Efficacy of Ultrasound Guided Pectoral Nerves Block in patients undergoing Unilateral Breast Surgery: A Randomized Controlled Trial

DR ABDUL JABBAR BIN ISMAIL

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE ANAESTHESIOLOGY

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Alhamdulillah, with the courage and compassion, and with guidance and blessings from Allah SWT, I managed to complete this dissertation.

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ABSTRAK

Tajuk: Keberkesanan pembiusan saraf pektoris II (PECS II Block) berpandukan imej ultrabunyi untuk pembedahan sebelah payu dara: Penyelidikan klinikal terkawal.

Pengenalan: Pembiusan saraf pektoris II berpandukan imej ultrabunyi adalah satu teknik pembiusan alternative kepada penggunaan ubat narkotik kuat seperti Morphine. Ia sebahagian daripada teknik rawatan kesakitan bebas narkotik untuk pembedahan sebelah payu dara.

Objektif: Kajian ini adalah mengenai keberkesanan dan keselamatan teknik pembiusan saraf pektoris II berbanding ubat narkotik Morphine yang menjadi kebiasaan di dalam praktis pembiusan untuk pesakit pembedahan sebelah payu dara.

Metodologi: Ini adalah penyelidikan klinikal terkawal. Seramai 60 pesakit yang didiagnosa kanser payu dara tahap I atau II telah menjalani pembedahan sebelah payu dara dengan pembuangan lengkap system linfa di ketiak. Mereka dipilih secara rambang untuk pembahagian kepada dua kumpulan. Kumpulan pertama diberi pembiusan saraf pektoris II dengan ubat pelali Ropivacain 3.75% dan kumpulan kedua menerima ubat narkotik Morphine 0.1mg/kg sebelum pembedahan. Kesemua pesakit diberi bius penuh sepanjang pembedahan berlangsung.

Keputusan: Tiada perbezaan statistik ketara dari segi umur, tinggi, berat badan dan indeks jisim badan (BMI) di antara pesakit ($p > 0.05$). Masa pelaksanaan pembiusan saraf adalah 17.7 (±7.72) minit dengan tiada sebarang komplikasi. Ketika pembedahan berlangsung, kumpulan Morphine menunjukkan penurunan tekanan darah sistole ($p = 0.03$), jumlah penggunaan ubat narkotik Fentanyl ($p < 0.01$) dan ubat penguat tekanan darah Phenylephrine ($p = 0.04$) yang lebih tinggi dengan perbezaan nilai statistik ketara. Walaupun kedua-dua kumpulan menunjukkan penurunan tahap kesakitan secara signifikan dalam 24 jam pertama selepas pembedahan ($p < 0.01$), tiada perbezaan tahap

kesakitan selepas pembedahan (p = 0.51) dan penggunaan ubat narkotik secara permintaan (PCA Morphine) (p = 0.86) di antara kedua-dua kumpulan tersebut. Penurunan ketara sebanyak 50% untuk risiko loya dan muntah (p = 0.015) selepas pembedahan didapati dalam kalangan pesakit pembiusan saraf pektoris II.

Rumusan: Pembiusan saraf pektoris II (PECS II Block) adalah teknik yang berkesan seperti Morphine, selamat dan mengurangkan risiko loya dan muntah selepas pembedahan sebelah payu dara.

ABSTRACT

Title: Efficacy of ultrasound guided pectoral nerves block (PECS II Block) in patients undergoing unilateral breast surgery: A randomized controlled trial.

Introduction: PECS II Block is an alternative technique to Morphine for patients undergoing unilateral breast surgeries as a part of multi-modal opioid-free post-operative analgesia.

Objective: Assessment of efficacy and safety of PECS II Block against the routine use of strong opioid Morphine in patients undergoing unilateral breast surgeries.

Methods: It was a randomized controlled clinical trial which had enrolled 60 patients diagnosed with breast cancer stage I and II undergoing unilateral breast surgery with axillary clearance. Participants were randomized into two treatment groups, one group receiving PECS II block with Ropivacaine 0.375% and another group receiving IV Morphine 0.1mg/kg prior to surgery. General Anaesthesia was administered throughout the surgery for both groups of patients.

Results: Demographically, both groups were comparable in terms of age, height, weight, BMI, pre-operative blood pressure and heart rate ($p > 0.05$). The average time to perform PECS II Block was 17.7 (±7.72) minutes with no associated complications encountered. In the controlled group, there were statistically significant lower intra-operative systolic blood pressure ($p = 0.03$), and higher usage of intraoperative fentanyl ($p < 0.01$) and phenylephrine ($p = 0.04$), however, the absolute difference was not clinically significant. Although both groups show significant post-operative pain score reduction in the first 24 hours ($p < 0.01$), there were no statistically significant difference between the groups in terms of post-operative pain score ($p = 0.51$) and PCA morphine usage ($p = 0.86$). However, patients receiving PECS II block had up to 50%

reduction in post-operative nausea and vomiting compared to the controlled group ($p = 0.015$).

Conclusion: PECS II Block is a safe technique and as effective as intravenous morphine as an analgesic modality for unilateral breast surgery in addition to significantly reducing PONV risk.

LIST OF TABLES & FIGURES

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS

BP	Blood pressure
ID	Identification
mm Hg	Millimeter mercury
GA	General Anesthesia
PECS II Block	Pectoral Nerves Block
PONV	Post-operative Nausea & Vomiting
NRS	Numerical Rating Scale
Post-op	Post-operative
ASA	American Society Of Anaesthesiologists'
BMI	Body mass index
IBM	International Business Machine
SPSS	Statistical Package for the social science
vs	Versus
BCS	Breast conserving surgery
mg	Milligram
cm	Centimeter
kg	Kilogram
mcg	Microgram
IV	Intravenous
Spo2	Pulse oximetry
G	Gauge
LA	Local anesthetic
MAC	Minimum alveolar concentration
MAP	Mean arterial pressure
PCA	Patient control analgesia
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
HR	Heart Rate
bpm	Beats per minute
TPVB	Thoracic paravertebral block

CHAPTER 1 : INTRODUCTION

1.1 Scientific background

The clinical workload of surgeries for breast cancer are increasing in trend

Breast cancer remains the highest number of cases of cancer among female patients. National cancer registry in 2006 for peninsular Malaysia, documented 3525 breast cancer cases registered, amounting to 16.5% of all cancer (1). The definitive treatment for breast cancer inevitably would be surgery, mainly categorized into either breast conserving surgery or mastectomy, with or without axillary clearance of affected lymph nodes, the choice of which will usually be according to the staging of the breast cancer (2).

In the past decade, there is an evidence that breast cancer incidence is rising, almost doubled, mainly due to the widespread use of screening tools such as ultrasound imaging and mammogram screening (3). The trend of rising incidence of breast cancer incidence would inevitably require increase in cases requiring anaesthetic care, which would warrant further scrutiny into this specific field of Anaesthesia.

Common clinical practice regarding analgesia technique in breast surgeries

Currently, the conventional anaesthetic technique employed for breast surgeries is General Anaesthesia (GA) using intravenous (IV) anaesthetic agent for induction of anaesthesia and volatile anaesthetic agent for maintenance of anaesthesia (4). Commonly, strong IV opioid such as Morphine would be used, with or without other analgesics for intraoperative and postoperative analgesia for the patient (4).

1.2 Problem Statement

The alternative to General Anaesthesia for breast surgery are not without problems

As breast cancer is the most common cancer in the female patients in Malaysia (1), and most of them will require breast surgery at some point, thus there is a need to explore several potential mode of anesthesia or analgesia for patient undergoing breast surgery.

Alternative to GA has been investigated in the past with the use of regional anaesthesia (RA) technique and have been shown, in comparison to GA (with strong opioid), resulting in better post-operative pain control, potentially reducing stress response from surgery and as well reducing post-operative nausea and vomiting (PONV) (4). However, RA techniques such as thoracic paravertebral block (TPVB), thoracic epidural, multiple intercostal blocks and intrapleural blocks, despite having a superior patient outcome compared to GA, it also have been associated with many side effects such as a high failure rate, hypotension, pneumothorax, epidural hematoma, and urinary retention (4).

Regional anaesthesia are superior in terms of analgesia and PONV but associated with serious side effects and failure rates

Among the 4 regional anaesthesia technique listed above, TPVB previously have been the established method of RA for breast surgery it offers superior analgesic efficacy, reduction in PONV and reduced post-operative morphine requirements (5, 6). However, TPVB is associated with risks such as high failure rate (10%), vascular puncture, and pneumothorax as demonstrated by Lonnqvist in his prospective study to

investigate the safety of TPVB (7, 8), as well as the recent meta-analysis by Schnabel (6).

Breast surgery have also been associated with high incidence of PONV, up to 30-40% (4). Thus there is a need to find a better method of anaesthesia or analgesia technique as PONV is associated with delayed discharge from post-operative care unit (9), and some patients reported as PONV being the most unpleasant experience, even more than pain (10).

1.3 Justification of the study

Exploring novel regional anaesthesia technique in breast surgery

In 2011, Rafael Blanco describe a new, groundbreaking regional anaesthesia technique in order to search for alternative to GA for breast surgery other than TPVB (11), and this technique was initially called The Pecs Block. Later in 2012, Blanco described another technique to address the inadequacy of coverage of anesthesia to the lower part and the axillary part of the chest wall through another modified Pecs block technique called 'PECS II block' (12).

Meta-analysis: Interfascial thoracic plane block (PECS II Block) is a very safe technique

Since 2012, there were 8 prospective, randomized, interventional trial and 1 peer-reviewed abstract have been published on the use of PECS II block, against a controlled intervention, either GA or TPVB (13). PECS II Block considered a safe RA technique that can be employed in breast surgery especially for analgesia, as all 9 studies described in meta-analysis published by Singh et al, all 9 studies have shown no complications encountered during administration of PECS II Block (13).

Our study: Addressing the issue of placebo as the controlled treatment in previous study

This study was done mainly to explore the relatively new regional anesthesia technique, thoracic interfascial plane block, specifically named PECS II Block designed by Rafael Blanco, for which, the effectiveness, as well as the safety profile have only been properly studied in 8 prospective, interventional, controlled trials (14)

In addition, none of the 8 controlled trials described in the meta-analysis described by Singh et al, have compared PECS II Block against commonly used analgesic which is a single bolus of IV Morphine given intraoperatively early at the start of the surgery. All of the studies published so far have been using placebo as the controlled group when comparing PECS II block efficacy rather than strong and longer acting opioid such as the commonly used Morphine.

Our study: using Morphine in the controlled group is more pragmatic in terms of clinical practice

Thus, this study was designed to compare the effectiveness of pectoral nerves block as an analgesia technique for breast surgery in comparison to the routinely used method, which is intravenous opioids, of which, commonly used was the long acting opioid Morphine.

The importance to establish the potential of PECS II Block as an alternative to IV Morphine is imperative as some patients could be either allergic or unsuitable for long acting opioid in view of several adverse effects, including post-operative nausea and vomiting, drowsiness, post-operative ileus, constipation, reflux, rigidity, pruritus, and respiratory depression (15).

Benefits of the study

- Encourage pectoral nerves block as part of the opioid-free anesthetic technique to be employed as an analgesia in breast surgeries
- Establishment of safety profile of pectoral nerves block with more data will build more confidence in anesthetic personnel to administer this regional block
- Pectoral nerves block can be used with confidence as an alternative to intravenous morphine in patients which are allergic and unsuitable for long acting opioids.
- Reducing uncomfortable side effects of intravenous morphine especially during post-operative period.

Limitations of the study

- Requirement of training to employ and administer pectoral nerves block.
- The limitation on the ultrasound machine that is compulsory for pectoral nerves block administration.
- High volume of local anesthetic used in pectoral nerves block, will be limited by the maximal safety dose, and body weight of the patients.

CHAPTER 2 : OBJECTIVES OF THE STUDY

2.1 General Objectives

This study was aimed to establish the comparative effectiveness with routinely given analgesic during breast surgery which was IV Morphine. It was also planned to observe for safety profile during and after pectoral nerves block administration

2.2 Specific objectives

- To compare mean post-operative pain score using NRS (numerical rating scale) between the group receiving PECS II Block and controlled group within 24-hours post-operative period.
- To compare mean difference of PCA Morphine usage between the group receiving PECS II Block and controlled group within 24-hours post-operative period.
- To compare intra-operative vital signs assessment between the group receiving PECS II Block and controlled group within 24-hours post-operative period.
- To compare the incidence of post-operative nausea and vomiting between the group receiving PECS II Block and controlled group within 24-hours post-operative period.
- To identify any complications arising during or after administration of PECS II Block

2.3 Research Hypothesis

Null Hypothesis

- There is no significant difference in terms of post-operative pain score using NRS (numerical rating scale) between the group receiving PECS II Block and controlled group.
- There is no significant difference in terms of PCA Morphine usage between the group receiving PECS II Block and controlled group.
- There is no significant difference in term of Intra-operative vital signs assessment between the group receiving PECS II Block and controlled group.
- There is no significant difference in term of the incidence of post-operative nausea and vomiting between the group receiving PECS II Block and controlled group.

Alternative Hypothesis

- There is a significant difference in terms of post-operative pain score using NRS (numerical rating scale) between the group receiving PECS II Block and controlled group.
- There is a significant difference in terms of PCA Morphine usage between the group receiving PECS II Block and controlled group.
- There is a significant difference in term of Intra-operative vital signs assessment between the group receiving PECS II Block and controlled group.
- There is a significant difference in term of the incidence of post-operative nausea and vomiting between the group receiving PECS II Block and controlled group.

CHAPTER 3: MANUSCRIPT

3.1 TITLE PAGE

Article Title

Effectiveness of PECS II Block versus intravenous Morphine for post-operative analgesia in unilateral breast surgery with axillary clearance

Running Head

A randomized controlled trial comparing between PECS II Block versus intravenous Morphine in patients undergoing unilateral breast surgery with axillary clearance investigating the difference between post-operative pain score, post-operative patient-controlled analgesia (PCA) usage of intravenous Morphine as well as evaluating the safety of PECS II Block administration. (49 out of 50 words)

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- This manuscript has not been published elsewhere or submitted elsewhere for publication.
- The result of this study has been presented at Borneo Anaesthesia, Intensive Care, and Pain Conference 2018, in Kota Kinabalu, Sabah as a Poster form
- There is no conflict of interest and no source of financial support in this study

Main Document

Title

Effectiveness of PECS II Block versus intravenous Morphine for post-operative analgesia in unilateral breast surgery with axillary clearance

3.2 ABSTRACT

Introduction: Ultrasound guided pectoral nerves block (PECS II Block) is a new technique, an alternative to intravenous morphine for patients undergoing unilateral breast surgeries as part of multi-modal opioid-free post-operative analgesia.

Objective: Assessment of efficacy and safety of PECS II Block against the routine use of intravenous morphine in patients undergoing unilateral breast surgeries

Methods: It was a prospective, single blinded, randomized controlled clinical trial involving 60 patients with breast cancer stage I & II whom underwent unilateral breast surgery with axillary clearance under general anaesthesia. Participants were randomized into two treatment groups, one group receiving PECS II block with Ropivacaine 0.375% prior to induction (total volume of 35ml) and another group receiving IV Morphine 0.1mg/kg. Post-operative pain score and PCA morphine usage at 6 hours interval over 24 hours were assessed

Results: In the controlled group, there were statistically significant lower intra-operative systolic blood pressure ($p = 0.03$), and higher usage of intraoperative fentanyl ($p < 0.01$) and phenylephrine ($p = 0.04$), however, the absolute difference was not clinically significant. Although both groups show significant post-operative pain score reduction in the first 24 hours ($p < 0.01$), there were no statistically significant difference between the groups in terms of post-operative pain score ($p = 0.51$) and PCA

morphine usage (p = 0.86). However, patients receiving PECS II block had up to 50% reduction in post-operative nausea and vomiting compared to the controlled group (p = 0.015).

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Conclusion: PECS II Block is a safe technique and as effective as intravenous morphine as an analgesic modality for unilateral breast surgery. (275 out of 275 words)

Keywords

PECS II Block, breast surgery with axillary clearance, pectoral nerves block, regional block

3.3 INTRODUCTION

The definitive treatment for breast cancer inevitably would be surgery, mainly categorized into either breast conserving surgery or mastectomy, with or without axillary clearance of affected lymph nodes, the choice of which will usually be according to the staging of the breast cancer (2). Currently, the conventional anaesthetic technique employed for breast surgeries is General Anaesthesia (GA) using intravenous (IV) anaesthetic agent for induction of anaesthesia and volatile anaesthetic agent for maintenance of anaesthesia (4). Commonly, strong IV opioid such as Morphine would be used, with or without other analgesics for intraoperative and postoperative analgesia for the patient (4).

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Thus, this study was designed to compare the effectiveness of pectoral nerves block as an analgesia technique for breast surgery in comparison to the routinely used method, which is intravenous opioids, of which, commonly used was the long acting opioid Morphine. The importance to establish the potential of PECS II Block as an alternative to IV Morphine is imperative as some patients could be either allergic or unsuitable for long acting opioid in view of several adverse effects, including post-

operative nausea and vomiting, drowsiness, post-operative ileus, constipation, reflux, rigidity, pruritus, and respiratory depression (15).

3.4 METHODOLOGY

Trial Design

This was a prospective, interventional, single blinded, randomized and controlled trial.

Participant flow

Figure 1 shows the study flow chart following the CONSORT 2010 guidelines. A total of 60 female patients was enrolled as planned according to the study protocol. Patients randomized into equal group of 30 participants in each group, in which Group A received Pectoral Nerves Block and Group B received Intravenous Morphine.

Recruitment

Period of the conducted study

This study was conducted after ethical approval was obtained in 20th October 2015, and 60 patients was enrolled throughout the study until the final participant enrolled in the month of October 2017

Conclusion of the study

This study was concluded after the final participants enrolled into the study, and no more enrollment occurred after ethical approval for the study lapses on 10th October 2017.

Settings & Location of the study

It was done in Hospital Queen Elizabeth II, Kota Kinabalu, Sabah. This study was conducted between November 2015 and concluded on October 2017. Locations that were involved were:

- Female Surgical ward during pre-operative assessment for informed consent taking and enrollment for the study, as well as during post-operative period for outcome assessments.
- Operating theater induction room, where patients that were randomized into the interventional group received pectoral nerves block.
- Operating theater recovery bay to educate patients regarding post-operative pain score, and usage of PCA Morphine machine as well as for 1-hour post-operative period outcome assessment.

Participants & Study Location

Patients identified from female patients admitted to the ward and was planned for unilateral breast surgeries with axillary clearance. Derived from power and sample analysis, 60 patients were enrolled and randomized into 2 groups, which were labelled as Group A, interventional group with 30 patients receiving pectoral nerves block, and Group B, controlled group with 30 patients receiving intravenous morphine. Both group of patients underwent general anesthesia throughout the surgery.