① Title

The effect of ultrasound-guided bilateral thoracic retrolaminar block on analgesia after pediatric open cardiac surgery: a randomized controlled double-blind study

② Authors information

Ibrahim Abdelbaser¹*(MD), Nabil A. Mageed¹ (MD), Sherif I. Elfayoumy² (MD), Mohamed Magdy¹ (MD), Mohamed M. Elmorsy³ (MD), Mahmoud M ALseoudy¹ (MD)

1- Department of Anesthesia and Surgical Intensive Care, Faculty of Medicine, Mansoura University, Mansoura, Egypt.
2- Department of Anesthesia and Surgical Intensive Care, Faculty of Medicine, Portsaid University, Portsaid, Egypt.
3- Department of Anesthesia and Surgical Intensive Care, Faculty of Medicine, Damietta University, Damietta, Egypt.

③ Running title

Retrolaminar block in cardiac surgery

④ Corresponding Author

Ibrahim Abdelbaser, MD, Department of Anesthesia and Surgical Intensive Care, Faculty of Medicine, Mansoura University, 2 El-Gomhouria Street, Mansoura 35516, Egypt.
Tel: +20 100 497 6825
Previous presentation in conferences

Not applicable

Conflict of interest

Not applicable

Funding

Not applicable

Acknowledgments

Not applicable

IRB number

Institutional Review Board (IRB): The Institutional Research Board, Faculty of Medicine, Mansoura University approved the study protocol on December 3, 2020 (IRB code: R 20.11.1073)

Clinical trial registration number

The study protocol was registered at Pan African Clinical Trial Registry with unique ID (PACTR202012621958228).
The effect of ultrasound-guided bilateral thoracic retrolaminar block on analgesia after pediatric open cardiac surgery: a randomized controlled double-blind study

Running title: Retrolaminar block in cardiac surgery
Abstract

Background: Thoracic retrolaminar block (TRLB) is a relatively new regional analgesic technique that can be used as an alternative to thoracic paravertebral block. This study aimed to evaluate the postoperative analgesic effects of ultrasound-guided TRLB in children undergoing open cardiac surgery via median sternotomy incision.

Methods: Sixty-six patients aged 2 to 8 years undergoing cardiac open cardiac surgery via median sternotomy incision were recruited. In the TRLB group, 0.25% bupivacaine 0.4mL/kg was injected into the retrolaminar space on each side at the level of T4 lamina. Patients in the control group were injected with 0.9% saline. The primary outcome measure was the 24h post-extubation fentanyl consumption. The secondary outcome measures were total intraoperative fentanyl consumption, postoperative modified objective pain score (MOPS) and time to extubation.

Results: The mean±SD total intraoperative fentanyl requirements (μg/kg) and the 24h post-extubation fentanyl consumption (μg/kg) were significantly lower (P<0.001) in the TRLB group (9.3±1.2&6.9±2.1 respectively) than the control group (12.5±1.4&16.6±2.8 respectively). The median (Q1, Q3) time (h) of extubation and the mean±SD time (h) of ICU length of stay were significantly shorter (P<0.001) in the TRLB group (2 [1–3] &23.8±3.2 respectively) in comparison with the control group (6 [4.5–6] & 30.3±3.2 respectively). MOPS was significantly lower (P<0.05) in the TRLB group than the control group at the following time points, 0, 2, 4, 8, 12 and16 hours after extubation.

Conclusions: Bilateral ultrasound-guided TRLB is effective in providing postoperative analgesia in children undergoing open cardiac surgery via median sternotomy incision.

Keywords: Analgesia; Child; Fentanyl; Retrolaminar block; Sternotomy; Ultrasonography.
Introduction

Cardiac surgery via median sternotomy incision causes moderate to severe postoperative pain that can be avoided by the use of an appropriate multimodal analgesic regimen [1]. Regional analgesia is an essential component of postoperative multimodal analgesia in all surgical patients including, children undergoing cardiac surgery. The use of ultrasound guidance in anesthesia increases the safety and efficacy of various regional anesthetic techniques [2]. Nowadays, the use of neuraxial analgesia including, epidural, caudal and spinal analgesia has been gradually replaced by the more safe ultrasound-guided fascial plane blocks specially in cardiac surgery to avoid the potential risk of epidural hematoma in fully anti-coagulated patients [3,4].

Ultrasound-guided thoracic retrolaminar block (TRLB) is a relatively new regional analgesic block that can be used as an alternative to thoracic paravertebral block as a component of multimodal analgesia to control postoperative pain [5]. In adults, the analgesic efficacy of TRLB has been reported in rib fracture [6], breast surgery [7,8] and transcatheter aortic valve replacement [9]. Retrolaminar injection of a local anesthetic blocks the ventral and dorsal rami of thoracic spinal nerves and the local anesthetic spreads laterally in the fascial plane to block the lateral cutaneous branch of intercostal nerve and the small branches arising from it [5]. The only pediatric randomized study for the use of TRLB for postoperative analgesia was conducted on patients undergoing inguinal hernia repair [10]. To the best of our knowledge, this is the first clinical trial that evaluated the analgesic efficacy of TRLB after open cardiac surgery.

This prospective, randomized, controlled study was designed to demonstrate the postoperative analgesic effects of single shot bilateral TRLB in terms of 24h postoperative opioid consumption and pain scores. We hypothesized that bilateral TRLB would decrease the postoperative opioid consumption and pain scores. The primary outcome was 24h post-extubation opioid consumption
and secondary outcomes were postoperative pain scores, time to the first rescue analgesia, time to extubation and the incidence of TRLB complications.
Material and Methods

This is a single-center, prospective, randomized, controlled, double-blind, superiority study with two parallel arms. The study protocol was approved by the Institutional Review Board of Mansoura faculty of medicine, Mansoura, Egypt (IRB code: R 20.11.1073) on December 3, 2020 and registered at pan African clinical trial registry (PACTR202012621958228) before patients recruitment. A written informed consent was obtained from the patient legal guardian before surgery to perform the retrolaminar block and to publish this study. This study was conducted according to ethical principles set by the Declaration of Helsinki and followed the guidelines of good clinical practice.

We conducted this study at the cardiac division of our Institutional Children's Hospital between December 2020 and September 2021. A total of 66 patients, aged 2 to 8 years of both sexes, ASA I& II who were scheduled to undergo cardiac surgery via midline sternotomy using cardiopulmonary bypass (CPB) for the repair of simple congenital heart diseases were recruited. Exclusion criteria were repeated cardiac surgery, emergency surgery, intubated patients, patients receiving inotropic support, presence of pulmonary hypertension, bleeding disorders, and allergy to the amide local anesthetics.

The patients were randomized to the either TRLB group or control group using computer-generated random numbers with an allocation ratio (1:1). The patient group assignment was kept in a sealed opaque envelope that was delivered to the operating room on the day of surgery and was opened just before the induction of anesthesia. The anesthesiologist who prepared the local anesthetic and placebo was not involved in the study. The anesthesia residents who collected the data and the nursing stuff who provided the postoperative care were all blinded to patient group allocation.

Patients were premedicated with 0.5 mg/kg oral midazolam 30min before the separation from their parents. Patients were monitored before induction of anesthesia with 5 leads electrocardiography,
pulse oximetry and non-invasive blood pressure cuff. Induction of anesthesia was either inhalational with sevoflurane or intravenous with propofol 1.5mg/kg depending on the presence or absence of intravenous line and the patient age. Rocuronium 0.9 mg/kg and fentanyl 2μg/kg were given before tracheal intubation. Then capnography was connected to the endotracheal tube to monitor end-tidal CO2, a 3Fr Leadercath (Vygon, Ecouen, France) was inserted into the femoral artery for invasive arterial pressure monitoring, a 5 to 5.5Fr central venous catheter was inserted into the right internal jugular vein to monitor the central venous pressure and a temperature probe was inserted into the nasopharynx to monitor patient temperature.

Anesthesia was maintained with sevoflurane (1%-2%) in a mixture of air-oxygen (1:1), fentanyl 1μg/kg/h and rocuronium 0.5mg/kg/h. Additional boluses of fentanyl 1μg/kg were given before skin incision, before sternotomy and when the mean arterial blood pressure and/or heart rate raised 20% above the baseline.

After the induction of anesthesia, the patient was placed in a prone position with a pillow under the chest to perform the retrolaminar block on both sides. The spinous process of the fourth thoracic vertebra was identified and marked. The ultrasound-guided TRLB was done under complete sterilization by using Sterillium®, sterile drapes, and putting the ultrasound probe in a sterile sheath. Ultrasound high frequency linear transducer of a GE Vivid S5 ultrasonography (General Electric Ving Med Systems, Horten, Norway) was placed in a parasagittal position just lateral to the spinous processes of thoracic vertebra to identify the muscles (trapezius, rhomboid major, erector spinae and paraspinal muscles) and vertebral lamina (Fig. 1). A 50 mm 22-gauge sonographic needle (stimuplex®; B .Braun Medical, Bethlehem, Pa) was inserted in an in-plane technique from a cephalad to a caudal direction and was advanced till touching the lamina of the fourth thoracic vertebra and then we injected 0.25% bupivacaine 0.4mL/kg on each side (Fig. 1). In the control group, we injected the same volume of 0.9% normal saline instead of 0.25% bupivacaine.
All surgeries were done via midline sternotomy incision (Fig. 2A). Before initiation of CPB, the patient received 3-4 mg/kg heparin via the central venous catheter to increase the activated clotting time above 480 seconds. Mild hypothermia was allowed. After the repair of cardiac defect, patient was rewarmed and separated from CPB, followed by administration of protamine to antagonize heparin. After completion of surgery and placing the drainage tubes (Fig. 2B), the patient was transferred to the intensive care unit (ICU).

The patients were monitored in ICU with the same monitoring parameters used during surgery. Extubation was accomplished once the patient fulfilled the extubation criteria (adequate level of consciousness, normothermia, hemodynamic stability, minimal inotropic support, absence of significant bleeding, adequate spontaneous respiration and acceptable arterial blood gases). Postoperative pain was assessed for 24 h after extubation using 10 points modified objective pain score (MOPS) [11]. All patients received a standard protocol of multimodal analgesia in the form of paracetamol 15mg/kg/8h and intravenous ibuprofen 10mg/kg/6h. Fentanyl 1μg/kg was given as a rescue analgesic when MOPS was more than 3.

The primary outcome measure was the 24h post-extubation fentanyl consumption. The secondary outcome measures were total intraoperative fentanyl consumption, postoperative pain score at rest, time to extubation measured after ICU arrival, time to the first rescue analgesia measured after extubation, ICU length of stay, and the incidence of TRLB complications (hypotension, pneumothorax, vascular or neurological injury, local anesthetic toxicity). The incidence of other complications (vomiting and pruritus) was also reported. Postoperative pain (MOPS) was assessed during rest at 0, 2, 4, 8, 12, 16, 24 h after extubation.

Sample size and statistical analysis
The sample size was calculated using PASS version 15.0.5 software for Windows (PASS, LLC, Kaysville, UT, USA) using a superiority test for the difference of two means. This study was designed as a superiority trial. Because there is no previous similar study, we calculated the sample size using the results of our pilot study that included 6 patients in each group (not included in this study). The mean±SD 24h post-extubation fentanyl consumption of our pilot study was 7.5±2.4 μg/kg in the TRLB group and 13±4.3 μg/kg in the control group. Group sample sizes of 25 and 25 achieve 80% power to detect superiority using a one-sided, two-sample t-test. The margin of superiority was 3 μg/kg. The true difference between the means was assumed to be 5.5 μg/kg. The significance level (alpha) of the test was 0.05. The data were drawn from populations with standard deviations of 2.4 and 4.3. The final sample size was increased to 32 patients per group to compensate for the probable 20% dropouts.

The statistical analysis of all data was done using IBM SPSS 21.0 (IBM Corp., Armonk, NY, USA) software for Windows. The Shapiro–Wilk test was used to determine the normality of data distribution. Normally distributed quantitative data were represented as mean±SD and were analyzed using independent t-test. Non-parametric variables were reported as median [interquartile range (Q1, Q3)] and analyzed using Mann–Whitney U test. categorical variables were expressed in number and were analyzed using Chi-Square test. The statistical analysis was performed by the comparison between the TRLB group and the control group. P < 0.05 indicates the statistical significance at the 95% confidence interval.
Results

Sixty-six patients were recruited, of whom 8 patients were excluded due to either refusal of their legal guardians (n=3) or the patients did not fulfill the inclusion criteria (n=5) (Fig.3). One patient in the control group lost to follow up due to re-exploration because of postoperative surgical bleeding. Fifty-seven patients completed the final analysis, 29 patients in the TRLB group and 28 patients in the control group (Fig.3).

There were no significant differences between the TRLB group and the control group in terms of patients and surgical characteristics (Table 1).

The comparison of analgesic profiles between the two study groups is shown in Table 2. The mean±SD total intraoperative fentanyl requirements (μg/kg) and the 24h post-extubation fentanyl consumption (μg/kg) were significantly lower (P<0.001) in the TRLB group (9.3±1.2 & 6.9±2.1 respectively) than the control group (12.5±1.4 & 16.6±2.8 respectively). The median (Q1, Q3) time (h) of the first rescue analgesia was significantly longer (P<0.001) in the TRLB group (7 [5–8]) than the control group (2 [1–2]). The median (Q1, Q3) time (h) of extubation and the mean±SD time (h) of ICU length of stay were significantly shorter (P<0.001) in the TRLB group (2 [1–3] & 23.8±3.2 respectively) in comparison with the control group (6 [4.5–6] & 30.3±3.2 respectively) (Table 2). There were no reported complications related to the TRLB (hypotension, pneumothorax, vascular or neurological injury, local anesthetic toxicity) (Table 2). There was no significant difference between the control and TRLB group as regard the incidence of vomiting and pruritus.

The comparison of MOPS between the TRLB group and the control group is shown in Figure 4. Postoperative pain score (MOPS) was significantly lower (P<0.05) in the TRLB group than the control group at the following time points, 0, 2, 4, 8, 12 and 16 hours after extubation. At 24 h after extubation, MOPS in the TRLB group was similar to that of the control group.
**Discussion**

In this randomized controlled superiority study, we examined 66 patients for eligibility, of whom 9 patients were excluded or lost to follow-up and the final analysis was performed on 57 patients (29 in the TRLB group and 28 in the control group). The main results of our study demonstrate that bilateral ultrasound-guided TRLB is associated with decreased perioperative fentanyl consumption, post-extubation pain scores, time to first analgesic request, time to extubation and ICU length of stay.

Pediatric open cardiac surgery causes moderate to severe postoperative pain that arises mainly from the median sternotomy incision and to a lesser extent the sites of drainage tubes [12]. An appropriate multimodal analgesic regimen including a regional anesthetic technique is usually used to control pain after cardiac surgery. Recently, most anesthetists prefer the use of ultrasound-guided muscle plane blocks instead of spinal, caudal, epidural and paravertebral analgesia to avoid the probable risk of epidural hematoma after full heparinization [3,4]. Bilateral ultrasound guided erector spinae plane block [13-15] and transversus thoracis muscle plane block [16,17] are associated with effective postoperative analgesia after pediatric cardiac surgery. The present study is the first to use bilateral TRLB for analgesia after cardiac surgery via midline sternotomy incision.

The retrolaminar block is simple and easy to perform fascial plane block that involves the deposition of local anesthetics between the posterior surface of the thoracic vertebral lamina and the overlying paraspinal muscles [18]. In this study we injected a relatively large volume of 0.25% bupivacaine (0.4mL/kg) because the distribution of local anesthetics and the analgesic efficacy of TRLB is a volume dependent [19]. The injectate increase the pressure in the non-compliant retrolaminar space allowing the ventral spread of local anesthetics into the paravertebral and the epidural spaces to block dorsal and ventral rami of spinal nerves. The injectate spreads also laterally in the fascial plane along the ventral surface of erector spinae muscle to block the cutaneous and
small branches of intercostal nerves producing analgesia of the hemithorax [5]. Actually, the exact mechanism of TRLB analgesia is still not completely known. We postulated that the principal mechanism of TRLB analgesia is the spread of the injected local anesthetics to the paravertebral and epidural spaces producing analgesia similar to or less that of the paravertebral block.

Several previous studies have demonstrated the analgesic efficacy of TRLB. Nobukuni K et al. compared the postoperative analgesic efficacy of TRLB and thoracic epidural analgesia after video assisted thoracoscopic surgery and they found that TRLB was effective as epidural analgesia in controlling the postoperative pain in terms of pain scores and opioid consumption [20]. Sotome S et al. found that the postoperative analgesia of TRLB is equivalent to that of the erector spinae plane block after breast surgery [21]. Zhao Y et al. found that the analgesic effects of TRLB were superior to that of the erector spinae block in patients with multiple rib fractures [22]. Wang Q et al. compared ultrasound-guided TRLB and paravertebral block for postoperative analgesia in patients undergoing video-assisted thoracoscopic surgery and they found that the paravertebral block produced better analgesia than TRLB [23]. In contrast to our findings, Hwang BY et al. in their randomized placebo study that aimed at assessing the analgesic efficacy of a single injection of ultrasound-guided TRLB after breast surgery reported that TRLB did not reduce postoperative analgesic consumption [24]. We postulated that the reason for the lack of efficiency of TRLB in reducing opioid consumption after radical mastectomy could be attributed to the complexity of the surgery that includes axillary lymphadenectomy.

In our study, TRLB was associated with reduced time to extubation and ICU length of stay. This is in agreement with other chest wall fascial plane blocks including bilateral erector spinae plane block [13-15] and transversus thoracis muscle plane block [16,17]. This can be explained by the reduction in the perioperative opioid consumption. Shortening the time to extubation and ICU stay allow fast track cardiac surgery, decreased costs and save resources.
In this study, the TRLB complications (hypotension, pneumothorax, vascular or neurological injury, local anesthetic toxicity) were not reported. Ultrasound-guided TRLB is simple, easy to perform and theoretically is safer than thoracic epidural analgesia and paravertebral block. The way of the block needle toward the vertebral lamina is away from any important vessels, the pleura and dura. The sonographic visualization of the block needle is better in children than adults.

Our study has several limitations. First, the sample size was small in this single-center study and we cannot determine the actual incidence of the complications of TRLB. Multicenter studies with large sample sizes are recommended in the future. Second, we didn’t assess the dermatomal spread of TRLB because we performed the TRLB in children after the induction of anesthesia. Further studies in awake adults are required. Third, the smallest effective volume of the local anesthetic is unknown; we used a relatively large volume (0.4mL/kg) of 0.25% bupivacaine to ensure the efficacy of the block. Fourth, a single injection of a local anesthetic was used in this study which resulted in a limited duration of analgesia; therefore, continuous infusion of local anesthetics is recommended in the future studies to get more prolonged analgesia. Finally, we did not measure the serum concentration of the bupivacaine because this is not available in our institutional hospital.

From the findings of this study, we can conclude that, ultrasound-guided bilateral TRLB performed at the level of the fourth thoracic vertebra is effective in providing postoperative analgesia in terms of opioid consumption and postoperative pain score in children undergoing open cardiac surgery via median sternotomy incision. Additionally, TRLB is associated with early tracheal extubation and short ICU length of stay.
References


Table 1. Patients and surgical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>TRLB group (n=29)</th>
<th>Control group (n=28)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>4.2 [2.9–6.7]</td>
<td>3.9 [3.2–5.7]</td>
<td>0.481</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>13/16</td>
<td>12/16</td>
<td>0.881</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>14.5±3.2</td>
<td>13.7±3.1</td>
<td>0.380</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>105±13</td>
<td>101±12</td>
<td>0.343</td>
</tr>
<tr>
<td>BSA (m2)</td>
<td>0.6±0.08</td>
<td>0.56±0.08</td>
<td>0.146</td>
</tr>
<tr>
<td>Aortic clamp time (min)</td>
<td>35 [22–43]</td>
<td>34 [23–40]</td>
<td>0.987</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>56±11</td>
<td>58±8</td>
<td>0.423</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>194±21</td>
<td>196±19</td>
<td>0.615</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD repair</td>
<td>12</td>
<td>9</td>
<td>0.765</td>
</tr>
<tr>
<td>ASD repair</td>
<td>15</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>CAVC repair</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Data are represented as median (Q1, Q3), number of patients and mean±SD. Thoracic retrolaminar block; BSA: body surface area; CPB: cardiopulmonary bypass; VSD: ventricular septal defect; ASD: atrial septal defect; CAVC: common atroventricular canal.
Table 2. Intraoperative fentanyl consumption and postoperative variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>TRLB group (n=29)</th>
<th>Control group (n=28)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative fentanyl consumption (μg/kg)</td>
<td>9.3±1.2</td>
<td>12.5±1.4</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Time to extubation (h)</td>
<td>2 [1–3]</td>
<td>6 [4.5–6]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Time to first rescue analgesia after extubation (h)</td>
<td>7 [5–8]</td>
<td>2 [1–2]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>24 h post-extubation fentanyl consumption(μg/kg)</td>
<td>6.9±2.1</td>
<td>16.6±2.8</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>ICU length of stay (h)</td>
<td>23.8±3.2</td>
<td>30.3±3.2</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TRLB complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Vascular, neurological injury</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Local anesthetic toxicity</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>6 (20.6)</td>
<td>8 (28.2)</td>
<td>0.550</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (24.1)</td>
<td>8 (28.5)</td>
<td>0.770</td>
</tr>
</tbody>
</table>

Data are represented as mean±SD, median (Q1, Q3), number (%) of patients. TRLB: Thoracic retrolaminar block; ICU: intensive care unit. *p<0.05 is statistically significant.
Figure legends

Fig. 1. Ultrasound image of thoracic retrolaminar block.
Fig. 2. (A) Sternotomy incision, (B) The sites of drainage tubes.
Fig. 3. Study flowchart. TRLB: thoracic retrolaminar block.
Fig. 4. Postoperative modified objective pain score (MOPS). Data are represented as median (Q1, Q3). The thick black line in the boxplot represents the median, the upper border represents Q3 and the lower border represents Q1. *p<0.05, †p<0.001 vs. TRLB group are statistically significant.