Pectoralis (II) Block with Liposomal Bupivacaine vs Bupivacaine plus Dexamethasone for Mastectomy with Immediate Reconstruction

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GHS Department of Anesthesiology
IRB Study Protocol

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Study Title: Pectoralis (II) Block with Liposomal Bupivacaine vs Bupivacaine plus Dexamethasone for Mastectomy with Immediate Reconstruction

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Background: Regional anesthesia has multiple benefits to patients undergoing surgery related to both analgesia and avoidance of opioids. Regional anesthesia requires accurate administration of local anesthetic medication to interrupt the function of sensory nerves to the surgical field. Multiple aqueous local anesthetics have been used for years, but in the past decade a liposomal formulation has been introduced with the reported ability to extend the duration of analgesia.

Study Purpose: To evaluate the duration of analgesia provided by PEC II block with liposomal Bupivacaine compared to Bupivacaine with dexamethason. Our hypothesis is that the block performed with liposomal bupivacaine will result in longer duration of analgesia.

Study Design: This pilot study is a self-controlled comparison of patients undergoing bilateral mastectomy with immediate reconstruction by breast surgeons at GHS. Ten patients will be enrolled after completing informed consent. Blocks will be performed and the duration of analgesia will be evaluated at regular intervals. At each interval the patient will also be asked to identify whether they can discriminate the level of pain based on laterality.

Our primary endpoint is the ability to discriminate analgesia. Secondary outcomes will include visual analog pain scores (by side), total morphine equivalent consumption; time to the first opioid request, and non-opioid pain medication administration. We also are planning to obtain demographic characteristics, intraoperative consumption of pain medication, and length of stay data. We will exclude all patients younger than 18 years old, patients with BMI >30, pregnant patients, patients with severe hepatic disease and patients with an active opioid prescription before surgery.

Methods and Duration:

Prospective data will be collected on 10 patients undergoing bilateral mastectomy with immediate reconstruction at Greenville Memorial Hospital or Patewood Memorial Hospital. Following informed consent, patients will be randomized to have PEC II blocks with 10cc liposomal Bupivacaine (133mg) plus 20cc 0.25% Bupivacaine HCl on one side and 30cc 0.25% Bupivacaine plus 4mg Dexamethasone on the other. Consistent with our current standard of care,

all patients will receive oral medications before surgery (1g acetaminophen, 75mg pregabalin, 400mg celecoxib) unless there are contraindications. The blocks will be placed following induction of general anesthesia in the operating room under sterile conditions and procedures. The anesthesiologist performing the block will be unblinded to which medication is placed on either side, but the surgeon and care team for the remainder of the perioperative stay will be blinded. All blocks will be performed by an anesthesiologist with expertise in regional anesthesia guided by ultrasonography. Intraoperative management will be consistent with our standard of care: ASA monitoring, maintenance with isoflurane, boluses of fentanyl or hydromorphone as needed.

Postoperative pain scores will be taken in throughout their hospitalization and by phone thereafter (2H, 4H, 6H, 8H, 12H, 18H, 24H, 30H, 36H, 42H, 48H +/- 1H after hour 6). At each time point the patient will be asked if they can discriminate pain to either side of their chest, and if so, which side has more pain. All pain scores will be taken at rest, if possible. Patient records will be queried to determine length of stay, opioid consumption, and time to first dosage.

Potential Risks to the Patients:

- This study does not increase the patient risks related to surgery or the PEC II block, nor does it increase risk of local anesthetic toxicity (lower total dosage).

Potential Benefits to the Patients:

The information gained from this study may be used scientifically and may determine the drug of choice for PEC II blocks at GHS and beyond. If liposomal Bupivacaine provides significantly longer analgesia, then patients would benefit from this pain relief on the side of liposomal Bupivacaine injection. Currently no patients receive this drug for PEC II blocks because it is unclear whether the potential benefit justifies the cost of the medication. We hope the information will be of future benefit to others in relation to:

- Better postoperative pain control
- Avoidance of opioid-related adverse events such a respiratory depression, sedation, nausea and vomiting, pruritus, urinary retention, and ileus
- Decrease length of stay and total cost

Privacy and Confidentiality:

The data collection sheets/jump-drives will be deposited in a locked collection box at the Department of Surgery at GMH. All collected data will be entered into a password-protected database (REDCap) in a password-protected GMH computer. In the database, patients will be identified only by a medical record and/or birth date. Only the PI and Co-Investigators will have access to this database.

Data Analysis:

Demographics, time to first narcotic request, and morphine equivalent pain medications will be described for the 10 patients. Patient ability to correctly discriminate difference in pain between the two locations will also be described. Additionally, intrapersonal differences in pain scores will be determined (liposomal Bupivacaine side - Bupivacaine plus Dexamethasone side) at each time interval. The median differences across the 10 patients will be aggregated to determine any trend in differences across the time intervals, as tested with a Kruskal-Wallis test.

Costs: This will not incur any additional costs to participants. Participants will not be compensated to take part in this study. The cost of the medication and pharmacy related charges will be paid by the investigator department(s).

References/Literature Review:

1. Bashandy GM, Abbas DN. Pectoral nerves I and II blocks in multimodal analgesia for breast cancer surgery: a randomized clinical trial. Reg Anesth Pain Med 2015;40(1):68-74.

- 120 Patients having mastectomy randomized to general anesthesia with or without PEC blocks. Lower pain scores and opioid consumption with the blocks. No complications.

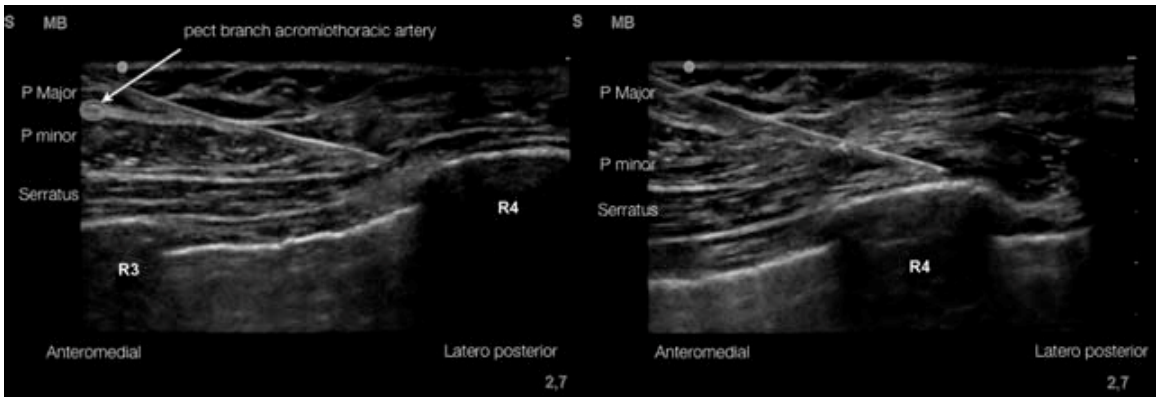
2. Gorfine SR, Onel E, Patou G, Krivokapic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. *Dis Colon Rectum*. 2011;54(12):1552-1559.

- Original prospective study with liposomal bupivacaine. Showed decreased pain scores and prolonged time until first opioid vs placebo. Multiple manuscripts available upon request, however PI endorses it remains unclear how much longer liposomal Bupivacaine lasts compared to aqueous Bupivacaine.

3. Amundson AW, Johnson RL, Abdel MP, et al. A Three-arm Randomized Clinical Trial Comparing Continuous Femoral Plus Single-injection Sciatic Peripheral Nerve Blocks versus Periarticular Injection with Ropivacaine or Liposomal Bupivacaine for Patients Undergoing Total Knee Arthroplasty. Anesthesiology 2017;126(6):1139-1150.

- Most recent article in quality anesthesia literature related to the multiple drug choices/modalities related to regional anesthesia. Includes discussion of liposomal Bupivacaine vs aqueous local anesthetics. Included to endorse the need for clarification of best practices.

PEC II block:



PEC II block ultrasound example

Expected area of analgesia with PEC II block

Reference for (modified) images (digital appendix): Blanco R, Fajardo M, Parras Maldonado T. Ultrasound description of Pecs II (modified Pecs I): a novel approach to breast surgery. Rev Esp Anestesiol Reanim. 2012 Nov;59(9):470-5.