Randomized prospective study comparing paravertebral catheters, single shot paravertebral block, thoracic epidural, for postoperative analgesia following Video-assisted thoracoscopic surgery

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1.0 Background

With the production of high quality imaging systems and improved surgical instruments, video-assisted thorascopic surgery (VATS) has increased in popularity. When compared to an open technique VATS has been shown to decrease opioid requirements, decrease length of stay and lead to decreased shoulder dysfunction. VATS surgery has also been shown to decrease time until patients resume their normal activity. Despite these statistics, pain following VATS can be severe and long lasting. In addition to non-steroidal anti-inflammatory drugs and systemic opioids, paravertebral nerve blockade and epidural with local anesthetics have emerged as viable adjuncts for control of post-operative pain. Chronic pain after thoracotomy has been studied extensively, and VATS has also been associated with similar rates of chronic pain when compared with open techniques.

Currently, there is no standard of care for post-operative pain control for these patients. The standard of care varies largely, depending on the anesthesiologist or the surgeon. Some anesthesiologists prefer thoracic epidural while others prefer paravertebral block. Each of these pain control techniques have been studied individually and have been shown to provide benefits. Komatsu et al showed that adequate post-thoracotomy pain control was accomplished by continuous paravertebral blockage, while Yoshioka et al showed that epidural analgesia provide effective pain control after surgery. Our study aim is to compare three different methods of pain control that have been proven to show benefit in VATS and compare the efficacy versus the side effects of each techniques. We also aim to look at the effect of these different regional techniques on pain 6 months after surgery.

As mentioned above, several regional techniques have been described for post thoracotomy pain and adapted to VATS. The three most common techniques are:

1) paravertebral block using anatomical or ultra-sound guidance

2) visual placement of extrapleural paravertebral catheter by thoracic surgeons

3) thoracic epidurals

Previous studies have demonstrated that both thoracic epidurals and paravertebral blocks provide adequate analgesia for VATS. Thoracic epidurals provide excellent pain relief but are associated with hypotension and more nausea/vomiting. Paravertebral catheters have the advantage of having a lower side effect profile than thoracic epidurals. Paravertebral blocks have also been shown to improve respiratory function after surgery. Single shot paravertebral blocks have been described as providing adequate post-VATS pain control, despite a shorter duration of action compared to catheter. In order to evaluate the effectiveness and the side effects of the different pain modalities for post-VATS pain control, we will compare these three different methods of pain blocks:

1)single shot paravertebral block

2)paravertebral catheters

3)thoracic epidural

Rationale and Specific Aims

All of the pain control modalities allow for titration and continuous infusion of local anesthetic to achieve adequate pain control for the duration that the catheter remains in place, except for the single shot paravertebral block. The specific aim of the study is to compare the difference between the three pain blocks in achieving the following:

1. Improved postoperative pain scores
2. Decreased opioid requirements
3. Improved patient satisfaction scores
4. Decreased opioid side effects (Nausea, sedation, ileus, urinary retention, respiratory depression)

The primary endpoint of this study will be VAS pain score. The VAS scores will be taken with both rest and movement.

The secondary endpoint includes intravenous opioid consumption and opioid side effects (nausea, sedation, ileus, urinary retention, respiratory depression). The IV and PO opioid doses will be quantified at 1, 24, 48, and 72 hours. We will also measure postoperative nausea and sedation scores at 1, 24, 48, and 72 hours. We will also measure time to first bowel movement, incidence of urinary retention, incidence of respiratory depression, and time to discharge. If subjects are discharged prior to completing the 72-hour endpoints, efforts will be made to contact them and obtain data points. If unable to be reached, or unable to collect data, we will not consider these deviations since it will not change the integrity of the study data.

All patients will receive a phone survey 6 months after surgery to assess for pain and quality of life. If the 6 month questionnaire is unable to be completed, we will not consider this a deviation since it will not affect the integrity of the study data. However, every attempt will be made to complete a follow up questionnaire.

2.0 Inclusion/Exclusion Criteria

Inclusion criteria:

- Pt undergoing VATS procedure at Indiana University Hospital
- ASA 1,2,3 or 4
- Age 18 or older, male or female
- Desires Regional anesthesia for postoperative pain control

Exclusion criteria:

- Any contraindication for Thoracic Epidural or Paravertebral block
- History of substance abuse in the past 6 months
- Patient staying intubated after surgery
- Known allergy or other contraindications to the study medications , which include dilaudid, bupivacaine, ropivacaine

3.0 Enrollment/Randomization

All VATS cases scheduled by thoracic surgeons at IU Health University Hospital will be identified. The subjects will be contacted face-to-face prior to surgery. They will be informed about the study and all questions will be answered. The potential subjects will be given a copy of the informed consent form and authorization form. The subjects will then be contacted face-to-face in POCU on the day of surgery and if participation is agreed, written consent will be taken.

A total of 120 subjects will be randomized by a computer program into three groups (40 per group):

1. US- Guided Paravertebral Catheter (PVB-A)- The Alaris pump will deliver 0.2% Ropivicaine at a rate of 10 ml/hr
2. Single Shot Paravertebral Block- placed by ultrasound using 0.2% Ropivicaine bolus.
3. Thoracic Epidural- The Alaris pump will deliver an epidural mixture of 0.125%bupiv/hydromophone

Randomization will be stratified by prior opioid experience (opioid naïve or opioid tolerant). Separate randomization lists will be used for the two strata.

4.0 Study Procedures

All the thoracic epidurals and ultrasound-guided paravertebral blocks will be placed preoperatively. All procedures will be done using sterile technique with masks, hats, and sterile gloves. All procedures will be placed under the supervision of the attending anesthesiologist on the acute pain service or the attending anesthesiologist in the VATS room.

Thoracic epidurals will be placed using the Arrow thoracic epidural kit. Fentanyl and midazolam will be given prior to epidural placement. The epidural will be placed at the appropriate level to cover the entry site for the VATS procedure. Placement will be determined by anatomical landmarks. The epidural needle will be advanced toward the epidural space utilizing a Paramedian approach and loss-of-resistance technique. A sterile catheter will then be secured in place and the epidural infusion will be started at the end of the case.

Ultrasound guided paravertebral catheter and single shot paravertebral block will be accomplished using an ultrasound transducer at the thoracic level. This will be done using an in-plane or out-of-plane approach, at the discretion of the anesthesia staff performing the procedure. Then a needle will be inserted the needle into the paravertebral space and local anesthetic injected. Then a catheter will be placed within the injectate and secured in place in the case of the paravertebral catheter. The 0.2% Ropivicaine will be delivered by OnQ pump.

General anesthesia will be induced and the patient will be placed in the lateral position for the VATS procedure. The patients will be intubated with dual lumen endotracheal tubes and placed on one-lung ventilation for the procedure.

All patients will receive intravenous patient-controlled analgesia (PCA hydromorphone) post-operatively for breakthrough pain. Usual standard of care for pain control following a VATS procedure include scheduling PO acetaminophen and PO oxycodone PRN on POD 1 once patients tolerate diet.

Opioid usage at 1,24,48,72 hours after the block will be recorded by a member of the research team. Pain scores at rest and on movement (knee flexion) will be measured by the investigator using Visual Analog Scale (VAS). Nausea will be measured using a categorical scoring system (none=0; mild=1; moderate=2; severe=3). Sedation scores will also be assessed by a member of the study team using a sedation scale (awake and alert=0; quietly awake=1; asleep but easily roused=2; deep sleep=3). All these parameters will be measured at 1, 24, 48 and 72 hours after the epidural or PVB. Patients will be encouraged to ambulate on postoperative day 1 under supervision.

All catheters will be removed by APS (Acute Pain Service) while patients are still in the hospital. APS will continue to follow the patients until catheter removal. Patient's hospital length of stay and readmission rate will be recorded from NSQIP (National Surgical Quality Improvement Program) data.

All patients will receive a phone call 6 months after surgery for assessment for chronic post-surgical pain. Patients will be assessed by a member of the research team over the phone. They will be assessed on their pain score and narcotic usage by using the Brief Pain Inventory. Study participation will conclude after the 6 month follow questionnaire has been completed.

5.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

Patients will be monitored by the primary team during the postoperative period which is after surgery, through hours, 24, 48, and 72. We will also follow up in 6 months with a telephone call to complete a questionnaire which will conclude all study participation. The potential complications or risks associated with all three procedures are risks that are normally expected and we will not consider these adverse events. Any post-operative complication that is associated with the required medication per study protocol such as drug toxicity or nausea and vomiting related to taking the scheduled Tylenol and PRN (as needed) oxycodone for pain will be reported as an adverse event. This required drug regimen is specific to the study. All of these events will be reported to the Principal investigator and will be addressed immediately. These adverse events will be assessed to determine if they meet prompt reporting criteria, and if so, we will report these events to the IRB committee using the prompt reporting form. Events not promptly reportable will be reported to the IRB at the time of study renewal, if applicable."
Normal post-operative adverse events such as nausea, vomiting, and pruritus will not be considered a recordable or reportable event to the IRB since it's part of the post-operative course expected with these procedures.

6.0 Study Withdrawal/Discontinuation

The patient can withdraw from the study at any time by contacting the research team or acute pain anesthesia resident. In such an event, the catheter will be removed immediately, provided no anticoagulants had been administered. Patient may still have access to Alaris pump and will have access to all the IV and oral pain medications. Anesthesia acute pain team will continue to follow the patient for 24 hours. 24 hours after catheter removal, anesthesia acute pain team will sign off and all further pain management will be done by the primary team.

7.0 Statistical Considerations

Primary outcome: VAS score at 24 and 48 hours

Primary Research Hypothesis: Thoracic epidural and Ultrasound guided paravertebral block with continuous catheter will provide lower pain scores compared to single shot paravertebral block.

Secondary outcomes: Opioid usage after 1, 24, 48 and 72 hours. Pain scores using VAS at rest and on movement at 1, 24, 48 and 72 hours. Patient satisfaction scores at 24 and 48 hours. Nausea scores at 1, 24, 48 and 72 hours. Sedation scores at 1, 24, 48 and 72 hours. Time to first bowel movement, incidence of urinary retention, and incidence of respiratory depression will be recorded as well.

Secondary Research Hypotheses: Thoracic epidural anesthesia and Ultrasound guided paravertebral catheter will show improved pain control, improved patient satisfaction scores, and decreased nausea and sedation scores compared to single shot paravertebral.

Statistical analysis will be performed using a standard statistical program (SAS or SPSS). All data will be summarized (means, standard deviations, standard errors, and ranges for continuous variables; frequencies and percentages for categorical variables) by group. Demographic data will be compared between the four groups using ANOVA or chi-square tests as appropriate. The primary outcome, VAS at 24 and 48 hours, will be compared between the groups using repeated measures ANOVA; the model will include fixed effects for group, time, and the group by time interaction and random effects to allow correlations between the two times and different variances for the two times. Pain and satisfaction scores and opioid usage over time will be analyzed using repeated measures ANOVA. Nausea and sedation scores will be compared between groups at each time point using Mantel-Haenszel chi-square tests for ordered categorical data. Distributions of the continuous variables will be examined, and a transformation of the data (e.g. natural logarithm) or nonparametric tests will be used as necessary. A 5% significance level will be used for all comparisons.

Based on prior studies, the coefficient of variation for the VAS score at 24 and 48 hours is estimated to be 0.70. With a sample size of 40 per group the study will be able to detect a 60% decrease in VAS score between any two groups, assuming two-sided tests each conducted at a 5% significance level.

8.0 Privacy/Confidentiality Issues

All study papers containing patient identifiers will be kept in each subjects confidential study file accessible to only the research team. All records will be kept in a locked room in a locked cabinet that only authorized staff enters. Collected data from each enrolled participant will be recorded on Redcap which is a secure web-based data collection tool. At the end of the study, all electronic information and paperwork containing patient identifiers will be deleted or shredded.

9.0 Follow-up and Record Retention

The study will start at the beginning of 2017 and will end when a sample size of 120 subjects is achieved. The estimated time frame to enroll 120 study subjects is 24 months. After 120 subjects have been enrolled, the study will be stopped and the data collected will be analyzed using statistical methods.

At the end of the study, all study papers with patient identifiers will be shredded and only data without any patient identifiers will be retained by the research team for an indefinite time.

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