RESEARCH PROPOSAL

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General Information

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Study Information

Study location: George Washington University Hospital
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Study Title: Postoperative pain control with Systemic Lidocaine vs Regional Anesthesia in Renal Transplant Patients

Study Type: Randomized trial

Study Duration: 36 months (Jan 2021 - Dec 2023)

Title: Postoperative Pain Control with Systemic Lidocaine vs Regional Anesthesia in Renal Transplant Patients

Background
GWU does about 75 kidney transplants a year. Adequate postoperative pain control is an important part of the patients' recovery. Renal transplant patients often have multiple comorbidities, that when combined with poorly controlled postoperative pain, can lead to tachycardia, hypertension, and increased risk of respiratory complications, which can in turn affect overall recovery and graft survival.

The use of patient-controlled analgesia (PCA) pumps is currently considered the standard of care in treating surgical pain in the immediate postoperative period [1]. Although a traditional mainstay of therapy, opioids have an unfavorable side effect profile that includes respiratory depression, nausea, postoperative ileus, sedation, and pruritus. Additionally, long-term opioid use is linked with opioid tolerance, addiction, and patient death. Patients that have high-level opioid use in the first year post-transplant have been found to have high rates of death and all-cause graft failure [2].

Recently, there has been a shift in post-operative pain management to utilize a multimodal approach of both non-pharmacologic and pharmacologic therapies. As a result, the use of other non-opioid therapies, such as lidocaine infusions and regional anesthetic techniques, like transverse abdominis plane blocks, have recently increased in popularity in perioperative pain management of renal transplant patients [3].

Intravenous lidocaine has an off label indication as analgesic and has good evidence for use in other areas such as colorectal surgery, trauma and orthopedics. Lidocaine infusions have a strong record of safety with relatively benign adverse side effects. Although data is promising, there is little established evidence of perioperative lidocaine infusions in renal transplant populations.

Transverse abdominis plane (TAP) blocks have emerged as a significant regional technique in the application of multimodal analgesia for abdominal surgeries. Historically, TAP catheters are avoided due to concern about infection near the operative site in immunosuppressed transplant patients. Establishing intravenous lidocaine as an effective treatment option will allow physicians to avoid the side effects of opioids and the infection risks of TAP catheter blocks.

Aims:
1. To see if Lidocaine infusion is non-inferior to TAP catheters for postoperative pain control
2. To see if higher rates of complications arise from non-opioid techniques (infection rates from TAP catheters, anesthetic toxicity from lidocaine infusion)

Recruitment: Recruitment for this study will take place in the preop waiting area. During that time, the purpose and method of the study will be explained to the patient. Patients will be informed of risks, benefits, and alternatives to participation in the study and will have the opportunity to sign consent after review of documentation and having all questions answered.

Recruitment cannot be done prior to the preop area because transplant surgeries are not scheduled far in advance. The organ recipient is called into the hospital when a match is found. The research team will be notified as soon as possible when a renal transplant is scheduled to allow for maximum amount of time to obtain consent.

Inclusion: Single Kidney transplant, >18 years old

Exclusion: Long term use of opioids (e.g. Chronic pain patients), history of substance abuse
Local anesthetic allergy
Complicated surgical course
- Intraoperative damage to other organs e.g. bowel

- Return to OR within 72 hours
- Postoperative ventilation

Methodology

Groupings
Patients will be randomly allocated into 2 groups: Lidocaine + PCA (L group) and TAP + PCA (T group). A member of the research team will perform the randomization and will notify the surgeon and the anesthesiologist on the case. This study is not blinded.

Sample size
The goal will be to recruit at least 55 patients for the Lidocaine group and 25 patients for the TAP block group for a total of 80 patients in all. Sample size for this study is based on information gained from a retrospective study of renal transplant patients. The aim is to demonstrate non-inferiority of lidocaine to TAP block where non-inferiority is defined as <10% difference in OME consumption (with a 95% confidence interval) between the groups.

Intervention
When a renal transplant case is posted to the OR schedule, the research team will be notified. A team member will then meet with the patient in the preop area to obtain informed consent. Once consent is obtained, the medical records of the patient will be screened for exclusion criteria. If the patient meets all criteria, they will be randomized to one of the two study groups.

The anesthesiologist and surgeon on the case will be informed immediately of the group assignment.

In addition to the treatments assigned to each group, all patients will receive the standard of care medications given pre-op, intra-op, and post-op. These medications include oral Tylenol, oral oxycodone as needed, IV morphine or hydromorphone as needed, ketamine as indicated, and Ondansetron as needed. All patients will receive a dilaudid PCA 0.5mg bolus Q10min postoperatively as standard of care.

Following the case, the research team will review the operative note and anesthesia postoperative note to identify any disqualifying surgical complications (injured bowel, patient remains intubated, complication requiring return to OR within 72 hours). If there are disqualifying complications, the anesthesiologist and the surgeon will be notified and the patient removed from the study. Any further treatment for postoperative pain will be per standard of care and the surgeon's discretion.

If there are no disqualifying surgical complications, the following orders for postoperative pain control will be placed per the patient's assigned group:

- Lidocaine (+PCA): 1.0-1.5 mg/kg/hour for 48 hours post-operatively.
- TAP (+PCA): 0.2% Ropivacaine at 6-10ml/hour for up to five days post-operatively.

Nursing will routinely record VAS scores for all patients per nursing standard of care.
The research team will review patient charts daily to obtain the VAS scores and total narcotics used at 12 hours, 24 hours, and 48 hours as well as any notes regarding complications.

Signs of complications due to the treatment methods will be reason to terminate the study and remove that patient from the study. Possible risks are listed below. The surgical team may terminate these treatment modalities as soon as a complication is identified, and may inform the research team as soon as possible afterwards.

Measures:
Demographics (age, gender, race, ASA)
Pain metrics at 12, 24, 48 hours (Time zero is arrival in PACU)

- Oral morphine Equivalents
- VAS score

Duration of operation
Surgeon
Length of stay (date of operation to date of discharge)
Complications

- Sepsis requiring antibiotic therapy
- Acute rejection of transplant
- Local Anesthetic Systemic Toxicity
- Need for CVVHDF
- Opioid toxicity requiring naloxone
- Ileus

Risks:
Risk of lidocaine infusion: Lidocaine toxicity (lightheadedness, dizziness, visual disturbances, confusion, tinnitus, and perioral numbness/peripheral paresthesia)
Risk of TAP block: local infection, hematoma, poor placement leading to inadequate pain control

Endpoints:

- VAS score
- Total opiate usage in morphine equivalents

Expected outcome and significance:
It is expected that patients with patients receiving lidocaine infusion will have equivalent opioid consumption and pain scores compared to patients receiving TAP blocks in the first 48 hours after surgery. If lidocaine infusion is demonstrated to be non-inferior to TAP blocks, this would provide physicians with an alternative to TAP blocks in controlling post-surgical pain while reducing total opioid usage.

Timetable: 36 months

References

1. Farag E, Guirguis MN, Helou M, et al. Continuous transversus abdominis plane block catheter analgesia for postoperative pain control in renal transplant. *J Anesth*. 2015;29(1):4-8.

2. Lentine KL, Lam NN, Naik AS, et al. Prescription opioid use before and after kidney transplant: Implications for posttransplant outcomes. *Am J Transplant*. 2018;18(12):2987-2999.

3. Siddiqui MR, Sajid MS, Uncles DR, Cheek L, Baig MK. A meta-analysis on the clinical effectiveness of transversus abdominis plane block. *J Clin Anesth*. 2011;23(1):7-14.