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ID: PRO44982 Lidocaine Patches in Elderly Patients With Traumatic Rib Fractures NCT05714631

Background:

Rib fractures occur in approximately 20% of all patients who suffer a traumatic injury and can be associated with functional implications, pulmonary infectious complications including pneumonia, and death, particularly among patients over the age of 65[1]. Multimodal pain control is the hallmark of treatment with particular interest in options that allow for decreased use of opioids which carry risks of delirium, abuse and dependence. One commonly prescribed analgesic choice is topical therapy with lidocaine patches. The theory is that the lidocaine will diffuse through the skin and subcutaneous tissue to provide analgesia without causing systemic side effects or requiring invasive procedures required for regional therapies (epidurals, serratus anterior blocks) which can be difficult in geriatric patients due to altered anatomy with degenerative bone and disk disease in the spine as well as the contraindication of anticoagulant or antiplatelet therapy.

While the idea behind the use of lidocaine patches is appealing, the data supporting their use in trauma patients is mixed. Original interest was developed in a retrospective study that showed decreased pain scores in patients who utilized lidocaine patches as part of a multimodal pain control regimen [2]. However, a up double blinded placebo controlled randomized control trial failed to show efficacy [3]. There were several limitations to the generalizability of this study however as the patients all had suffered polytrauma, not isolated ribs fractures, and therefore overall pain scores likely were not truly reflective of the local effects of the patch itself. Additionally, patient BMI was not reported or controlled for which makes the makes the penetrance of the patch a concern. An additional randomized controlled trial based out of Tawian, did note a decrease in pain scores when lidocaine patches were used for rib fractures however this was only a 1.5-point decrease on a 1-10 scale, which raised question of the clinical significance [4]. Most recently a retrospective study noted a 50% decrease in the in hospital opioid use of patients utilizing lidocaine patches, however, this study was limited in that length of stay was longer in the non-patch group which likely factored in to the total oral morphine equivalent utilization[5].

The aim of this pilot study is to determine if it is feasible to perform a larger scale trial looking to answer the question on the efficacy of decreasing opioid use in elderly patients with rib fractures but minimal other injuries by utilizing 4% topical lidocaine patches vs a placebo. An additional arm with standard of care treatment which does not require lidocaine patches at our institution) will be included to help determine if the placement of a patch itself also provides a placebo effect, which has never been noted in the two prior RCTs.

Purpose:

Many patients are prescribed lidocaine patches for rib fractures despite mixed evidence to their efficacy. **The outcome of this trial offers significant benefit to patient care if it finds benefit of their use or if it does not.** Reducing opioid use and increasing functional outcomes in older adults patient suffering rib fractures can improve quality of life and ability to return to prior levels of function. Limiting the need for opioid prescriptions dispensed in the community,

particularly to vulnerable older adults individuals, is also a key aspect in curbing the opioid epidemic. However, even if no difference is found, it would support stopping the use of lidocaine patches in this population as a waste of money and resources. The novel approach of adding the 3rd arm to assess for placebo effect will also carry clinical value, as a placebo effect that reduces opioid use may in fact be enough to support continued use of the products given their overall low side effect risk profile compared to opioids and other pain control medications

Hypothesis:

We hypothesized that lidocaine 4% epidermal patch will lead to a reduction in pain score, OME, and 30-day post discharge opioid use

Aim/Objective:

AIM 1: Determine if a 3-armed placebo controlled randomized trial evaluating the efficacy of 4% lidocaine patches is feasible on a large scale with up to 500 enrolled patients across multiple institutions.
Objective 1: Evaluate the study design, randomization system, drug delivery and placebo creation processes to determine barriers to a larger multicenter study design.

AIM 2: Determine if the use of 4% lidocaine patches decreases the utilization of opioids in older adults (Age ≥50) patient with rib fractures and minimal other injuries by 50% or more during the first 72 hours of hospitalization.
Objective 2: Determine an appropriate target opioid reduction rate and appropriate enrollment numbers for a future a larger scale trial. We suspect a 50% opioid reduction may be larger than would be expected for a single aspect of multimodal pain control treatment. While the study will be powered to identify this difference, it is more likely that a 20-40% reduction could be achieved and therefore help determine appropriate power calculations for a future trial.

AIM 3: Determine if there is a potential placebo effect of topical patch therapy.
Objective 3: Utilizing a 3rd arm increases the number of patients needed to enroll but will help clarify if there is a significant placebo effect from the application of a non-medicated patch over rib fractures. There may be clinical benefit from this placebo effect itself which would need to be accounted for clinical recommendations generated from this and future studies.

AIM 4: Include post discharge opioid usage in analysis to determine the prolonged pain needs of patients suffering rib fractures.
Objective 4: Assess the feasibility of incorporating opioid prescription data using the Wisconsin Prescription Drug Monitoring Program (WI PDMP)as part of a clinical trial as a measure of post discharge opioid use.

Design:

Approved study staff will be screening the trauma surgery patients list. Elderly patients (>/=50) with traumatic rib fractures will be approached within 24 hours after admission. Approved study staff will explain the project and informed consent in its entirety. Patients will then be

randomized to one of 3 arms: 4% Lidocaine Patches, Placebo, Standard of Care (no lidocaine patch). Randomization will take place using RedCap database. The patients will receive the study drug or placebo as recommended by the manufacturer as 12 hours on, 12 hours off regimen. The patch location will be selected by the patient and nurse based on site of maximal pain. The patient will receive 1 drug or placebo patch for unilateral rib fractures and 2 drug or placebo patches for bilateral rib fractures. The 4% Lidocaine patches will be obtained from the Froedtert Investigational Drug Office and dispensed with enough supply to last for 1 or 2 patch cycles in 5 days. The patches will then have kinesio tape (designed for topical application) applied over the patch to blind, providers, and patients to whether it is a study drug or placebo. For placebo, a double thickness similarly shaped piece of kinesio tape will be used. Based on drug efficacy, all patches can be prepared at the time of study enrollment and remain viable for use during the duration of the study. Patients in the standard of care arm will not receive a patch. All other pain medications will be prescribed at the discretion of treating providers based on standard of care (see section 52.1 Pain Management Protocol Lidocaine RCT). Approved study staff will be accessing patient's electronic medical record 5 days after enrollment; approved study staff will gather information regarding pain score (scored out of 10) and oral morphine equivalent (OME). Dr. Jacob Peschman is the director of outpatient services; he will be accessing patient's 30-day post discharge opioid use utilizing the Wisconsin Prescription Drug Monitoring Program (PDMP). Patients will be approached by approved study staff 30-days post discharge. Patients will be asked several questions regarding pain score and control.

Research personnel (including post-doctoral research fellows, research nurses and/or, research assistants) will be the only project team members unblinded to the randomization outcome. Research personnel will be responsible for randomizing patients using the REDCAP database. Research personnel will be consenting the patients prior to knowing the randomization status. After which, no direct contact between project team members and nurses will take place. Moreover, nurses will be made aware that project team members (including Drs. Peschman, Carver, Peppard, and Trevino, who might be responsible for clinically duties pertaining to enrolled patients) are blinded. As such, no direct contact between nurses and project members will occur. In addition, the EPIC order for the patch will appear as Lidocaine/Patch, hence maintaining project team members blinding. Research personnel will inform IDS pharmacy of the randomization outcome after which IDS will dispose the required patches to the nurses. Finally, study team members will organize an educational session for nurses (led by OCRICC and nurse managers responsible for floor or intensive care units) to explain the study design, drug disposal, drug administration, and the blinding process.

Prior to commencing this pilot study, a nurse educational session will take place. Project team members, constituted of trauma surgeons, APP, and research nurse will be responsible for providing the nurse education. This includes explanation of study design, drug order, drug disposal, and patch administration. Nurses will be made aware that all project team members, besides Researcg personnel, will be blinded to the randomization process. Accordingly, no direct contact between nurses and project team members will take place. Additionally, nurses will be educated on the appropriate patch administration and disposal processes to maintain patient blinding. This includes proper handling and administration to patients' chest while maintaining the blinding process. Nurses will make sure to hide the applied side of the patch while

administrating the patch. Moreover, nurses will be required to treat placebo patches as a lidocaine patch. This includes performing accurate disposal of patches and rinsing/watching hands after drug administration or removal. Finally, nurses should not provide any recommendations to patients with regards to patients reported pain score and/or frequency of opioid request. An operational planning meeting with nurse managers will be conducted, if deemed necessary.

Inclusion criteria

1. Age >/=50

2. Patient with injuries meeting an AIS score </=2; (see section 52.1 AIS screening sheet) - Disclaimer: Patient will be asked about the location of the worst pain.

3. Patient presenting with traumatic rib fractures

4. Patient admitted to trauma service

5. Patient able to consent

Exclusion criteria:

1. Age <50 years

2. Unable to consent to study participation

3. Chronic pain medication usage; defined as >/= 3 weeks of >/= 30 mg oral morphine equivalent

4. History of allergic reaction to lidocaine or adhesive tape

5. Prisoners

6. Patient will be excluded if pain is worse in non-ribs location

7. Patient will be excluded if he has injuries not meeting our criteria (see section 52.1 AIS screening sheet)

Data Collection/Analysis:

Data on daily opioid use, standard pain scores, and additional pain therapies will be collected prospectively for the entire duration of their hospital stay. At the end of the 5 days or at discharge if before that time, patients will return to standard of care. 5 days was selected as a

common length of stay for this injury pattern. Post discharge disposition will be collected, and at 30 days post discharge the patient's WI PDMP record will be reviewed to assess for opioid use. A follow up during their scheduled clinical follow up and at 30 days call will be performed by a member of the study team to confirm post discharge pain medication usage as well as functional pain score. Additional data will be obtained from their electronic medical record including basic demographics, prior medication use, comorbid conditions, pre-hospital functional status, and thickness of their chest wall on CT imaging (if performed) as calculated by the study PI. Data will be inputted into a secure MCW BOX PLATFORM database for analysis. Data will be analyzed for the primary outcome of reduction of opioid use (as oral morphine equivalents) in the first 5 days of hospitalization with use of the study drug and pain score reported by the patient. Secondary outcomes will include reduction in post discharge opioid use. All of these will be compared between participants in each of the 3 arms/groups of the study.

References:

1. Bulger, E.M., et al., *Rib fractures in the elderly.* J Trauma, 2000. **48**(6): p. 1040-6; discussion 1046-7.
2. Zink, K.A., et al., *Lidocaine patches reduce pain in trauma patients with rib fractures.* Am Surg, 2011. **77**(4): p. 438-42.
3. Ingalls, N.K., et al., *Randomized, double-blind, placebo-controlled trial using lidocaine patch 5% in traumatic rib fractures.* J Am Coll Surg, 2010. **210**(2): p. 205-9.
4. Cheng, Y.J., *Lidocaine Skin Patch (Lidopat® 5%) Is Effective in the Treatment of Traumatic Rib Fractures: A Prospective Double-Blinded and Vehicle-Controlled Study.* Med Princ Pract, 2016. **25**(1): p. 36-9.
5. Johnson, M., et al., *Do Lidocaine Patches Reduce Opioid Use in Acute Rib Fractures?* Am Surg, 2020. **86**(9): p. 1153-1158.