the efficacy of postoperative 1 g paracetamol/6 h, ketorolac tromethamine 30 mg/8–12 h as conventional analgesia versus bupivacaine plus magnesium sulfate through a single presternal catheter for postoperative pain relief after cardiac surgery. Forty patients were scheduled for valve replacement cardiac surgeries and were randomly assigned into two groups (20 patients in each group). Group M: each patient has received bupivacaine 0.125% with 5% magnesium sulfate through the presternal soft catheter at a fixed rate of 5 ml/h. Group B: each patient only has received postoperative 1 g paracetamol/6 h, ketorolac tromethamine 30 mg/8 h. For postoperative breakthrough pain, rescue analgesia in the form of 25 μg fentanyl was used, with recording of total required doses in both groups.

Results

The mean numeric pain scale was significantly lower in group M than in group B at most time points. The overall fentanyl requirements over the first 48 h were significantly lower in group M than in group B (33 ± 11.7 vs. 150 ± 1.6 μg, respectively). There was no statistically significant difference between the two groups regarding ICU stay and blood glucose level.

Conclusion

Local presternal bupivacaine with magnesium sulfate provided adequate postoperative analgesia and less opioid requirements.

Keywords:
bupivacaine, cardiac surgery, magnesium sulfate

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Introduction

Effective pain relief after cardiac surgery has assumed importance with the introduction of fast-track discharge protocols that requires early weaning from mechanical ventilation. Inadequate pain control reduces the capacity to cough, mobility, increases the frequency of atelectasis, and prolongs recovery [1–5]. A major cause of pain after cardiac surgery is the median sternotomy particularly on the first 2 postoperative days [6]. The most often used analgesics in these patients are parenteral opioids which can lead to undesirable side effects such as sedation, respiratory depression, nausea, and vomiting [3–8]. Infiltration of local anesthetics near the surgical wound has shown to improve early postoperative pain in various surgical procedures [8–11]. Magnesium is the fourth most plentiful cation in our body. It has antinociceptive effects in animal and human models of pain [12]. It has been mentioned in a systematic review that it may be worthwhile to further study the role of supplemental magnesium in providing perioperative analgesia, because this is a relatively harmless molecule, is not expensive, and also because the biological basis for its potential antinociceptive effect is promising [13]. These effects are primarily based on physiological calcium antagonism, that is voltage-dependent regulation of calcium influx into the cell, and noncompetitive antagonism of *N*-methyl-d-aspartate receptors [14].

Aim

To compare the efficacy of postoperative 1 g paracetamol/6 h and ketorolac tromethamine 30 mg/8–12 h as conventional analgesia versus bupivacaine 0.125% plus magnesium sulfate 5% through a single presternal catheter for pain control after cardiac surgery. Our primary outcome is postoperative

measurement of pain scores, the secondary outcomes are ICU and hospital stay duration, and blood glucose level.

Patients and methods

This study was approved by our Local Ethics Committee of Faculty of Medicine, Assiut University (IRB 17100392), and registered in clinical trials (NCT03230227). This research was designed as a randomized, controlled study in patients undergoing valve replacement cardiac surgeries. It was conducted in Al-Orman Heart Institute, one of the Assiut University Hospitals, Assiut, Egypt between July 2016 and July 2017. All patients were adult patients (age > 18 years), both sexes were eligible for Study, American Society of Anesthesiologists physical status II and III patients scheduled for open heart surgery with sternotomy. We excluded patients with emergency surgery, previous sternotomy, patients with preoperative poor left ventricular function [ejection fraction (EF)<40%], pre-existing pulmonary or neurological dysfunction, clinically significant kidney or liver disease, patients allergic to local anesthetic, pre-existing coagulopathy, patients with prolonged cardiopulmonary bypass (CPB) time (>120 min), postoperative hemodynamic instability (including the occurrence of serious arrhythmia), or bleeding that required surgical re-exploration and those who received high inotropic support that interferes with separation and weaning from mechanical ventilation. Informed consents were obtained from all study participants.

Forty patients scheduled for valve replacement cardiac surgeries were randomly assigned into two groups (20 patients in each group) group M: each patient has received bupivacaine 0.125% with 5% magnesium sulfate by infusion through a small diameter multihole soft catheter generally used for epidural analgesia (Portex Epidural Catheter 18-G; Smith Medical ASD Inc., Keene, New Hampshire, USA) positioned anteriorly to the sternum above the fascia in the subcutaneous tissue during wound closure for 48 h postoperatively. A bolus of 5 ml of the study solution was injected into the catheter after aspiration test and before connection to an elastomeric infusion pump that delivers a fixed rate of 5 ml/h. Group B: each patient has received postoperative 1 g paracetamol/6 h, ketorolac tromethamine 30 mg/8 h. For postoperative breakthrough pain, rescue analgesia was used in the form of 25 μg fentanyl, intravenous, with a recording of total required doses in both groups. Preoperative evaluation of eligible patients included physical examination and checkup of patients and echocardiographic reports. Preoperative cardiac medications have been continued up to the operative time except that warfarin (when it was indicated) was stopped 5 days preoperatively and bridging therapy with low molecular weight heparin has been used. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and diuretics have been stopped 24 h preoperatively. Lorazepam 1.5 mg has been given in the night preceding the surgery. Fasting was 6 h for semisolids and 2 h for oral nonparticulate fluids preoperatively. On arrival at the operating room, 18 G, intravenous, cannula and a 20-G radial arterial cannula were inserted under local anesthesia. Basic monitoring included an electrocardiogram, invasive blood pressure, pulse oximetry, capnography, temperature (oropharyngeal), urine output, airway volume, and pressure. General anesthesia was induced with fentanyl 2 μg/kg, midazolam 0.1 mg/kg, and propofol 1–2 mg/kg, lidocaine 1-2 mg/kg cisatracurium 0.1 mg/kg was administered to facilitate endotracheal intubation and was repeated during surgery as required to ensure proper muscle relaxation. Anesthesia was maintained using 0.5–1.5% isoflurane in an oxygen–air mixture (1: 1 ratio). Fentanyl infusion in the dose of 1 μg/kg/h until the end of anesthesia procedure. Mechanical ventilation was provided by a Narkomed anesthesia machine (Datex-Omeda, Telford, Pennsylvania, USA) using a Tidal volume 6-8 ml/predicted body weight in kg. A 3-port central jugular venous line was inserted (Certofix Duo; B. Braun Melsungen A.G., Melsungen, Germany) for central venous pressure monitoring and fluid infusion management. All operations were performed by the same surgical team in a standard method through a median sternotomy incision. By the end of the operation, with coagulation reversal, separation from CPB was done, and just before sternal wire placement, the patients were managed according to randomization to be in group M or the control group (group B). The patients were observed for 10 min for any bleeding caused by an inadvertent vascular injury before the closure of the sternum. After sternal wiring, the small diameter multihole soft epidural catheter was positioned anteriorly above the fascia in the subcutaneous tissue during wound closure in group M. Steri-strips (3M Germany GmbH, Neuss, Germany) and wound dressing were used to secure the catheters. A bolus of 5 ml of the study solution was injected in the catheter after aspiration test before connection to the infusion pump (Accufuser Plus P 4003; Chungbuk, S. Korea) which consists of a disposable 50 ml elastomeric reservoir that delivers continuous infusion of the solution at a fixed rate of 5 ml/h. At the end of surgery, neuromuscular block was not antagonized. Stoppage of fentanyl infusion was done and the patients were transferred intubated to the postoperative ICU, where they were mechanically ventilated (Engström Carestation; GE Healthcare). In the ICU, the criteria for extubation were

hemodynamic stability, absence of arrhythmias, adequate airway reflexes, normothermia, mediastinal drainage (<100 ml/h for 2 h), and acceptable blood gas analysis (pH > 7.30, arterial oxygen tension > 60 mmHg and arterial carbon dioxide tension <50 mmHg) at an inspired oxygen fraction of 0.4.

Numeric pain scale (NPS) was used for pain assessment (0 = no pain, 10 = the worst pain imaginable). The patients were asked to take a deep breath and the intensity of pain was recorded. If the patients were still intubated, the observer asked whether he or she had a pain score of 10 points, if this was not the case, the observer repeated the question decreasing the score 1 point each time until the patients confirmed the answer by nodding. Rescue analgesia was given if the NPS pain score was at least 3 and the total amount of fentanyl given during the first postoperative 48 h was recorded. The occurrence of any postoperative sternal wound infection or delayed wound healing during hospitalization was also recorded. The pain score was recorded postoperatively on patient's arrival in the ICU (T0), every 4 h for 12 h and then every 6 h for 48 h.Time to extubation (from arrival at the ICU till tracheal extubation), measuring serum glucose levels by the night of the first and second postoperative days consequently.

Data analysis

Data presented as mean ± SD unless otherwise stated, were analyzed using SPSS 20.0 for Windows (SPPS Inc., Chicago, Illinois, USA). Independent-samples *t*-test was utilized to compare means as appropriate. Categorical data were analyzed by χ^2-test. Nonparametric data was compared by the Mann–Whitney *U*-test. A two-tailed *P* value less than 0.05 was considered statistically significant.

Sample size estimation

A calculated sample size of 18 participants would have an 80% power to detect a difference of 20% in the primary outcome variable with type I error of α=0.05 using a confidence interval of 95%. Twenty patients were enrolled in each group to compensate for any dropouts during the study.

Results

The total of 40 patients were enrolled in this study as shown in Fig. 1. There were insignificant differences between bupivacaine/magnesium sulfate group (group M) and control group (group B) with respect to age, sex, body surface area, EF, CPB, surgery time preoperative EF, duration of surgery, cross-clamping, and CPB times (Table 1).

The mean NPS score of pain was significantly lower in group M than in group B at most time points (Fig. 2). The overall fentanyl requirements over the first 48 h in the ICU were significantly lower in group M than in group B (33 ± 11.7 vs. 150 ± 1.6 μg, respectively = 0.0006; Table 1).

There was no statistically significant difference between the two groups regarding the ICU stay nor does postoperative blood glucose level (Tables 1 and 2).

No recorded postoperative delayed wound healing or infection related to our used intervention in group M.

Discussion

The present study demonstrated that continuous subcutaneous presternal infusion of bupivacaine 0.125% with 5% magnesium sulfate at a rate of 5 ml/h for 48 h in patients undergoing valve replacement cardiac surgery with median sternotomy had resulted in better postoperative analgesia, reduction in fentanyl requirements, shorter time to extubation with no incidence of wound infection, and no difference in ICU and hospital duration compared with the control group.

Wound infiltration with local anesthetics has been studied for postoperative analgesia in different surgical settings and has proved to reduce postoperative pain effectively [8–11] although the same method applied directly to the sternotomy incision in cardiac surgery has been studied; the results were controversial [15–19].

Similar to our results, Chiu *et al.* [16] found that when bupivacaine 0.15% was infused continuously at a rate of

Table 1 Patients' demographic and clinical data

Variables	Group M (*n*=20)	Group B (*n*=20)	*P*
Age (years)	36.8±13.8	37.6±13.1	0.87
Male/female	17/3	15/5	0.43
BMI (kg/m^2)	28.8±1.6	28.2±2.4	0.63
EF (%)	56.9±8.6	55.14±5.6	0.52
CPB time (min)	91.6±14	95.64±12.4	0.37
Surgery (min)	222.8±16.8	221.36±15.4	0.8
Fentanyl (μg)	33±11.7	150±1.6	0.0006***
ICU stay (h)	49±1.7	53±6.4	0.2

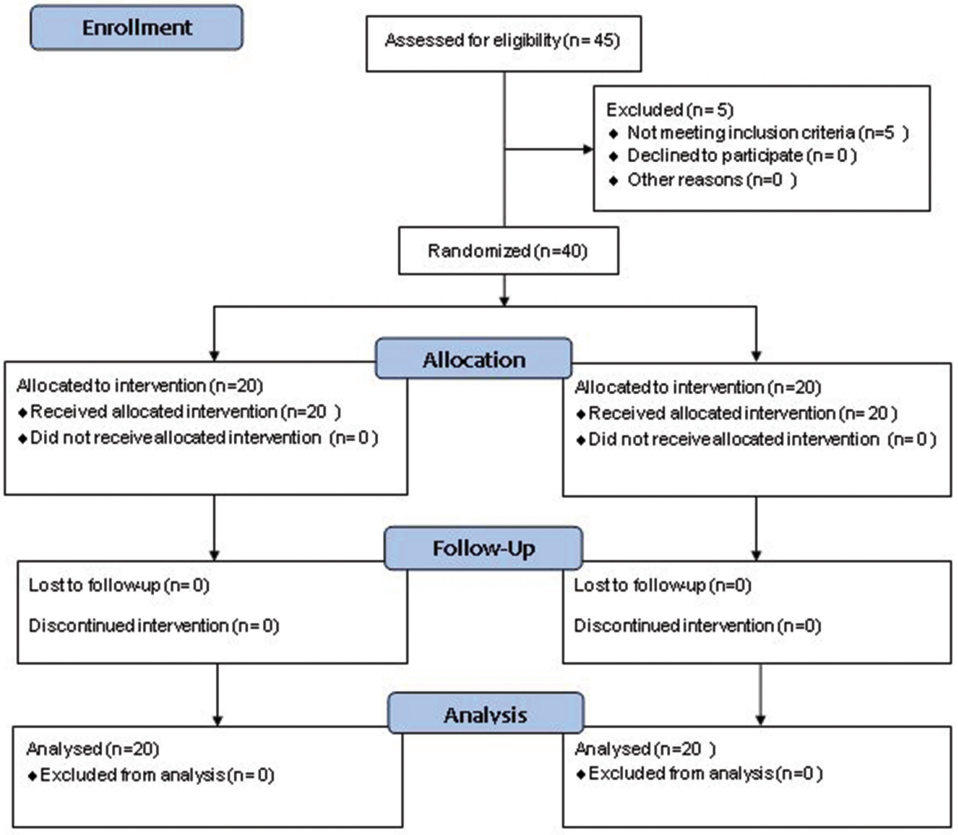
***Result is highly significant. Data are presented as mean±SD or ratio. CPB, cardiopulmonary bypass; EF, ejection fraction. *P*>0.05, statistically nonsignificant.

Table 2 Serum glucose level in the first and second postoperative days

Variables	Group M	Group B	*P*
Glucose first (mg/dl)	213±85	206±67	0.46
Glucose second (mg/dl)	193±59	190±70.6	0.9

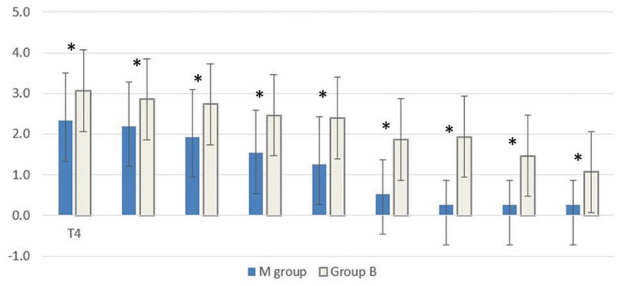
Data is presented as mean±SD. *P*>0.05, statistically nonsignificant.

Figure 1



Consort flowchart.

Figure 2



Postoperative numeric pain scale (NPS).

2 ml/h, initiated at the time of wound closure provided uninterrupted analgesia and contributed to short-term and long-term pain relief for thoracotomy patients. Four other trials studied different local anesthetic solutions applied directly to the sternal wound through two catheters with an elastomeric pump, the first study used bupivacaine 0.5% at 4 ml/h [3], the second and third used ropivacaine 0.2% at 4 ml/h [15,18], and the 4th one used ropivacaine 2 ml/h [20]. The results of the previous studies showed a reduction in postoperative pain and opioid consumption with a significant decrease in hospital stay duration.

On the contrary, Magnano *et al.* [17] used bupivacaine 0.5%; 10 ml for wound infiltration followed by continuous infusion of 10 mg/24 h and Agarwal *et al.* [19] used ropivacaine 0.3% for wound infiltration followed by continuous infusion of 4 ml/h for 64 h. Both studies showed that local anesthetic infusion after median sternotomy did not reduce postoperative pain, NPS, and time to extubation. Magnano *et al.* [17] attributed their results that they used a catheter with few holes only at the tip which was ineffective in long surgical incisions as in median sternotomy and that the lower portion of the wound was probably 'uncovered' by the anesthetic drug. They recommended to prolong the duration of bupivacaine infusion to be more effective in controlling delayed postoperative pain. Agarwal *et al.* [19] attributed the failure of their analgesic technique that their study was stopped earlier than planned due to wound infection. In our study, it was possible that placing catheters for sternal wound infusion closer to the anterior branches of the intercostal nerves has improved analgesic efficacy.

As regards ICU and hospital stay duration, White *et al.* [3] demonstrated no reduction in length of ICU stay probably because there were no attempts by the ICU staff in his study of fast-track cardiac patients. In our study, reducing pain and earlier tracheal extubation in the bupivacaine/magnesium sulfate group did not change the policy of the ICU team as regards ICU and also hospital stay durations (as they follow routine

discharge protocols), and hence differences between groups if found were not easy to identify. There were no serious adverse events reported in all the previous studies and this is what we have found but in one of the similar studies sternal wound infection occurred with increased incidence of catheter-related problems noticed which led to discontinuation of the trial [19].

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Conflicts of interest
There are no conflicts of interest.

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