Research Summary

1. Protocol Title:

Comparison of TAP, Anterior QL, or ESP Block for Elective Cesarean Section

2. Purpose of the Study:

The purpose of this prospective single center, randomized study is to determine if ultrasound guided Quadratus Lumborum (QL) and Erector Spinae Plane (ESP) blocks decrease opioid consumption compared to Transversus Abdominis Plane (TAP) in subjects undergoing elective cesarean section. Total opioid consumption and pain scores will be monitored for 48 hours postoperatively.

3. Background & Significance:

Cesarean section is an invasive surgery that can lead to significant postoperative pain. Well controlled postoperative pain in this specific patient population can help minimize the effect of surgery on a new mother's ability to care for her newborn and ease the transition back home, as well as allay any concerns regarding transfer of opiates through breastfeeding.

The typical anesthetic plan involves a spinal anesthetic or combined spinal epidural anesthetic as the primary anesthetic for the procedure followed by a combination of oral pain medications, including opioids, to control pain postoperatively. Side effects from opioid use, including nausea, vomiting, sedation, or respiratory depression, can hinder a new mother's ability to fully participate in the care of her newborn. Additionally, some women are leery to take opioids if they are breastfeeding for fear of transfer to their newborn [1]. Despite widespread postoperative prescription of opioids, women report poor pain control after cesarean section [2-4]. As part of a larger public health concern, unused postoperative opioids can be detrimental and the possibility of persistent opioid use after surgery is feasible in this patient population [5].

TAP blocks have been utilized for years to help control incisional pain after abdominal surgeries, including cesarean section [6, 7]. However, it is not without limitations and there is some question regarding efficacy [8]. TAP blocks often decrease somatic pain, but do not impact visceral pain which can contribute to uncontrolled postoperative pain after cesarean section. Additionally, it has been shown that TAP blocks do not improve analgesia when patients are already receiving intrathecal morphine[9].

With newer truncal blocks like anterior quadratus lumborum (QL) and erector spinae plane (ESP) blocks coming into practice, it will be helpful to identify which, if any, of the three blocks can benefit this unique patient population.

Studies involving earlier variations of the quadratus lumborum block have shown to be successful after cesarean section [10, 11]. At Duke University Hospital, we most commonly perform the anterior variation of the QL block which has not specifically been studied in this patient population. However, case series have demonstrated success in other abdominal procedures [12].

Erector spinae plane blocks were initially used to treat pain from rib fractures and thoracotomies, but have now been shown to be effective for open abdominal procedures [13-15]. However, there has only been one case report to date using an ESP block for cesarean section [16].

This study aims to answer if QL or ESP can impact postoperative opioid use and pain scores after cesarean section compared to TAP block.

4. Design & Procedures:

The typical anesthetic for cesarean section at Duke University Hospital includes a spinal or combined spinal epidural anesthetic with intrathecal dosing of 1.4-1.6 mL bupivacaine HCl 0.75%, 15 mcg fentanyl, and 150 mcg morphine. If the epidural component of a combined spinal epidural anesthetic is used, the subject will be withdrawn from the study. Patients also receive rectal acetaminophen 975 mg prior to incision, intravenous (IV) ondansetron 4 mg, metoclopramiden10 mg, famotidine 20 mg and dexamethasone 4 mg intraoperatively, and IV ketorolac 15 mg prior to skin closure. There will be no change to this typical practice.

Patients who consent to be in this study will be randomized to receive one of three truncal nerve blocks using an online randomization program by the study PI (AK/LG): (1) ultrasound-guided bilateral classic TAP block; (2) ultrasound-guided bilateral anterior QL (also known as transmuscular or QL type 3) block; (3) ultrasound-guided bilateral ESP block at the level of T9. These nerve blocks will be performed after delivery and within one hour of skin closure with 25 mL of 0.2% ropivacaine with epinephrine 1:400,000 per side. Nerve blocks will be performed by a dedicated and trained group of regional anesthesiologists. This non-blinded regional anesthesiologist will save an ultrasound image after local anesthetic administration while the needle is still in position on each side. The study team will review these images to ensure a high quality of block performance.

Patients will have standard postoperative pain medication orders, including acetaminophen 975 mg PO Q6H for 4 days (scheduled, starting 6 hours after intraoperative rectal dose), ketorolac 15 mg IV Q6H for 24 hours (scheduled, starting 6 hours after intraoperative dose), ibuprofen 600 mg PO Q6H for 3 days (scheduled, starting 24 hours after first dose of ketorolac) and oxycodone 5-10mg PO Q3-4H PRN for 4 days. If patients are unable to tolerate oral medication or oxycodone is insufficient, rescue medications may be ordered: IV morphine 1-2 mg or IV hydromorphone 0.3-0.5 mg Q4H as needed. There is no change from the standard postoperative order sets used for patients after cesarean section.

Subjects' verbal pain scores at rest and with movement as well as opioid consumption will be recorded at 2, 6, 24, and 48 hours postoperatively. The validated Obstetric Quality of Recovery-11 (ObsQoR-11) score will also be assessed at 24 and 48 hours postoperatively [17]. Additionally, the amount of antiemetics and antipruritics used will also be recorded at the above time points. These scores will be entered into a Duke University Hospital REDCap database. Subjects will also be sent a survey assessing their satisfaction with pain control one week after discharge via email or telephone. This information will be collected via Duke University Hospital REDCap.

5. Selection of Subjects:

Patients undergoing elective cesarean section will be identified the day prior to surgery. Patients will be contacted via telephone by a member of the study team the day prior to surgery to confirm eligibility and, if eligible and interested, the study will be explained. Inclusion and exclusion criteria will be assessed through self-reporting by the subjects and review of patient chart on EPIC. Patients will be given the opportunity to ask initial questions about the study over the phone. Patients interested in participating will have the protocol fully explained and written informed consent will be obtained on the day of surgery prior to the procedure. The patient's care team, including attending surgeons, attending anesthesiologists, anesthesia residents, and nurse anesthetists will be informed of the patient's inclusion via secure email with specifics for the case.

Inclusion Criteria:

1) American Society of Anesthesiologists (ASA) Physical Status 1-3
2) Age greater than or equal to 18 years
3) Scheduled cesarean section
4) English speaking

Exclusion Criteria:

1) ASA Physical Status 4-5
2) Diagnosis of chronic pain
3) Chronic opioid use (opioid use in the past 3 months)
4) Preoperative use of SSRIs (Celexa, Lexapro, Prozac, Paxil), SNRIs (Cymbalta, Effexor), gabapentin, or pregabalin (Lyrica)
5) Inability to cooperate with or understand protocol
6) Inability to communicate pain scores or need for analgesia
7) Infection at the site of block placement
8) Intolerance or allergy to local anesthetics
9) Neurologic deficit or disorder
10) Blood thinning disorder or taking anticoagulant medication
11) BMI > 50 kg/m^2
12) Suspected or known addiction to or abuse of illicit drug(s), prescription medicine(s), or alcohol within the past 2 years
13) Uncontrolled anxiety, schizophrenia, or other psychiatric disorder that, in the opinion of the investigator, may interfere with study assessments or compliance
14) Current or historical evidence of any clinically significant disease or condition that, in the opinion of the investigator, may increase the risk of surgery or complicate the subject's postoperative course

6. Subject Recruitment & Compensation:

Only patients who are having elective cesarean sections are eligible for this study. We will not bias any demographic groups in identifying patients eligible for this study. A total of 75 patients will be consented from Duke University Hospital. An IRB approved phone script will be used to discuss the study with eligible patients. Patients will not receive any additional compensation for enrollment in this study.

7. Consent Process:
Potential subjects will be contacted and screened the day prior to surgery via telephone. If the patient is interested in the study, the consent process will take place in a private preoperative room on the Labor and Delivery ward prior to surgery. The consent process will be conducted by a member of the research team. Throughout the consent process, measures will be taken to maintain privacy, such as conducting face-to-face conversations in private rooms. As much time as necessary will be spent with each potential subject to sufficiently explain and answer all questions, and address all concerns they may have in regard to the study and/or consent process. Under HIPAA waiver, the study team will identify potential subjects from clinic schedules, OR schedules, and Maestro Care.

8. Subject's Capacity to Give Legally Effective Consent:
Patients who do not have the capacity to give legally effective consent will not be approached for participation in this study.

9. Study Interventions:
See 4 above.

10. Risk/Benefit Assessment:
Patients will be consented regarding the standard risks associated with regional anesthesia. These standard risks include: minor pain or discomfort; bruising; infection at the needle insertion site; injury to arteries, veins, or nerves affecting the abdomen, back, or legs; residual numbness, weakness, or paralysis; headache; muscle soreness. If patients are allergic to the local anesthetic (ropivacaine) or have an adverse drug reaction, they could possibly have a reaction that is severe enough to cause cardiac arrest and/or respiratory arrest. If there is injection of local anesthetic into a blood vessel, patients could possibly have loss of consciousness, seizure, or cardiac arrest.

There have been rare case reports of hip or knee weakness after quadratus lumborum block. Therefore, patients will be encouraged to have someone with them to help them of bed the first time after the nerve block is performed.

Benefits include contributing to general knowledge to improve future patient care. Benefits also include potential analgesic benefit, decreased pain scores, and improved patient satisfaction. Conversely, this study may show no benefit of the block, thereby invalidating the technique.

11. Costs to the Subject:
Subjects will not incur any additional costs to participate in the study. A MaestroCare build will be created to ensure that any subjects are not charged for researched related procedures, equipment, or medications.

12. Data Analysis & Statistical Considerations:
A randomized trial of 75 subjects (25 per group) will provide 80% power to detect a 35% decrease in opioid use between treatment groups in a t-test at an alpha level 0.017 utilizing Bonferroni's correction,

(parametric), Mann-Whitney U Test (nonparametric), or repeated measures ANOVA as appropriate. Sample size and power calculations were performed using PASS v15 (NCSS, LLC. Kaysville, Utah).

Patient and surgical characteristics will be summarized by standard descriptive statistics and will be compared between groups using t-tests, ANOVA, or Wilcoxon sum ranked tests as appropriate. We will report odds ratios, 95% confidence intervals, and p-values to assess significance and clinical importance of the observed treatment effect. Additional measures of treatment efficacy (pain scores, ease of mobility, overall pain experience) will be summarized overall and between groups to further characterize the treatment effect in this population.

13. Data & Safety Monitoring:

In accordance with federal regulations the PI will monitor for, review, and promptly report to the IRB, appropriate institutional officials, sponsor, coordinating center and the appropriate regulatory agency head all unanticipated problems involving risks to subjects or others that occur in the course of a subject's participation in a research study (45 CFR 46.103(b)(5)(i) and 21 CFR 56.108(b)(1)), all AE reports will be reported per the DUHS IRB policies. PI will be monitoring all AEs and submitting reports to the IRB per DUHS IRB policy.

14. Privacy, Data Storage & Confidentiality:

Potential subjects and their families will be approached in private rooms. Any guests not involved in the consent process will be asked to leave the room during any such communications, unless the patient allows them to be present. Efforts to maintain subject confidentiality will include following Federal Privacy Regulations which provide safeguards for privacy, security, and authorized access. Except when required by law, subjects will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Duke University Health System (DUHS). Subjects will not be revealed in any reports or publications resulting from this study. For records disclosed outside of DUHS, subjects will be assigned a unique code number. The paper and electronic data will be stored as per the RDSP.

15. References:

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17. Ciechanowicz, S., et al., *Development and evaluation of an obstetric quality-of-recovery score (ObsQoR-11) after elective Caesarean delivery.* British Journal of Anaesthesia, 2019, 122 (1): 69-78.