A Comparison between dexmedetomidine and fentanyl as adjuvants to thoracic epidural in patients undergoing thoracotomy surgery: A randomized controlled trial

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Introduction:

Thoracotomy surgeries are associated with painful surgical incisions which increase the need for intraoperative and postoperative analgesia. Thoracic epidural analgesia (TEA), when combined with general anesthesia, provides good intraoperative and postoperative pain relief, and also facilitates deep-breathing exercises and early ambulation. (1) Opioids, such as fentanyl, have traditionally been used as adjuvants for epidural administration in combination with local anesthetics to achieve the desired analgesic effect. [2] The addition of opioids provides superior analgesia and prolongs the duration, but there is always a possibility of an increased incidence of pruritus, urinary retention, nausea, vomiting and respiratory depression. [3, 4]
Recently α2 -agonists have shown promise as an adjuvant to local anesthetics in epidural anesthesia. (5−6) Dexmedetomidine, a highly selective α2 -adrenoreceptor agonist, has effective analgesic and sedative properties (7, 8) and lacks opioid-related side effects. (9) One study compared the analgesic efficacy of dexmedetomidine versus fentanyl as an adjuvant for thoracic epidural combined with general anesthesia in patients undergoing upper abdominal surgery (10). Moreover, another study compared the analgesic efficacy of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. (11) These studies show that Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides effective perioperative analgesia, prolonged post-op analgesia, lower consumption of rescue analgesia during the postoperative period, and much better sedation levels.
However, the use of dexmedetomidine in thoracic surgery has not been well investigated.

In this study, we aim to compare the analgesic efficacy of bupivacaine with dexmedetomidine versus bupivacaine with Fentanyl administered in epidural anesthesia in patients undergoing thoracotomy surgery under general anesthesia.

Aim of the work:

This thesis aims to investigate whether the addition of dexmedetomidine to epidural bupivacaine provides effective intraoperative analgesia comparable to fentanyl.

Objectives:

To find out if there is a benefit from adding dexmedetomidine to epidural bupivacaine as regards:

- Intra and postoperative opioid consumption
- Pain score (numerical rating scale)
- Hemodynamic stability,
- Patient satisfaction.

Hypothesis:

We hypothesize that adding dexmedetomidine to bupivacaine in thoracic epidural would lead to better intraoperative and postoperative analgesia compared to fentanyl, with fewer side effects.

Ethical Considerations:

The study will be conducted after taking approval of research ethical committee; Informed consent will be obtained from the patients. Documentation of any motor or neurological deficit if present.

Methodology

- ### Study design
  This is a randomized controlled, double-blinded study.

- ### Study setting and location
  The study will be conducted at Cairo University Hospital – cardiothoracic surgery unit.

Study population

Participants will be adult patients, ASA I, II, and III, scheduled for thoracic surgeries with posterolateral thoracotomy.

Eligibility Criteria

Inclusion criteria:

- Age 18 – 60 years old
- ASA physical status I-II-III
- Good mental function.
- Patient scheduled for thoracic surgery with posterolateral thoracotomy.
- BMI of patient (18 – 30).

Exclusion criteria:

- Age less than 18 or more than 60 years old
- Any contraindications to epidural injection (patient refusal, local infection at the site of injection, coagulopathy, patients on anticoagulant or antiplatelet drugs, known allergy to local anesthetics, significant spine deformity)
- Inability to provide informed consent or pain score

Study Procedures

Randomization

Patients will be randomly allocated by a computer-generated table into one of the study groups; the randomization sequence will be concealed in sealed envelopes. Patients and data collector will be blinded to group assignment.

Study Protocol

Following approval from Research Committee of Anesthesia Department and the Ethics Committee of the Faculty of Medicine, Cairo University, 50 patients will be included in the study (25 patients per group). After obtaining written informed consents, all patients will be subjected to systematic preoperative assessment including history taking, physical examination, and review of the results of routine investigations. Upon arrival to the preparation room, a 20G IV cannula will be inserted into a peripheral vein and midazolam 2-3 mg will be administered unless contraindicated. A 20G arterial catheter will be inserted into the radial artery of the dependent (non-operative) side, after local infiltration with lidocaine 2%. Patients will be transferred to the operating room where routine monitoring is applied, including electrocardiography (ECG), invasive Blood Pressure (IBP) and pulse oximetry are attached. Baseline heart rate, blood pressure, oxygen saturation and respiratory rate will be recorded.

A thoracic epidural catheter will be inserted at the T6- T7 intervertebral space, with the patient in the sitting position with standard aseptic precautions using an 18-G Touhy needle via a midline or paramedian approach with a loss of resistance method. A test dose of 3 ml of 2% lignocaine with adrenaline 5 µ/ml will be administered.

For thoracic surgery the sensory dermatome blockade needs to cover the incision and intercostal drains and may extend from T4 to T8.

The epidural drug will be administered according to the group allocation over a period of 10 minutes as follows:

Group A:

Patients will receive 50 µg dexmedetomidine with 10 ml of 0.125% bupivacaine followed by a continuous infusion of (10 ml bupivacaine + 25 µg dexmedetomidine + 39 ml saline with rate of 5 ml per hour).

Group B:

Patients will receive 50 µg fentanyl in addition to 10 ml 0.125% bupivacaine followed by a continuous infusion (10 ml bupivacaine + 100 µg fentanyl + 38 ml saline with rate of 5 ml per hour).

After documenting the sensory blockade by using a piece of ice or cold object,

If sensory level fail to be achieved, patient will be out of the study.

Anesthesia will be induced with Propofol 2–3 mg/kg, together with fentanyl 2 mg/kg until loss of verbal response. Muscle relaxation will be achieved with atracurium 0.5 mg/kg and the patient's trachea will be intubated using a single or double-lumen tube, as indicated by the surgical procedure. Anesthesia will be maintained by isoflurane, and muscle relaxation will be maintained with atracurium 0.3 – 0.5 mg/kg/hr.

The lungs will be ventilated with positive pressure ventilation to maintain end-tidal carbon dioxide (EtCO2) between 32 and 36 mmHg. Patients' heart rate, blood pressure will be monitored continuously and recorded at ten-minute intervals until the end of surgery. Any attack of hypotension, defined as a drop of > 20% of baseline blood pressure, will be managed by ephedrine 0.2 mg/kg IV, and administering I.V. fluids. On the other hand, hypertension, defined as an increase of > 20 % of baseline blood pressure, will be managed by increasing the depth of anesthesia and administering bolus doses of fentanyl 1 mic/kg (up to 3 mic/kg maximum dose).

Bradycardia (heart rate < 50 beats/min) will be managed by atropine 0.02 mg/ kg IV

At the end of surgery residual neuromuscular blockade will be reversed and the endotracheal tube will be removed. Patients will be transferred to the ICU and will be monitored for 24 hours. Patients' heart rate, blood pressure, oxygen saturation and respiratory rate will be monitored at regular intervals and the pain score and sedation level as well.

Epidural infusion will be continued with the same infusion rate. A fixed dose of paracetamol (10 – 15 mg/kg) every 8 hours and NASID (0.5 – 2/kg/ day divided in 2 doses will be administered I.V.

Pain will be assessed using the **numerical rating scale (NRS)** and if the pain score is more than 3, 3mg morphine I.V. will be administrated intra venous as rescue analgesia (up to .4 mg/kg morphine maximum dose every 24 Hours).

Side effect of drugs may appear like
(Nausea, vomiting that will managed by antiemetic drugs , Shivering will be managed by 25 mg Pethidine , Hypotension will manage by ephedrine 0.2 mg/kg IV, and administering I.V. fluids).

Measured Parameter

1. Demographic data of the patient (Age, Sex, Weight, Height).
2. Hemodynamic parameters (heart rate, systolic diastolic, and mean arterial blood pressure) will be recorded at baseline (before epidural analgesia), ten and twenty minutes after epidural activation, immediately after induction, and every 10 minutes till end of surgery.
3. Total intraoperative fentanyl consumption
4. Total postoperative morphine consumption
5. Postoperative pain score (numerical rating scale (NRS))
6. Patient satisfaction.
7. Sedation Score (The Modified Ramsay Sedation Score).
8. Time to ambulation
9. Incentive spirometry (It will measure the total amount that you were able to exhale, called the forced vital capacity (FVC), as well as how much was exhaled in the first second, called the forced expiratory volume in 1 second (FEV1).
10. The incidence of side effects (nausea, vomiting, shivering, hypotension, dizziness, dry mouth, and respiratory depression)
11. Time for the first analgesia

VI. Study outcomes

Primary outcome

Total morphine consumption in the first 24 hours.

Secondary outcomes

- Hemodynamics parameters (systolic and Diastolic blood pressure, Mean blood pressure, Heart rate) will be recorded at baseline (before epidural analgesia), ten and twenty minutes after epidural activation, immediately after induction, and every 10 minutes till end of surgery).

- Total intra operative fentanyl consumption.
- Pain score (numerical rating scale (NRS))
- Sedation score (The Modified Ramsay sedation score).
- Patient satisfaction after the procedure
- The incidence of side effects (nausea, vomiting, shivering, hypotension, dizziness, dry mouth, and respiratory depression)
- Time to the first analgesia request.

Statistical Analysis:

1. Sample size:

Based on a previous study (12) the total morphine consumption for rescue analgesia in patients receiving thoracic epidural after thoracotomy was 9.6 ± 4.3 mg/24 hours. Sample size calculation yielded a total number of 44 patients to detect a difference of 30% between the two groups with a power of 80% and an alpha error of 0.05. The number was increased to 50 patients (25 patients/group) to compensate for possible dropouts.

2. Statistical analysis:

Data will be summarized as mean ± SD, median (range), or frequency (%) as appropriate. Categorical variables will be analyzed using the Chi squared or Fisher's exact test. Intragroup comparisons will be analyzed using ANOVA with repeated measures. Comparisons between the two groups will be made using the unpaired *t*-test or the Mann-Whitney U-test as appropriate. A *p*-value <0.05 will be considered statistically

significant.

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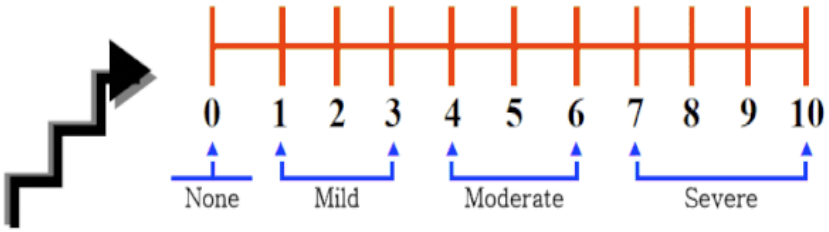
Appendix:

Numerical rating scales (NRS)



The-Modified-Ramsay-Sedation-Score

Score	Definition
1	Awake and alert, minimal or no cognitive impairment
2	Awake but tranquil, purposeful responses to verbal commands at conversation level
3	Appears asleep, purposeful responses to verbal commands at conversation level
4	Appears asleep, purposeful responses to verbal commands but at louder than usual conversation level or requiring light glabellar tap
5	Asleep, sluggish purposeful responses only to loud verbal commands or strong glabellar tap
6	Asleep, sluggish purposeful responses only to painful stimuli
7	Asleep, reflex withdrawal to painful stimuli only (no purposeful response)
8	Unresponsive to external stimuli, including pain

Patient satisfaction score:

How satisfied are you with the result of your anesthesia?

5	Very satisfied
4	Somewhat satisfied
3	Neither satisfied nor dissatisfied
2	Somewhat dissatisfied
1	Very dissatisfied

We will calculate patient satisfaction scores from answers to previous Questions to range between (1) to (5).