

Evaluating the efficacy of continuous nerve block vs combination of single-injection block plus intravenous lidocaine for postoperative pain.

Study Title: *A Prospective, Randomized, Active-Comparator, Open-Label, Non-Inferiority Study of the Efficacy of Continuous Nerve Block vs. Single block plus intravenous Lidocaine for Post-Operative Pain*

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Background

A multimodal approach to perioperative pain including regional anesthesia is recommended for thoracic and abdominal surgeries^(1, 5, 6, 8, 17, 18, 29, 35, 38, 39, 42, 47). Thoracic paravertebral blocks (TPVB) have been demonstrated to be effective for the management of perioperative pain following thoracic and abdominal surgery, but widespread adoption of this technique is limited by the requirement for advanced training^(5, 8, 17, 38, 42, 47). In the last several years, various fascial plane blocks including the erector spinae plane (ESP) and quadratus lumborum (QL) block have emerged as an alternative to TPVB. These techniques have experienced a surge in popularity in clinical practice because they are technically easier and less prone to the serious complications of TPVB while retaining similar clinical efficacy^(1, 8, 29, 40). In our institution, both ESP and QL blocks in combination with a multimodal approach have become the standard of care for perioperative pain management in patients undergoing thoracic and abdominal surgeries, respectively.

The ESP block, originally described by Forero et al, involves injection of local anesthetic under ultrasound guidance in the plane between the erector spinae muscle and the thoracic transverse processes^(1, 8, 24, 38, 39, 42). The proposed mechanism of action of the ESP block is spread of local anesthetic to the paravertebral space, blocking the ventral and dorsal rami of thoracic spinal and sympathetic nerves^(1, 8, 18, 42). The ESP block has been reported to be an effective analgesic technique for a variety of surgical procedures including video-assisted thoracoscopic surgery (VATS)^(1, 3, 8, 13, 17, 18, 29, 35, 42, 44). This literature includes a randomized controlled trial by Fang et al, who found no difference in pain scores between patients who received ESP and TPVB following thoracotomy⁽¹⁷⁾.

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The Quadratus Lumborum block (QLB) was first described by Blanco (2007) as a variant of the traditional Transversus Abdominis Plane block (TAP). The QLB involves injection of local anesthetic between the quadratus lumborum muscle and the thoracolumbar fascia (TLF), resulting in spread along the TLF to the paravertebral space and to the celiac ganglion or sympathetic trunk via splanchnic nerves ^(2, 9, 12,15, 41). QLB has been described as an effective alternative analgesic technique to TPVB for a wide variety of abdominal and urologic surgeries^(2, 3, 7, 10, 14, 19, 25, 26, 32, 33, 46, 48, 49).

Although significant improvements in postoperative analgesia have been reported with the use of single-injection ESP and QL fascial plane blocks, the relatively short lasting effects of these blocks have led to the placement of a perineural catheter to extend the duration of perioperative analgesia^(9, 20, 21, 24, 34, 35, 37, 50). Although rare, continuous blocks carry their own set of risks and limitations, including catheter dislodgement, migration, kinking and leaking at the site, increased risk of bleeding, especially in case of concomitant use of anticoagulants, and infection^(4, 20, 23, 31, 36). Lastly, from a cost point of view, the use of continuous nerve blocks is overall more expensive compared to single block, especially in our institution where the pump used to continuously infuse the local anesthetic mixture requires disposal and much more expensive cartridges (\$48 vs \$15).

Perioperative intravenous (IV) lidocaine is considered one of the safest local anesthetics and its use has been shown to provide analgesia and reduce opioid requirements, and to shorten the time to return of bowel function and decrease hospital length of stay following colorectal surgery^(11, 27, 28, 30, 43, 45). Furthermore, it has been hypothesized that part of the analgesic efficacy of continuous peripheral nerve blocks may be due to the systemic effects of the local anesthetic infused at the site^(27, 43). Therefore, it is possible that the combination of a single block followed

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by an infusion of IV lidocaine may provide the same benefits as a continuous nerve block at a significantly lower cost. Thus, our database review indicated that both techniques produced similar postoperative analgesia. Since no prospective, randomized study has been conducted to compare these two techniques, the purpose of this study is to compare a single-shot fascial plane block technique plus IV lidocaine to a continuous nerve block technique. For the purpose of this study we chose two surgical models--VATS and major abdominal surgery--and ESP and QL blocks, respectively.

Specific Aims

This study will prospectively investigate the efficacy of continuous Erector Spinae Plane block (ESP) or Quadratus Lumborum block (QLB) versus the combination of single shot ESP or QLB plus postoperative intravenous (IV) lidocaine infusion for postoperative pain management in patients undergoing VATS and major abdominal surgery. The primary outcome measure will be total opioid medication consumption at 24 hr following the surgery, reported as total Morphine PO equivalent in 24 hours after surgery. Secondary outcomes include opioid consumption at 48 and 72 hours after surgery, pain scores at 6, 12, 24, 48, and 72 hours after surgery, total dose of local anesthetic administered at 12, 24, 48, and 72 hours after surgery - reported in (mg), serum lidocaine levels at 24, 48, and 72 hours postoperatively, total hospital length of stay from admission to discharge, patient satisfaction, and incidence of adverse events. Lastly, the cost of each technique will be assessed.

Morphine equivalents will be calculated using ClinCalc - Equianalgesic dosage conversion calculator ⁽²²⁾. Pain scores will be reported using the Numeric Pain Rating Scale, with 0 meaning no pain and 10 meaning worst possible pain ⁽¹⁶⁾.

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All variables including opioid consumption, non-opioid analgesics, pain scores, local anesthetic medication consumption, serum lidocaine levels, and adverse events will be recorded on a case report form.

Hypothesis

There will be no difference in efficacy between the two groups.

Study Design

The study will be conducted as a prospective, randomized, open-label, non-inferiority, active-comparator trial at the University of Pittsburgh Medical Center (UPMC) Shadyside Hospital. Institutional review board approval will be obtained before eligible patients are recruited and consented. The trial will be registered at www.clinicaltrials.gov before beginning recruitment.

Recruitment

Potential subjects will be recruited in the preoperative area of Shadyside hospital on the day of their scheduled thoracic or abdominal surgery. Patients who agree to participate in the trial will sign an IRB approved Informed Consent Form. Sixty patients are expected to be enrolled in this trial, with thirty in each group (group 1= continuous nerve block and group 2 = single block + IV infusion of lidocaine). Within each group, half of the patients will be scheduled for a unilateral VATS and half for major abdominal surgery.

Randomization Process

After obtaining a signed informed consent, participating patients will be randomized by computer generated random numbers to either the control group to receive continuous Erector Spinae Plane block (in the case of thoracic surgery) or continuous Quadratus Lumborum block (in the case of abdominal surgery), or the treatment group to receive single shot Erector Spinae Plane block (in the case of thoracic surgery) or single shot Quadratus Lumborum block (in the case of abdominal surgery) with postoperative intravenous lidocaine infusion.

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Inclusion Criteria

1. 18-90 years old
2. Primary unilateral VATS or major abdominal surgery
3. BMI 20-36, weight \geq 50kg

Exclusion Criteria

1. Patient refusal
2. Inpatient status at the time of surgery
3. ASA class 4 or greater
4. Pregnancy
5. Non-English speaking or inability to participate in the study
6. Patients with coagulopathy or on therapeutic anticoagulation
7. Chronic steroid use
8. Opioid use disorder
9. Contraindication to performing any of the proposed blocks - active infection at the block site, systemic infection, allergy to local anesthetic medications
10. Patients undergoing second surgery or urgent/emergent surgery
11. Patients weighing < 50kg
12. History of chronic pain and/or opioid tolerant
13. Anticipated requirement for patient-controlled analgesia (PCA)
14. Allergy or intolerance to any medication specified in the study protocol or postoperative pain management regimen
15. Liver disease

Treatment Groups

Group 1, Continuous nerve blocks: A total of 30 subjects equally distributed to either CESP for VATS , or CQL for major abdominal surgery. Patients in this group will receive 20ml 0.5%

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ropivacaine per block performed after positioning of the needle followed by continuous perineural infusion of 0.25% lidocaine (10ml/hr) beginning in the post-anesthesia care unit (PACU) and continued for 72 hours or until 12 hours prior to patient discharge, whichever comes first, which is standard of care at this institution.

Group 2, single nerve blocks plus IV lidocaine infusion: A total of 30 subjects equally distributed to either ESP for VATS, or QL for major abdominal surgery, will be included .

Patients in this group will receive 20ml 0.5% ropivacaine per block after proper positioning of the Tuohy needle. Upon patient arrival in the recovery room a continuous infusion of IV lidocaine 50 mg /hr will be started and continued for 72 hours or until 12 hours prior to patient discharge, whichever comes first, which is standard of care at this institution.

Block techniques

I. Group 1= Continuous nerve blocks.

A total of 30 subjects equally distributed to either CESP for VATS , or CQL for major abdominal surgery will be enrolled.

A. Continuous ESP Block Approach: The patient will be positioned in seated position with side or sides to be blocked marked. The T5 spinous process will be identified by palpation starting with C7 and continuing caudad. C7 is the most prominent spinous process anatomically. The T5 spinous process will be marked with a marking pen. The block area will be cleaned using 2% chlorhexidine solution. The entire block procedure is performed under strict aseptic technique. An ultrasound probe covered in a sterile probe cover will be placed at the T5 spinous process in a cephalad to caudad orientation and moved lateral until the T5 transverse process is identified. 1-2ml of 1% lidocaine will be administered just above the ultrasound probe for local skin infiltration. An 18 gauge Tuohy needle will then be inserted in plane in a cephalad to caudad direction under ultrasound visualization until the tip of the needle touches the T5 transverse process.

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The T5 transverse process is the anatomical target for this block. 20ml of 0.5% ropivacaine will then be injected using slow fractionated injection, aspirating every 5ml to ensure the needle tip is not intravascular. Local anesthetic spread in the appropriate plane will be confirmed with ultrasound. Once injection is complete, a 20 gauge nonstimulating catheter will be inserted through the Tuohy needle. Catheter tip placement will be confirmed with ultrasound. If bilateral blocks are to be performed, the procedure will then be repeated on the contralateral side.

B. Continuous QL Block Approach: The patient will be positioned in lateral decubitus position with the side to be blocked facing up and the side or sides to be blocked marked. The block area will be cleaned using 2% chlorhexidine solution. The entire block procedure is performed under strict aseptic technique. An ultrasound probe covered in a sterile probe cover will be placed transversally between the iliac crest and the costal margin at the level of the anterior axillary line and the three muscles of the anterolateral abdominal wall (external oblique, internal oblique and transversus abdominis) will be identified. The probe will then be moved posteriorly until the transversus abdominis muscle (TAM) tapers off into its aponeurosis approximately at the level of the posterior axillary line, and posteriorly to this the intersection of the transversalis fascia with the lateral side of the QL muscle will be identified. An 18 gauge Tuohy needle will then be inserted in plane in an anterior to posterior direction until the tip of the needle is visualized at the intersection of the transversalis fascia with the lateral side of the QL muscle. The intersection of the transversalis fascia with the lateral side of the QL muscle is the anatomical target for this block. Once the initial injection of local anesthetic is complete, a 20 gauge nonstimulating catheter will be inserted through the Tuohy needle. Catheter tip placement will be confirmed with ultrasound. If bilateral blocks are to be performed, the patient will be repositioned, the area to be blocked will

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be cleaned and prepared in a strict aseptic fashion as described above, and the procedure will then be repeated on the contralateral side.

2. Group 2, Single shot nerve blocks with IV lidocaine: A total of 30 subjects equally distributed to either single-shot ESP for VATS , or single-shot QL for major abdominal surgery will be enrolled. A 22 gauge Tuohy needle will be used to perform these blocks. After the proper positioning of the needle 20ml of 0.5% ropivacaine plus, 4mg dexamethasone, plus 20mcg dexmedetomidine per injection site (30mcg if unilateral block only) will be deposited. In the recovery room an infusion of IV lidocaine at 50mg/hr for be initiated for 72 hours or until 12 hours prior to patient discharge.

A. Single Shot ESP Block with Postoperative IV Lidocaine Approach: The same technique described for the CESP will be used except that in this case a single ESP block will be used.

B. Single Shot QL Block with Postoperative IV Lidocaine Approach: The same technique described for the CQL will be used except that a single QL block will be used.

After the proper positioning of the 22 gauge Tuohy needle, 20ml of 0.5% ropivacaine, 4mg dexamethasone, and 30mcg dexmedetomidine (20mcg if bilateral blocks are to be performed) will then be injected using slow fractionated injection, aspirating every 5ml to ensure needle tip is not intravascular.

Anesthetic Management

Both treatment groups will receive the standard anesthetic technique and multimodal analgesic technique at our institution, including preoperative gabapentin 300mg PO and acetaminophen 1000mg PO, intraoperative IV propofol infusion-based general anesthetic combined with sub-anesthetic dose IV ketamine infusion, IV dexmedetomidine infusion, IV acetaminophen, and avoidance of intraoperative opioids. Postoperative pain management will also follow standard protocol, using IV hydromorphone (0.2-0.3 mg) and PO oxycodone (5-10 mg) on request by the

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patient for moderate to severe pain (VAS >5), scheduled ketamine 20-50mg PO q 8hrs for 48 hours, scheduled acetaminophen 1000mg IV or PO q 6hrs, scheduled gabapentin 100-300mg PO at bedtime, and dexmedetomidine infusion 0.2mcg/kg/hr IV for 24 hours if the patient is located in the Intensive Care Unit.

Data Collection and Outcome Measures

Once the patient has signed the informed consent document, they will be randomized to receive CESP or CQLB, or SESP or SQLB with postoperative IV lidocaine infusion. The person administering the block and the patient will be unblinded. The outcome assessors will be blinded to the treatment group allocation. The primary outcome measure is total opioid medication consumption, reported as total Morphine equivalent in 24 hours after surgery. Secondary outcomes include opioid consumption at 48 and 72 hours after surgery, pain scores at 6, 12, 24, 48, and 72 hours after surgery, total dose of local anesthetic administered at 12, 24, 48, and 72 hours after surgery - reported in (mg), serum lidocaine levels at 24, 48, and 72 hours postoperatively, total hospital length of stay from admission to discharge, and incidence of adverse events - nausea and vomiting requiring treatment, hypotension, and bradycardia or tachycardia. Opioid medication consumption, pain scores, local anesthetic medication consumption, serum lidocaine levels, and adverse effects will be recorded on worksheets included in patient research folders, with each study participant having their own research folder identified only by randomly assigned patient study number.

Statistics

Demographics will be presented as mean \pm SD. Pain and opioid consumption data will be presented as median (75% confidence interval). This study is designed as a non-inferiority trial. All continuous variables will be compared between the two groups by Wilcoxon rank sum test and dichotomous variables will be compared by Chi-square test. $P < 0.05$ will be considered

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statistically significant. SPSS 12.0 software will be utilized for statistical analysis. Intention to treat analysis will be utilized for this study.

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