MU Health

EM Research Working Group

Project Proposal

Administrative Summary

Project Title	*Methylnaltrexone versus Naloxegol in the Treatment of Opioid-Induced Constipation in the Emergency Department*
Primary Investigator	*Kara B. Goddard, PharmD, BCPS*
Others Involved	*Jeanise Butterfield, MD; Julie Stilley, PhD; Matthew Robinson, MD*
Estimated Budget	*Methylnaltrexone oral tablet - $17.07 per tablet* *Methylnaltrexone 12mg subcutaneous injection - $93.96* *Naloxegol 25mg oral tablet - $9.14 per tablet* *For 20 doses of each medication:* *$51.21x 20 = $1,024.20* *$93.96 x 20 = $1,879.20* *$9.14 x 20 = $182.80* *Total: $3,086.20*
Funding Source	Missouri College of Emergency Physicians
Protocol Version	v2
Protocol Date	04/18/2023
Special Considerations	*None*

Project Overview

Background / Significance:

Opioid-induced constipation can lead to serious complications, including small bowel obstruction, fecal impaction, and bowel perforation.[1] Not only are the medical complications potentially severe, patient quality of life can also be impacted.[2] Two agents are currently available for opioid-induced constipation – oral and subcutaneous methylnaltrexone and oral naloxegol. Mechanistically, both agents antagonize the

peripheral mu-opioid receptor in the gastrointestinal tract to decrease constipation without reversing the systemic analgesic effects of opiates.[3] The literature currently available has evaluated the effectiveness of each agent, not the comparative effectiveness of these agents.

Purpose / Study Aims:

The purpose of this study is to compare the efficacy of subcutaneous versus oral mu-opioid receptor antagonist therapy in opioid induced constipation that is refractory to other bowel regimens.

Primary Outcome: The primary outcome of this study is to determine the effectiveness of peripherally acting mu-opioid receptor antagonist therapy for patients presenting to the emergency department (ED) with opioid-induced constipation.

Secondary Outcomes: The secondary outcome of this study is the time to effectiveness of subcutaneous versus oral therapy.

Feasibility (sample size, frequency of eligible patients, duration of study):

Sample size: 15 patients (due to changes in standard of care procedures the enrollment goal had to be reduced)

Duration: 2 years

Study Procedure

1. Methods
    a. Patients presenting to the Emergency Department with opioid induced constipation will be screened for inclusion in one of three groups:
        i. Methylnaltrexone oral tablets (total 450 mg)
        ii. Methylnaltrexone 12mg subcutaneous injection
        iii. Naloxegol oral tablets (total 25 mg)
    b. A pregnancy test will be administered to females of childbearing potential before administration of the study drug.
    c. After treatment patients will
        i. Have a successful bowel movement, thus completing their time in the study to continue with standard patient care
        ii. Not have a successful bowel movement after 3 hours, continue with standard patient care, and be contacted in 24 hours to record the time of any successful bowel movements after the 3 hours study period

2. Data collected
    a. Age
    b. Sex
    c. Current medications
    d. History of constipation
    e. Time of last bowel movement
    f. Attempts to alleviate current constipation
    g. Time to successful bowel movement after treatment
    h. Phone number or other contact information
    i. Side effects noted by patient or staff

3. Subjects
    a. Inclusion criteria
        i. Complaint of opioid-induced constipation refractory to other therapy (enemas, laxatives, stool softeners)
        ii. Age≥18y/o
        iii. Not pregnant or lactating (negative urinary pregnancy test)
        iv. No contraindication to Methylnaltrexone or Naloxegol
    b. Exclusion criteria
        i. Age<18y/o
        ii. Pregnancy or lactation
        iii. Contraindication to Methylnaltrexone or Naloxegol
        iv. Assigned NPO
        v. Small bowel obstruction

4. Treatment of subjects
    a. If the subjects are eligible for inclusion they will be offered inclusion in the study by one of the Emergency Department faculty. If they refuse participation they will be treated in a standard fashion. Patient follow-up will cease after 24 hours
    b. Benefits
        i. Patient benefits: patient may achieve relief from opioid-induced constipation
        ii. Society benefits: To our knowledge, this is the first time these two drugs are being compared for their efficacy
    c. Risks: *Allergic reaction, stomach/abdominal pain, gas, nausea, diarrhea, dizziness, increased sweating, hot flashes, flushing, tremor, chills, black or bloody stools, coughing up blood*
    d. Compensation: The patients will not be compensated for study inclusion

5. References

1. Jones R, Prommer E, Backstedt D. Naloxegol: A Novel Therapy in the Management of Opioid-Induced Constipation. Am J Hosp Palliat Care 2016;33(9):875-880.
2. Anantharamu T, Sharma S, Gupta AK, et al. Naloxegol: First oral peripherally acting mu opioid receptor antagonists for opioid-induced constipation. J Pharmacol Pharmacother. 2015;6(3):188-92.
3. Bowers BL, Crannage AJ. The Evolving Role of Long-Term Pharmacotherapy for Opioid-Induced Constipation in Patients Being Treated for Noncancer Pain. J Pharm Pract. 2017 Jan 1:897190017745395. doi: 10.1177/0897190017745395. [Epub ahead of print].