Quantitative observational comparative effectiveness of quadratus lumborum block with liposomal bupivacaine (Exparel®) versus thoracic epidural analgesia in patients undergoing laparoscopic colectomy

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Purpose of the Study

We believe that a quadratus lumborum block with lipsomal bupivacaine(Exparel®) or a quadratus lumborum block with an admixture of bupvicaine will provide roughly equivalent analgesia and opioid use when compared with postoperative analgesia in a historical cohort that received thoraic epidural analgesia. We believe participants who receive the quadratus lumborum block will result in improved early mobilization, fewer complications such as block failure, urinary retention, and pruritis, and decreased overall pharmacy costs compared to the patients who received thoracic epidural analgesia.

Background & Significance

Laparoscopic colectomy is a surgical procedure that is primarily performed for resection of a GI malignancy. While most of the procedure is performed via laparoscopic ports in the anterior abdominal wall, the resected specimen is typically delivered through a small lower abdominal laparotomy, which results in a moderately severe burden of pain for these patients. Enhanced recovery after surgery (ERAS) protocols are aimed at improved return to function with minimal disruption in the functional capacity, and have been shown to reduce hospital length of stay, complications, and costs. One standard therapeutic component of the ERAS program at Duke for colorectal surgery is thoracic epidural analgesia (TEA), which is typically maintained for 2 days postoperatively. While TEA usually provides high-quality analgesia of the abdomen, drawbacks include technical difficulties with insertion, patchy or non-functioning block, pruritis and/or urinary retention due to epidural opioids, impairment of mobility due to leg weakness or the presence of a pump apparatus on an IV pole, and most importantly, associated hypotension which often results in the epidural local anesthetic infusion being discontinued. Alternatives to TEA include infiltrative blocks of the wall of the abdomen. The quadratus lumborum block (QLB) is a novel, ultrasound-guided infiltration technique whereby local anesthetic is deposited in the fascial plane between the quadratus lumborum and psoas major muscles at the level of L3-4.(1) Performed bilaterally, the QLB has been shown to provide a dermatomal block of the entire anterior abdominal wall. This may be the principal advantage of QLB over transversus abdominis plane (TAP) block, which is often patchy and restricted to a smaller area of the abdominal wall. In our institution, QLB is replacing TAP blockade for many abdominal procedures that have both upper and lower incisions or port sites. The QLB appears (both in the scant literature to date and in our institutional experience) to be reliable and technically simpler to perform that TAP blocks, as the needle is not moved once the fascial plane is breached. We wish to compare the effectiveness of QL blocks for postoperative analgesia in this population with a historical cohort that received thoracic epidural analgesia. Based on our experience, we believe that infiltrating this space with an admixture of bupivacaine and liposomal bupivacaine will result in excellent pain relief for an extended duration of time. Liposomal bupivacaine (Exparel®) is a slow-release, long-acting form of bupivacaine that has been shown to provide extended duration of analgesia and opioid sparing

in a number of surgical settings. (2, 3) Liposomal bupivacaine is FDA approved for surgical infiltration, field blocks, fascial plane blocks of the abdomen, dental blocks, and interscalene brachial plexus blocks. A number of new abdominal wall block techniques have been developed over the last several years, and following some initial confusion related to the wording of the label, the FDA issued a clarification letter that stated that truncal fascial plane blocks such as the transversus abdominis plane (TAP) block are an on-label use of the medication (see attached clarification letter). The quadratus lumborum (QL) block is a type of TAP block, wherein local anesthetic is infiltrated into the fascial plane between muscles of the lateral abdominal wall.

Design & Procedures

This is a single center, observational prospective and retrospective cohort study.

Prospective: On the day of surgery, subjects will receive a QLB in the preoperative holding area as follows:

Subjects will be positioned in the right lateral decubitus position, and will be attached to standard ASA monitors (pulse oximetry, EKG, non-invasive blood pressure). Oxygen 5 L/min will be supplied via a face mask. Sedation/analgesia with midazolam 1- 2 mg IV and fentanyl 25- 100 mcg IV will be administered.

After appropriate skin preparation and draping, a 60 mm, 2-5 MHz curvilinear ultrasound transducer will be placed on the skin over the intercristal line (approximately L3/4 disc space) on the midline of the back. The transducer will be translated laterally to the left until the quadratus lumborum and psoas major muscles are identified. The transducer will then be rotated until the quadratus muscle is seen in its long axis, just below its attachment on the 12th rib.

A 21 gauge, 10 cm echogenic block needle (Pajunk Sonoplex, Norcross, GA) will then be inserted from the inferior aspect of the transducer and advanced until the tip is visualized in the fascial plane between the QL and psoas major muscles. Following negative aspiration for blood, 30 ml of injectate will be slowly administered with intermittent aspiration. Each 30 ml aliquot will contain 10 ml of liposomal bupivacaine (133 mg) and 20 ml of 0.25% bupivacaine (50 mg). The block will then be repeated on the right side.

Following the block, subjects will proceed to the operating room where they will undergo a standard general anesthetic with endotracheal intubation (desflurane or isoflurane in a mixture of air/oxygen). The dosing of intraoperative opioids will be left to the discretion of the attending anesthesiologist in the room.

In the Post-Anesthesia Care Unit (PACU) and on the postoperative floor, subjects will have access to oxycodone 5-15 mg PO q3h prn for rescue analgesia (the primary outcome measure). In the PACU, patients will also have access to intravenous hydromorphone if the oral opioid

provides inadequate relief. Finally, subjects may receive a standard multimodal analgesia regimen consisting of:

- Acetaminophen 975 mg PO q6h (beginning in preop holding)
- Gabapentin 600 mg PO once in holding, then 100 mg PO tid thereafter
- Ketorolac 15 mg IV prior to skin closure

While this standard regimen is expected, it may vary per clinical care team judgement and/or preference. Any alterations in this standard regimen will not be considered a protocol deviation.

Assessments

Patient assessments will be performed or recorded by a research assistant twice daily (unless otherwise specified). Assessments made after discharge will be recorded by subjects who will be provided with a diary to document the outcomes. Outcomes to be measured include:

Opioid consumption. Cumulative opioid consumption over 48 hours is the primary outcome measure. Data will be drawn from PACU records and from the nursing medication records on a twice-daily basis. Post discharge opioid use will be tracked in the take- home patient diary. The patient will be called at 7 days after surgery to collect.

NRS-11. The 11-point Numeric Rating Scale (0-10) will be used as a secondary outcome measure. Two measures will be taken with each assessment, one at rest and one with coughing. These will be conducted preoperatively, 30 minutes after arrival to PACU, and at time points 8 hrs., 24 hrs., 36 hrs. 48 hrs, 72 hrs, 96 hrs., 120 hrs., 144 hrs. and 168 hrs.

Block success and adverse events. Presence of demonstrable sensory block over 4 points on the abdomen (one in each of the 4 quadrants), as tested by response to pinprick. Subjects will be asked to report whether the stimulus feels “sharp” or “dull”, indicating block failure and success respectively. This will be done at the time of pain assessment (30 minutes after arrival to PACU, and at time points 8 hrs., 24 hrs., 36 hrs. and 48 hrs. and 72 hrs.). Subjects will be evaluated for potential adverse events related to the block including evidence of hematoma, infection, unexpected sensory or motor deficit, local anesthetic systemic toxicity, as well as transient weakness of the hip flexor muscles (a known possible side-effect of QL block).

Satisfaction with postoperative pain control. Overall subject satisfaction with pain control will be recorded on postoperative day 0 and 1 (11-point scale: 10=highly satisfied, 0=completely unsatisfied)

Hospital length of stay. Measured both by raw length of stay and by time to achieving “discharge readiness”, defined by the presence of 3 criteria: a pain score of 3 or less with ambulation, no opioids required in the preceding 6 hours, and the ability to perform self-care (go to the toilet, dress, and shower).

Incidence of opioid-related adverse events. Incidence of nausea, vomiting, ileus, constipation, orthostasis, pruritis, urinary retention, respiratory depression

Time to first mobilization. Measured from time of arrival in PACU (time zero)

Cost. Hospital costs including pharmacy-related costs, costs due to opioid-related adverse events, the cost associated with nursing interventions and drugs to treat opioid-related adverse events, and overall hospital admission costs will be calculated.

Sleep Quality. Two measures will be taken for sleep quality assessment. How much did pain interfere with falling asleep (0= no interference, 10= completely interferes). How much did pain interfere with staying asleep (0= no interference, 10= completely interferes). Measures will be taken once daily from POD 1 to POD 7 (approximately 168hrs. after surgery). If the subject is sleeping at the time assessment collection is due, the subject will not be disturbed to collect the assessments, and this will not be considered a protocol deviation.

Historical data of 30 patients that meet inclusion criteria and meet no exclusion criteria, will be collected and for the retrospective group. The anesthesia statisticians will evaluate the following data from the patient's electronic medical record if available, including but not limited to hospital notes, anesthesia notes, medical history, medications, pain service notes, and flowsheets from admission to discharge. Electronic medical records will be used to assess the following items to compare to the prospective cohort.

Opioid consumption. Cumulative opioid consumption at 24hours, 48 hours and 72 hours. 48 hours is the primary outcome measure. Data will be drawn from PACU records and from the nursing medication records.

NRS-11. The 11-point Numeric Rating Scale (0-10) will be used as a secondary outcome measure. These will be collected from the preoperative assessment record, 30 minutes after arrival to PACU, and at time points 8 hrs., 24 hrs., 36 hrs. 48 hrs. and 72 hrs.

Thoracic epidural success and adverse events. Evidence of epidural block success/failure (as described in the anesthesia record and in daily Inpatient Pain Service notes). This will be done at the time of pain assessment (30 minutes after arrival to PACU, and at time points 8 hr, 24 hr, 36 hr and, 48 hr and 72 hr). Subject data will be collected for potential adverse events related to the epidural including evidence of hypotension, urinary retention, inability to ambulate per physical therapy. (known possible side-effect of thoracic epidural approach).

Hospital length of stay. Measured both by raw length of stay and by time to achieving "discharge readiness", defined by the presence of 3 criteria: a pain score of 3 or less with ambulation, no opioids required in the preceding 6 hours, and the ability to perform self-care (go to the toilet, dress, and shower).

Incidence of opioid-related adverse events. Incidence of nausea, vomiting, ileus, constipation, orthostasis, pruritis, urinary retention, respiratory depression

Time to first mobilization. Measured from time of arrival in PACU (time zero)

Cost. Hospital costs including pharmacy-related costs, costs due to opioid-related adverse events, the cost associated with nursing interventions and drugs to treat opioid-related adverse events, and overall hospital admission costs will be calculated.

Selection of Subjects

Criteria for inclusion in Prospective cohort:

- Patients scheduled for elective, laparoscopic colonic resection by one of three surgeons: Drs. Thacker, Mantyh or Migaly. These surgeons perform this procedure in the same manner
- Age 18-85 years
- American Society of Anesthesiologists (ASA) Physical Class I-III
- BMI 18-35 kg/m2

Criteria for exclusion in Prospective Cohort:

- Inability to consent
- Inability to speak English
- Pregnancy
- Emergency surgery
- Contraindications to regional blockade: coagulopathy or bleeding diathesis, local infection, allergy to local anesthetics
- Allergies/intolerances/contraindications to any of the multimodal agents (acetaminophen, gabapentin, ketorolac)
- Daily opioid equivalent use of 30 mg of morphine or greater at time of consent
- History of drug or alcohol abuse
- Uncontrolled anxiety, schizophrenia or other psychiatric disorder that, in the opinion of the investigator, may interfere with the study assessments of compliance.

Criteria for inclusion in Retrospective cohort:

- Patients that have had a laparoscopic colonic resection in the past year by Drs. Thacker, Mantyh or Migaly and received thoracic epidural analgesia.
- Thoracic epidural analgesia must be placed in preoperatively, must be sited between levels T8 and T12, and must be started while the case is going- i.e. not started in PACU.
- Age 18- 85 at the time of the procedure.
- American Society fo Anesthesiologists (ASA) Physical class between I- III.
- BMI 18- 35 kg/m^2.

- Received the standard multimodal medication regimen for pain as outlined in the ERAS protocol for colorectal surgery

Criteria for exclusion in Retrospective cohort:

- Emergency surgery
- Daily opioid equivalent use of 30 mg of morphine or greater at time of consent.
- History of drug or alcohol abuse.
- Uncontrolled anxiety, schizophrenia or other psychiatric disorder.

Risk/Benefit Assessment

Risks of the study intervention relate to those associated with the quadratus lumborum block. These include routine risks of block procedures including bleeding, infection, nerve damage, local anesthetic systemic toxicity, as well as transient weakness of the hip flexor muscles (a known possible side-effect of QL block).

If subjects receive the quadratus lumborum block, they may experience improved pain control and/or reduced side effects compared to the epidural pain relief option, but it is not known yet whether this will be the case.

Data Analysis & Statistical Considerations

We will use descriptive statistics (mean (SD) or frequency (%)) and group comparisons via Wilcoxon rank sum or fisher exact tests to measure differences between cohorts in opioid consumption, pain scores with rest and activity, and other secondary outcome measures.

Sample Size Justification

A difference in opioid consumption less than 20% would be considered non-inferior. Based on typical postoperative opioid consumption following laparoscopic colectomy (20mg +/- 5.2 mg), a total of 54 subjects (27 in each group) would be required to reject the null hypothesis that QL blockade is inferior in the first 48 hours with the study intervention, given an alpha of 0.05 and a power of 0.8. We plan on recruiting 45 subjects to account for dropout.