Effect of Continuous Paravertebral Dexmedetomidine Administration on Intraoperative Anesthetic Drug Requirement and Post-Thoracotomy Pain Syndrome After Thoracotomy: A Randomized Controlled Trial

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Objectives: **To assess the effect of paravertebral administration of dexmedetomidine as an adjuvant to local anesthetic on the intraoperative anesthetic drug requirement and incidence of post-thoracotomy pain syndrome.**

Design: **Prospective, randomized, controlled, double-blind trial.**

Setting: **Single university hospital.**

Participants: **The study comprised 30 patients who underwent elective thoracotomy and were assigned randomly to either the Ropin or Dexem group (n = 15 each).**

Interventions: **All patients received the study medications through paravertebral catheter. Patients in the Ropin group received a bolus of 15 mL of 0.75% ropivacaine over 3-to-5 minutes followed by an infusion of 0.2% ropivacaine at 0.1 mL/kg/hour. Patients in the Dexem group received 15 mL of 0.75% ropivacaine plus dexmedetomidine, 1 μg/kg bolus over 3-to-5 minutes followed by an infusion of 0.2% ropivacaine plus 0.2 μg/kg/hour of dexmedetomidine at 0.1 mL/kg/hour.**

Measurements and Main Results: **The primary outcome of the study was intraoperative anesthetic drug requirement. The secondary outcome was the incidence of post-thoracotomy pain syndrome 2 months after surgery. The amount of propofol required for induction of anesthesia was significantly less in the Dexem group (Dexem 49.33 ± 20.51 *v* 74.33 ± 18.40 in the Ropin group, p = 0.002). End-tidal isoflurane needed to maintain target entropy was significantly less in the Dexem group at all time points. Intraoperative fentanyl requirement was lower in the Dexem group (Dexem 115.33 ± 33.77 *v* 178.67 ± 32.48 in the Ropin group, p = 0.002). Postoperative pain scores and morphine consumption were significantly less in the Dexem group (p <0.001). The incidence of post-thoracotomy pain syndrome was comparable between the 2 groups (69.23% *v* 50%, p = 0.496).**

Conclusions: **Paravertebral dexmedetomidine administration resulted in decreased intraoperative anesthetic drug requirement, less pain, and lower requirements of supplemental opioid in the postoperative period. However, it had no effect on the incidence of post-thoracotomy pain syndrome.**

KEY WORDS: paravertebral block, dexmedetomidine, post-thoracotomy pain syndrome

POST-THORACOTOMY PAIN often causes alterations in chest wall mechanics and impedance of effective chest expansion and coughing. This predisposes patients to ventilation/perfusion mismatch, atelectasis, hypoxemia, infection, and delayed recovery.[1,2] Effective analgesia is essential to decrease these complications.[3] In addition, inadequately treated acute pain predisposes patients to the development of chronic pain syndrome, whereas good-quality perioperative analgesia has been demonstrated to decrease its incidence.[4,5] Thoracic epidural analgesia is considered to be the gold standard for treatment of post-thoracotomy pain. However, it may result in devastating complications, such as spinal hematoma, epidural abscess, and resulting paraplegia.[6] Recently, paravertebral blocks have been shown to be as good as or even superior to epidural analgesia for post-thoracotomy pain relief.[7,8]

Administration of dexmedetomidine as an adjuvant to local anesthetic via epidural and the paravertebral route has been shown to decrease surgical stress response, improve quality and duration of postoperative analgesia, and decrease opioid requirements with no respiratory depressant effect.[9–14] However, its use may be associated with bradycardia and/or hypotension.[14] The role of dexmedetomidine as an adjuvant to local anesthetic for paravertebral block in reducing the intraoperative anesthetic drug requirement and its effect on the incidence of post-thoracotomy pain syndrome have not been studied.

The authors hypothesized that the addition of dexmedetomidine to ropivacaine via the paravertebral route would reduce the intraoperative anesthetic drug requirement (primary outcome), improve postoperative pain scores, and reduce rescue analgesic requirement, with a resultant decrease in the incidence of post-thoracotomy pain syndrome (secondary outcome) in patients undergoing thoracotomy.

METHODS

This study was conducted at a cardiothoracic center of a tertiary care hospital from June 2014 to June 2015. Approval was obtained from the ethics committee (intramural) of the Postgraduate Institute of Medical Education and Research, Chandigarh, India (Ref. Histo/14/1771) in April 2014, and the trial was registered at ctri.nic.in (CTRI/2016/01/006565). After providing written, informed consent, 34 adults between 18 and 70 years old who were undergoing elective lung surgery via thoracotomy (anterolateral or posterolateral) were enrolled in this prospective, double-blind, randomized trial. Patients who experienced local site infection, coagulopathy, and allergy to amide local anesthetics or dexmedetomidine were excluded from the study.

All patients received oral alprazolam as a premedication on the night before and the morning of surgery. Before induction

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of anesthesia, thoracic paravertebral block was administered at the level of the surgical incision between the T4 and T6 paravertebral spaces using real-time ultrasound guidance with a 16G Toughy needle, 9L Transducer (3-10 MHz), and Vivid E9 ultrasound machine (GE Healthcare, Little Chalfont, United Kingdom), as described by Riain et al.[15] A 18G multipore epidural catheter was threaded 3 cm into the paravertebral space, and a test dose of lignocaine 2% (3 mL) with adrenalin was administered.

Patients were allocated randomly into 1 of 2 groups using a computer-generated random number and sealed envelope method. Patients in the Ropin group received a bolus of 15 mL of 0.75% ropivacaine over 3 to 5 minutes, followed by an infusion of 0.2% ropivacaine at 0.1 mL/kg/hour. Patients in the Dexem group received 15 mL of 0.75% ropivacaine plus dexmedetomidine, 1 μg/kg bolus over 3 to 5 minutes followed by an infusion of 0.2% ropivacaine plus 0.2 μg/kg/hour of dexmedetomidine at 0.1 mL/kg/hour. The level of sensory block was assessed using the cold (ice) sensation test 15 minutes after administration of the paravertebral block and after arrival in the intensive care unit (ICU) at a predefined interval. Paravertebral infusion was stopped and the catheter was removed 72 hours after surgery. The study drugs were prepared in a 50-mL identical syringe by a person not involved in the study. The anesthesiologists involved in the intraoperative management were blinded to the group allocation of the patients.

Anesthesia was induced using fentanyl and titrated doses of propofol. Vecuronium was used as the muscle relaxant to facilitate endotracheal intubation. Maintenance of anesthesia was achieved using inhalation administration of isoflurane and air/oxygen mixture. The depth of anesthesia was monitored using entropy (GE Datex-Ohmeda Entropy Module; GE Healthcare). Target state entropy between 40 to 60 was achieved by changing the dial setting of isoflurane vaporizer.

The heart rate (HR), arterial oxygen saturation, invasive arterial blood pressure, and central venous pressure were monitored throughout the surgery and in the postoperative period. Fentanyl boluses were administered if the difference between state and response entropy was more than 20 or if mean arterial blood pressure (MAP) and HR exceeded more than 20% of the baseline value for more than 30 seconds despite maintaining target entropy. Hypotension was defined as a decrease in MAP 20% below the baseline or MAP <60 mmHg that persisted for more than 30 seconds. Hypotension was treated with 250-mL boluses of normal saline to maintain central venous pressure 6-to-8 mmHg. Persistent hypotension refractory to fluid administration was managed using boluses of 0.1 mg/kg of mephentermine. Bradycardia was defined as a fall in HR <60/min and was treated with atropine, 0.6 mg.

Administration of inhalation isoflurane was discontinued at the time of the last skin suture. At the end of the procedure, neuromuscular block was reversed with equivalent doses of neostigmine and glycopyrrolate. Patients' airways were extubated after standard extubation criteria were fulfilled, and the patients were transferred to the ICU. All patients were observed for 24 hours in the ICU. A nurse blinded to group allocation assessed the pain scores in the ICU using the visual analog scale (VAS) (0-10), 0 meaning no pain and 10 meaning worst pain. A rescue analgesic (intravenous morphine, 3 mg) was administered to maintain VAS ≤ 4. The patient's level of sedation was assessed using the Observer's Assessment of Alertness/Sedation (OAA/S) scale,[16] with a score of 5 being fully awake and a score of 1 being asleep or unarousable. A patient's satisfaction with the analgesic technique was assessed by the ICU nurse 24 hours after the surgery and at the time of paravertebral catheter removal using the VAS scale (0-10), 0 being unsatisfied and 10 being fully satisfied.

Hemodynamic parameters—HR and blood pressure—were recorded at baseline, before administration of paravertebral block, at 1-minute intervals until 5 minutes after the block, before skin incision, at 1-minute intervals 5 minutes after skin incision, and at 15-minute intervals thereafter until the end of the procedure. In the postoperative period, hemodynamic parameters, pain scores using the VAS scale, and sedation scores using the OAA/S scale were noted at 1, 2, 3, 4, 8, 12, 16, 20, and 24 hours after surgery.

The incidence of post-thoracotomy pain syndrome was assessed 2 months after surgery during a follow-up visit, by telephonic interview, or through response of a letter to determine whether patients still were experiencing post-surgical pain and whether any pain interfered with their daily routine of activity. The severity of pain was assessed using a 10-point VAS score.

Statistical Analysis

Statistical analysis was performed with SPSS Statistics, Version 15.0 (SPSS Inc, Chicago, IL). The mean or medians were calculated for quantitative variables. For measures of dispersion standard deviation or interquartile range were calculated. Normality of quantitative data was checked using the Kolmogorov-Smirnov test. For normally distributed data, means of 2 groups were compared using the *t*-test. For skewed or ordinal data, the Mann-Whitney *U*-test was used. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using the chi-square or Fisher exact test, whichever was applicable. All statistical tests were 2-sided and performed at a significance level of $\alpha = 0.05$. Sample size calculation was performed using an online power sample size calculator based on a previous study that demonstrated a decrease in end-tidal sevoflurane requirement (0.5 ± 0.2 in the dexmedetomidine group *v* 1.3 ± 0.2 in the control group) after caudal dexmedetomidine administration.[17] To detect a 50% change in anesthetic requirement with a standard deviation of 0.2, the sample size was determined to be 12 per group at a power of 80% and confidence interval of 95%. To adjust for possible dropouts, the authors enrolled a total of 34 patients.

RESULTS

Of 50 patients screened for enrollment, 34 were enrolled in the study, and of those, 4 were excluded due to failed paravertebral block (catheter found in pleural cavity). The remaining 30 patients (10 females and 20 males) were assigned to a treatment group and completed the study (Fig 1). The type of surgery and location of the thoracotomy incision site are