PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF MASTER'S DEGREE IN ANESTHESIOLOGY, INTENSIVE CARE AND PAIN MANAGEMENT

Title of the Protocol

Ultrasound-Guided Modified Pectoral Plane (PECS II) Block versus Erector Spinae Plane Block (ESPB) for Postoperative Analgesia of Modified Radical Mastectomy

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What is already known on this subject? What does this study add?

Modified Radical Mastectomy (MRM) is a surgical procedure that removes the entire breast, including the skin, breast tissue, areola, and nipple, along with most of the axillary lymph nodes. However, most of the chest muscles are left intact. It is a less invasive surgery than a radical mastectomy, which also removes the chest muscles. It is a standard option for treating breast cancer that has spread to the axillary lymph nodes.

Postoperative pain in MRM is a common problem that can affect the quality of life and recovery of patients. Postoperative pain management is becoming an integral part of anesthesia care. Optimal pain control in patients undergoing MRM is imperative for good rehabilitation and functional outcomes. Current modalities in use aim to reduce postoperative opioid consumption to control postoperative pain thus minimizing its side effects in what is recently known as multimodal analgesia techniques.

Regional blocks have been introduced for postoperative pain relief such as thoracic epidural block (TEB), thoracic paravertebral block (TPVB) and intercostal blocks. The use of ultrasound guidance has much improved the success rate of the nerve blocks and the development of new techniques.

Newer pain control modalities have been used providing adequate pain relief, not affecting muscle strength and utilized as excellent solutions for multimodal analgesia peri-operatively. Examples of these modalities are serratus anterior plane (SAP) block, pectoral nerve (PECS) block and erector spinae plane block (ESPB).

In this study we will compare the analgesic efficacies of modified pectoral plane (PECS II) block versus erector spinae plane block (ESPB) after MRM surgery.

1. INTRODUCTION / REVIEW:

Breast cancer (BC) is the most common type of female cancer in Egypt with an age-specific incidence rate of 48.8/100,000. Although incidence rate in Egypt is lower than the global figures, mortality is higher at an age-standardized rate of 20.4/100,000 compared with the US rate of 12.3/100,000 and the developed countries' rate of 12.8/100,000 ***(Sung et al., 2021) (Globocan, 2020)***.

It is the most commonly diagnosed cancer worldwide, with estimated new cases exceeding 2 million in 2020. Furthermore, it represents the leading cause of cancer death in women, with more than 680,000 deaths ***(Sung et al., 2021)***.

During MRM, some of the nerves in the chest are affected so most women have some level of pain in the days after the procedure. Severe acute postoperative pain following breast surgery is an independent risk factor in the development of chronic post-mastectomy pain ***(Bakeer et al., 2020)***, not only increasing the risk of persistent agony and prolongs hospitalization, it also affects recovery and increases healthcare costs ***(Deng et al., 2020)***.

Multimodal techniques for pain management have been recommended by the American Society of Anesthesiologists (ASA) for the management of acute postoperative pain ***(Apfelbaum et al., 2012) (Nagaraja et al., 2018)***. These techniques include oral analgesics as opioids, paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) ***(Nagaraja et al., 2018)***, intravenous (IV) and regional analgesia. Inappropriate postoperative analgesia may increase morbidity and mortality ***(Blanco R, 2011)***.

PECS-II block is an interfascial plane block in which local anesthetic is injected between serratus anterior and pectoralis muscles that blocks the pectoral nerve as well as the long thoracic, intercostobrachial and lateral cutaneous branches of the inter-costal III, IV, V, and VI nerves. PECS-II is a less invasive and easier to be performed alternative to thoracic paravertebral block (TPVB). This block, defined by ***Blanco et al.***, provides safe and adequate post-operative analgesia in the anterior chest wall after breast surgery. The most common complications are pneumothorax, vascular puncture, infection, local anesthetic systemic toxicity (LAST), allergy and failed block ***(Blanco et al., 2012) (Wang et al., 2018)***.

ESPB is a paraspinal fascial plane block in which local anesthetic is injected between the tip of the transverse process of the spine and the anterior fascia of the erector spinae muscles blocking the dorsal and ventral rami of the spinal nerves, as well as the sympathetic chain, resulting in analgesia of chronic thoracic neuropathic pain, breast and upper abdominal surgeries. The block, defined by ***Forero et al.***, can cover several spinal nerve levels above and below the injection site as the local anesthetic spreads along the fascial plane, depending on the volume and concentration of the local anesthetic ***(Forero et al., 2016) (Bonvicini et al., 2017) (Chin et al., 2017)***. The main advantages of this technique include the ease of performing it, the analgesic efficacy and the low risk of complications as Pneumothorax, hemi-diaphragmatic paralysis, motor weakness, and neurological findings related to local anesthesia toxicity ***(Tulgar et al., 2019)***.

2. AIM / OBJECTIVES:

This study aims to compare the analgesic efficacies of the modified pectoral plane block (PECS II) and the erector spinae plane block (ESPB) after modified radical mastectomy surgery.

3. METHODOLOGY: Patients and Methods

- **Type of Study:** Prospective randomized comparative clinical study.
- **Study Setting:** Ain Shams University Hospitals, Cairo, Egypt.
- **Study Period:** 6 months to 12 months, starting from approval of the protocol, both from scientific and ethical committee.
- **Study Population:**

- **Inclusion Criteria:**

1- Female patients scheduled for MRM.

2- Age eligible ≥ 40 & ≤ 65 yrs.

3- Patients with American Society of Anesthesiologists (ASA) physical status I, II who will be scheduled for MRM surgery.

- **Exclusion Criteria:**

1- Age < 40 & > 65 years old.

2- Declining to give written informed consent.

3- History of allergy to the medications used in the study.

4- Contraindication to regional anesthesia [including coagulopathy (platelet count ≤ 80,000, INR ≥ 1.5) and local infection].

5- Severe hepatic impairment (INR ≥ 1.5, Bilirubin ≥ 2, Albumin ≤ 2).

6- Renal dysfunction [GFR < 50 ml/min calculated by MDRD (Modification of diet in renal disease) equation for GFR estimation ***(Livio et al., 2008)***].

7- Psychiatric disorder.

8- Pregnancy.

9- Patient with history of thoracic spine surgery.

- **Sampling method:** Simple random sampling.
- **Sample Size:**

Using PASS 15 program for sample size calculation, setting power at 90% and alpha error at 0.05 and according to "***Bakeer & Abdallah, 2022***", the expected median VAS score 1-hour post-operative in PECS II group = 1(1-2) and in ESPB group= 2(1-3). Sample size of 10 patients per group will be needed to detect the difference between two groups.

- **Ethical consideration:**

Patient informed written consent and approval of the Research Ethical Committee of the Faculty of Medicine; Ain Shams University will be obtained before patient's allocation.

- **Study procedures:**

- **Preoperative settings:**

All patients will be assessed preoperatively by careful history taking, full physical examination, laboratory evaluation and other appropriate investigations.

At the preoperative visit, all patients will be instructed on how to evaluate their own pain by using a 10-cm visual analogue pain scale (VAS) (0 = no pain, 10 = maximum pain imaginable).

The nerve block will be performed in the preoperative block area following standardized monitoring, including non-invasive blood pressure (BP), electrocardiogram (ECG), and pulse oximetry (PO). Oxygen 2–3 L/min will be applied through the nasal cannula and IV midazolam 0.025 mg/kg will be given and dose may be repeated every 3-5 minutes until

sedation is adequate and patient still arousable up to 20 mg ***(Pedro et al., 2022)***. All blocks will be performed by the same two experienced senior attending doctors in ultrasonic-guided nerve blocks. Patients will be randomly divided according to a computer-generated random number table into two groups:

- Group 1 (**PECS II group**): patients will receive ultrasound guided PECS II block (10 patients).
- Group 2 (**ESPB group**): patients will receive ultrasound guided erector spinae plane block (10 patients).

Both blocks will be performed under complete aseptic precautions using ultrasound machine with high-frequency linear probe covered with sterile sheath (Sonosite M-turbo c, Bothell, Washington, USA) and linear ultrasound probe (2.5-7.5MHz) and a 22G 100 mm echogenic needle (B-Braun Medical Inc., Bethlehem, PA, USA) which will be inserted after standard skin disinfection and infiltration of 2 millilitres (mL) lidocaine 2% subcutaneously.

Pre-operative chest ultrasound will be done by the anesthesiologist to detect complications after puncturing of the blockade (hematoma in the puncture site by direct visualization and pneumothorax by Barcode/Stratosphere sign).

- **In the PECS II group: -**

The patient will lay supine with the ipsilateral arm abducted and externally rotated and the elbow flexed at 90 degrees. The high-frequency linear probe will be placed transversely between the clavicle medially and above and the shoulder joint laterally. After identifying the pectoralis major and minor muscles and the plane between them, the probe will be angled caudally to look for the pulsating pectoral branch of the thoraco-acromial artery; if it couldn't be found, the probe will be pushed 1-2 cm caudally and medially. In a caudal tilt, within a biconvex space, the artery will be recognised. After that, the block needle will be inserted in an in-plane approach to the artery's location and 10 mL of 0.25% bupivacaine will be administered ***(Pani et al., 2019)***. Then probe will be moved laterally and caudally towards the anterior axillary fold until the serratus muscle appears beneath the pectoralis minor muscle attaching to the underlying ribs. The third and fourth ribs will be detected. The needle will target the plane

between pectoralis minor and serratus muscles at the level of the third rib, followed by negative aspiration into the fascial plane then injection of 10 mL of 0.25% bupivacaine ***(Alshawadfy and Al-Touny, 2023)***.

- **In the ESPB group: -**

The block will be performed with the patient in a sitting position ***(Costache, 2016)***, The high-frequency linear probe will be placed in a longitudinal orientation 3 cm from the midline. Once the erector spinae muscle and the transverse processes identified, the block needle will be inserted in a caudad-to-cephalad direction until the tip lay in the interfacial plane deep to the erector spinae muscle, 20 mL of 0.25% bupivacaine will be administered for block performance ***(Forero et al., 2016)***.

- **Intraoperative settings:**

On arrival of the patients to the operative room, ECG, non-invasive blood pressure, pulse oximetry will be applied with capnography during ventilation till extubation. Baseline parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), heart rate (HR), and arterial oxygen saturation (SpO_2) will be also recorded.

Before surgery, 20-gauge venous access will be established in all patients, and infusion with 2-4 mL/kg/h ringer's acetate solution will be started, general anesthesia will be induced with IV injection of fentanyl (1.5 µg/kg) ***(Plaud et al., 2020)***, propofol (2 mg/kg) ***(Gelberg et al., 2014)*** and atracurium (0.5 mg/kg) ***(Plaud et al., 2020)*** in the same sequence. Endotracheal intubation will be performed, controlled mechanical ventilation will be maintained to keep the end-expiratory carbon dioxide (CO_2) values between 34 and 36 mmHg using capnography. Anesthesia will be maintained with isoflurane 1-2 MAC in 40 % oxygen in air. Incremental dose of atracurium (0.1 mg/kg) ***(Bhoi et al., 2019)*** will be given after assessment by nerve stimulator according to train of four. Granisetron 3mg ***(Dehghanpisheh et al., 2022)*** (EM-EX® ,3mg/3ml, Amoun pharmaceutical company, Cairo, Egypt) will be also administered to prevent postoperative nausea and vomiting.

Intraoperative fentanyl 0.5 µg/kg ***(Plaud et al., 2020)*** will be given if the HR or the blood pressure or both increase by >20% of the baseline. At the end of the procedure Isoflurane will be discontinued, neuromuscular blockade will be antagonized by using neostigmine 0.04 mg/kg ***(Choi et al.,***

2016) plus atropine 0.01 mg/kg ***(Elnasr et al., 2019)*** after assessment by nerve stimulator according to train of four and will be administered to reverse the effect of atracurium. After extubation, all patients will be transferred to the post-anesthesia care unit (PACU).

- **Postoperative settings:**

During the first 24 hr after surgery, Postoperative pain will be evaluated by VAS score at 0 point (on admission to the PACU), 2, 4, 8, 16 and 24 hours postoperatively and increments of intravenous meperidine 0.5 mg/kg ***(Friesen et al., 2016)*** (pethidine-HCL®, 50 mg/ml, Misr company for pharmaceuticals, Cairo, Egypt) will be given as a rescue analgesia at any time the patient feels any pain for a pain score more than 4 (maximum dose 600 mg per day) ***(Friesen et al., 2016)***, if the patient still in pain after using maximum dose meperidine per day, she will be given morphine 0.1 mg/kg ***(ElGhamry and Amer, 2019)*** (Morphine sulphate®,10 mg/ml, Misr company for pharmaceuticals, Cairo, Egypt), considered block failure to be excluded from the study and replaced by another patient to fulfill sample size criteria.

In the presence of nausea, with or without vomiting, granisetron 3 mg ***(Gelberg et al., 2014)*** will be given IV and repeated once if nausea persisted (maximum dose of 6 mg per day) ***(Gelberg et al., 2014)***.

- Complications after puncturing of the blockade (hematoma in the puncture sites, pneumothorax, bradycardia defined as heart rate (HR) <50 beats/min, tachycardia defined as HR >110 beats/min, hypotension defined as a decrease in mean arterial pressure (MAP) of >20% from the baseline value and hypertension defined as an increase in MAP of >20% from the baseline value) will be evaluated and well-managed.

➢ **Outcome measurement:**

The age, weight, height, the American Society of Anesthesiologists (ASA) class of each patient will be recorded and compared among both groups.

- **Primary outcome:**

Post-operative pain severity assessed by VAS at 0 point (on admission to the PACU).

- **Secondary outcomes:**

1. Post-operative pain severity assessed by VAS at 2 hr, 4 hr, 8hr, 16 hr

and 24 hr.

2. Time of first rescue analgesia.
3. Cumulative post-operative meperidine consumption in the first 24 hours.

➢ **Statistical Analysis:**

All data will be recorded, analyzed and statistically compared between both groups to describe the groups and identify any significant differences between them. The quantitative data will be presented as mean ± standard deviation and range. Qualitative data will be presented as a number and percentage. Non-parametric data will be presented as a median and inter-quartile range.

The following tests will be done:

- Independent samples t-test of significance will be used when comparing between two means.
- Mann Whitney U test: for two-group comparisons in non-parametric data.
- Chi-square (x^2) test of significance will be used in order to compare proportions between qualitative parameters.
- The confidence interval will be set to 95% and the margin of error accepted will be set to 5%. So, the p-value will be considered significant as the following:
  - P-value <0.05 will be considered significant.
  - P-value <0.001 will be considered as highly significant.
  - P-value >0.05 will be considered insignificant.

➢ **Statistical package:**

Recorded data will be analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA).

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