Title: Regional Blockade of the Sternum with Liposomal Bupivacaine Prior to Incision Decreases Opioid Use in Patients undergoing Cardiac Surgery

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Background:

Prolonged and excessive narcotic usage in the postoperative setting has been linked to multiple complications. Use of complimentary pain management techniques such as regional analgesia can reduce postoperative pain and narcotic usage. This can enhance patient recovery and improve quality of life in the immediate postoperative period. [1] Previous research investigating the benefits of local analgesia during cardiac surgery have been limited by the sparse amount of single-center randomized controlled trials, particularly evaluating the use of para-sternal injections.

Of the available studies, the use of local analgesia injections compared to controls has led to improved pain scores and overall decreased perioperative opioid usage. Studies have shown this efficacy using 0.2% ropivacaine, [2] 0.75% ropivacaine, [3] and 0.53% liposomal bupivacaine [4] all compared to control groups receiving normal saline injections in the para-sternal area. These studies all used injections just prior to sternal closure and no significant evidence is available for the use of ultrasound-guided regional block of the sternum prior to surgical incision. Injection of analgesia prior to surgical incision has been shown to decrease postoperative pain compared to injection after surgical closure. [5]

Hypothesis/Aims:

We hypothesize that injection of 1.3% liposomal bupivacaine and 0.5% bupivacaine (20mL dose) as a sternal block prior to surgical incision will lead to decreased pain and opioid usage in the intraoperative and postoperative setting for patients undergoing upper mini- and median sternotomy compared to controls (normal saline block).

Aim 1: To demonstrate decreased postoperative opioid usage and decreased pain scores in the postoperative setting in the treatment group compared to controls.

The amount of opioid medications used will be recorded during the routine postoperative course. Pain scores, set by a validated system, will be obtained daily during the routine postoperative course.

Aim 2: To demonstrate decreased intraoperative opioid usage in the treatment group compared to controls

Aim 3: To demonstrate improvement in key clinical components closely linked to narcotic usage.

Multiple variables specific to opioid usage will be recorded during the routine postoperative setting. These included, but are not limited to: time to extubation, incentive spirometer volume, return of bowel function, postoperative atrial fibrillation incidence, delirium and intensive care unit (ICU) and overall lengths of stay (LOS).

Methods

This is an investigator-initiated prospective randomized study with an 18-month patient accrual period and patient follow-up period dependent on postoperative length of stay following surgery.

Regional Block: Liposomal Bupivacaine (1.3%) solution (20 mL dose) is proposed for use during this study. This solution has demonstrated increased efficacy in prolonged analgesia following injection. This solution will be injected as an ultrasound-guided subpectoral interfacial plane block.

Normal Saline: Normal saline (0.9%) will be used as the control solution for patients not receiving the liposomal bupivacaine solution. Injection procedure of this solution will be identical to that of the liposomal bupivacaine solution.

Procedures: Patients undergoing a surgical procedure through mini- or full sternotomy will be considered for inclusion in this study. Qualified patients will be randomized 1:1 to a liposomal bupivacaine sternal block or a normal saline block. An unblinded research coordinator will use a password-protected spreadsheet to randomly generate the subject's randomization assignment. The unblinded coordinator will communicate the information to the unblinded anesthesiologist who will perform the block. This ensures the intraoperative (including a blinded anesthesiologist and surgeon) and postoperative staff (including the blinded research coordinator) will remain blind to the randomization assignment. The subject will also be blinded to the assignment. The amount of opioid medications given by the anesthesia team during the procedure will be recorded. Anesthesiologists will be encouraged to standard of care early extubation. There will be no deviation from routine surgical procedures following injection of para-sternal solution prior to surgical incision. Patients are considered part of the research study until they are discharged. After discharge, patients can be told which block they were given and the blinded coordinator can be unblinded to review all medical records.

Study Population

Patients undergoing a surgical procedure through mini- or full sternotomy from 7/1/2019 at THHBP will be included in this data set. A total of 150 patients is proposed for this study.
Inclusion Criteria:

1. Age greater than 18 years
2. Undergoing a surgical procedure through mini- or full sternotomy.

Exclusion Criteria:

1. Clinical instability

2. Allergic to liposomal bupivacaine solution or any of its ingredients
3. Maximum-allowed dosage of local analgesia will be exceeded by the injection amount of liposomal bupivacaine used in this study (<50 kg).
4. BMI >45
5. Pregnant or nursing
6. Chronic home opioid usage
7. LVEF< 30%
8. Low cardiac output requiring mechanical or inotropic support
9. End-stage renal disease
10. Cirrhosis
11. Re-do sternotomy
12. Endocarditis

Data elements

Patient Characteristics:

1. Age
2. Gender
3. BMI
4. Tobacco use
5. Chronic lung disease
6. Diabetes
7. HTN
8. HLD
9. Ethnicity (Hispanic & not Hispanic)
10. Race (Caucasian, African Americans, Asians and others)
11. CKD
12. CVA
13. Chronic home NSAID use (excluding ASA)

Intraoperative Variables:

1. Type of procedure being performed
2. Prior procedures performed

Postoperative Variables:

Time to extubation, time to ambulation, time to oral diet, return of bowel function (bowel movement), postoperative atrial fibrillation incidence (through discharge), and intensive care unit (ICU) length of stay (LOS) and overall LOS. Maximum incentive spirometer maximum volume at 24, 48 and 72 hours, Confusion assessment method (CAM) at 24, 48 and 72 hours, post op opioid usage up to 72 hours post op. If additional days of post-op opioid usage is documented in the existing medical record, this may be used also. CAMs are performed by the blinded research coordinator.

Pain scores (Scale 0-10) at 1, 2, 4, 8, 12,24,36,48, 60, and 72 hours after ICU arrival for extubated patients and CPOT scores (Scale 0-8) for intubated patients

Adverse Events: Allergic reaction, pneumothorax, pericardial tamponade, vascular injury, hematoma, intravascular injection, wound infection, paresthesia, persistent numbness. These adverse events will be monitored and reported from the start of the study procedure to discharge (study termination).

Protocol Deviations: If certain data elements are not in the existing medical record and were not collected, this is not a protocol deviation. Nevertheless, all effort will be made to collect these data points.

Funding: CVRRC

Journals in which you plan to publish or meetings where abstracts will be submitted: TBD

Risks and Benefits

Risks: The risks are the same as the Standard of Care surgery performed outside this study. This is discussed in the ICF. A confidentiality breach is a risk associated with research. However, all data collection protocols follow HIPAA guidance.

Benefits: If participants receive the drug, they could experience less pain than those that don't receive the drug. However, not all participants are likely to benefit from the proposed research. The investigators will benefit from the knowledge gained, as it will provide deepened insight on the main challenges, advantages and disadvantages of the procedure.

Data Analytic Methods

The mean, standard deviation, median, and interquartile ranges of narcotic usage (in morphine equivalent units) will be reported for each group. The difference of narcotic usage between the two groups will be reported as a single value. Additional variables analyzed in this study include the following:

Patient Characteristics:

1. Age
2. Gender
3. BM
4. Tobacco use
5. Chronic pain medication usage
6. Diabetes
7. HTN
8. HLD
9. Race & Ethnicity
10. CKD
11. CVA

Intraoperative Variables:

1. Type of procedure being performed
2. Prior procedures performed

Postoperative Variables:

1. Time to extubation
2. Time to ambulation
3. Time to oral diet (solid foods)
4. ICU LOS
5. Total LOS from date of sternotomy
6. Return of bowel function
7. Postoperative atrial fibrillation

8. Maximum spirometry at 24, 48, 72 hours post op
9. CAM at 24, 48, 72 hours post op
10. Pain Scores (Scale 0-10) at 1, 2, 4, 8, 12,24,36,48, 60, and 72 hours after ICU arrival for extubated patients and CPOT scores (Scale 0-8) for intubated patients
11. Post op opioid usage up to 72 hours post op

Standard descriptive statistics will be used throughout (mean, range, standard deviation, and median, IQR), with comparative statistics for normally and non-normally distributed data with $p<0.05$ considered as significant. For categorical variables, 2 Sample t-test or chi-squared test will be used to determine statistical significance. For continuous variables, logistic regression will be used to determine the value of significance to variables with postoperative outcomes. Depending on the enrollment rate, the stratification of data based on the type of sternotomy (full or mini) could be performed and analyzed respectively.

References

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4. Lee, C.Y., et al., *A Randomized Controlled Trial of Liposomal Bupivacaine Parasternal Intercostal Block for Sternotomy.* Ann Thorac Surg, 2019. 107(1): p. 128-134.
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