Efficacy of One Dose of Laxative on Post-Operative Constipation following Total Knee Arthroplasty

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Abstract

Postoperative constipation, defined as no fully satisfying bowel movement within the first three postoperative days, is a common occurrence with some researchers estimating that between 41 and 85% of postoperative patients experience symptoms. Causes include intraoperative medications, postoperative opioid analgesics, decreased mobility, and decreased oral intake. Constipation significantly impacts quality of life following surgery. Current standard of care for preventing postoperative constipation for patients having a single total knee arthoplasty at Cleveland Clinic is discharge on postoperative day one with either a prescription to be filled for docusate sodium (Colace®) 100 mg to be taken two times a day by mouth for twenty eight days or the filled prescription, plus discharge instructions on ways to avoid and treat constipation. Research results show that docusate sodium is ineffective for preventing postoperative constipation in orthopedic surgery patients, and anecdotal reports confirm this finding. The proposed study uses a 2-group non-equivalent cohort design to evaluate the effect of one standard dose (17 grams) of an over-the-counter osmotic laxative (propylene glycol (PEG 3350), brand name Miralax®) by mouth prior to discharge to the current standard of care. The primary outcome measure is whether patients report of a fully satisfying, normal for them, bowel movement within the first three postoperative days. Patient reported data will be collected by phone call four to seven days following surgery. Pertinent patient characteristics will be abstracted from the electronic medical record. The sample will consist of patients over twenty years old having a single total knee arthroplasty by Drs. Stearns, Molloy, or Murray who are admitted to unit 5D at Cleveland Clinic Lutheran Hospital postoperatively. Intent to treat analysis will be performed using logistic and linear regression models, adjusting for differences between groups on patient and surgical characteristics. Based on use of a two-sided Pearson chi-square test with 80% power and significance level of 0.05, 49 patients per group are required to detect a 25% decrease in constipation rate. To account for attrition we will oversample by 50% for a total of 74 per group or 148 total participants.

Constipation following orthopedic surgery is a common problem. Postoperative constipation is defined in the literature as no normal bowel movement within the first three postoperative days following surgery (Li et al., 2017; Trads, Deutch, & Pedersen, 2017; Turan & Asti, 2016). Estimates of postoperative constipation following orthopedic surgery range from 41% to 85% of patients experiencing this uncomfortable side effect (Davies, Green, Mottram, & Pirmohamed, 2008; Şendir, Büyükyilmaz, Aşti, Gürpnar, & Yazgan, 2012; Stienen et al., 2014). Constipation has a negative impact on quality of life following orthopedic surgery (Jing & Jia, 2019; Turan & Asti, 2016). Symptoms of postoperative constipation include abdominal pain, nausea, abdominal bloating, and difficulty passing hard stool (Turan & Asti, 2016). Despite the frequency of this problem and its impact on quality of life following orthopedic surgery, there is a dearth of rigorous scientific literature addressing preventative interventions.

The majority of research studies addressing postoperative constipation prevention and treatment use orthopedic surgery patients as their population of interest, test non-pharmacological interventions, and have relatively small sample sizes with no a priori sample size calculation noted in the manuscript. Regardless, results indicate that nursing interventions often work better than standard of care. In a quasi-experimental study examining the impact of development of a personalized postoperative constipation prevention care plan (helping patients figure out how they can increase fluids and fiber in their diet) for hip fracture surgery patients, researchers found that constipation rates were lower for those that used the individualized care planning process (Trads et al., 2017). Abdominal massage has also been tested as a non-pharmacological intervention to treat postoperative constipation. Study results from two quasi-experimental studies, orthopedic surgery patients in one study (Turan & Asti, 2016) and lung transplant patients in the other (Li et al., 2017), indicate that abdominal massage was superior to the existing standard of care at the study sites for preventing postoperative constipation. Turan and Asti's (2016) abdominal massage intervention was superior to a pharmacological standard of care treatment, either a rectally administered laxative suppository or saline enema. Interestingly, results for time to first normal stool were past the defined time limit for postoperative constipation of surgical day three.

Studies testing pharmacological interventions for prevention of postoperative constipation in the orthopedic surgery population also tend to have small sample sizes, yet results indicate significant differences between groups. Traditional preoperative mechanical bowel prep has been investigated as a postoperative constipation preventative intervention. A randomized controlled three arm trial investigated the efficacy of mechanical bowel prep using enema or suppository laxative versus the standard of care (no bowel prep) on postoperative constipation following spinal surgery. Sample sizes were small, 15 in each arm, yet results showed that time to bowel movement was shorter to a significant degree for those in the no bowel prep arm (Olsen et al., 2016). Researchers found in a pilot study (n=14) testing the feasibility of administering daily polyethylene glycol (PEG 3350 or brand name Miralax®) versus daily oral docusate sodium (Brand name Colace®) to prevent postoperative constipation following knee or hip arthroplasty a significant improvement in constipation rates with the PEG 3350 group having a bowel movement one day sooner before postoperative day four (Madsen, Magor, & Parker, 2010). As in the Madsen, Magor, and Parker study (2010), the current standard of care for preventing constipation for patients having knee or hip arthroplasty at Lutheran Hospital is a prescription for docusate sodium100 mg orally twice daily on discharge.

Docusate is one of the most often prescribed drugs for constipation prevention for hospitalized patients, but is essentially ineffective in preventing or relieving constipation (Fakheri & Volpicelli, 2019). Guidelines issued by The American Society of Colon and Rectal Surgeons (Paquette, et al, 2016) and a technical review issued by the American Gastroenterological Association (Bharucha, Pemberton, & Locke, 2013) both recommend the non-prescription osmotic laxative PEG 3350 over most other laxatives as it relieves constipation sooner than other treatments and is generally well-tolerated since it is not systematically absorbed. Results from a systematic review show that PEG 3350 performs better than another osmotic laxative (lactulose) at relieving constipation (Lee-Robichaud, Thomas, Morgan, & Nelson, 2010). Although none of these studies and guidelines specifically address the effectiveness of PEG 3350 on postoperative constipation, they demonstrate that PEG 3350 is the gold standard in laxatives.

Purpose

The purpose of this study is to determine if one dose of an over-the-counter laxative administered on postoperative day one is more effective at preventing postoperative constipation, no fully satisfying bowel movement in the first three postoperative days, than an over-the-counter stool softener taken two times a day by mouth for twenty eight days. The primary research question to be answered is:

What is the effect of one standard 17 gram dose of PEG 3350 given by mouth prior to discharge from single total knee arthroplasty surgery compared to current standard of care on frequency of postoperative constipation, defined as no fully satisfying bowel movement by postoperative day three?

Secondary research questions are:

What is the effect of one 17 gram dose of PEG 3350 given by mouth prior to discharge from total knee arthroplasty surgery compared to current standard of care on patient reported:

- Pain with bowel movement?
- Straining with bowel movement?
- Laxative use?

Method

This study uses a 2-group non-equivalent cohort design. Patients in cohort one will receive the current standard of care, a prescription for Colace to be taken twice a day for 28 days. Once the sample size needed for group comparisons has been reached, prescribing practices will change. Patients in cohort two will receive one standard dose (17 grams) of Miralax by mouth on postoperative day one. Both groups will receive the current standard discharge instructions.

Setting and Sample

The study will be conducted at Cleveland Clinic Lutheran Hospital on unit 5D, a 42 bed telemetry-capable inpatient unit in which the majority of patients have had either orthopedic or general surgery. Follow up phone calls will be made to study participants using the phone number they provide, and the setting for answering these questions is of participant's choosing.

The sample of patients for this study must meet the following criteria:

- Admission to Lutheran Hospital surgical unit 5D
- Single total knee replacement surgery by orthopedic surgeons Stearns, Murray, or Molloy

- Age greater than 20
- Discharge to home on postoperative day one

Excluded from the study are patients who:

- Have known allergy to PEG 3350
- Are unable to complete a follow up phone call in English
- Have known renal disease, irritable bowel syndrome, or inflammatory bowel disease (Crohn's disease or ulcerative colitis), contraindications for PEG 3350 use

Sampling and Sample Size

A convenience sample of those that agree to participate will be used. Based on prior research (Madsen, Magor, and Parker, 2010), the constipation rate at 3 days is expected to be high as high as 85% in the current standard. In order to detect a 25% decrease in this constipation rate with 80% power, 49 patients per group are needed. This assumes use of two-sided Pearson chi-square tests and a significance level of 0.05. Since any impact of covariates on this outcome is unknown, this is a reasonable approximation of the power based on a logistic regression. This sample size will also allow for adjustment of up to 4 covariates in our planned models based on recommendations of Vittinghoff and McCulloch (2007), if the event rate is similar to previous studies. To account for attrition, we will oversample by 50% for a total of 74 per group or 148 total participants.

Advertising and Recruitment

The recruitment process will occur in two phases. Study team member Karen Sanchez conducts a pre-operative joint replacement patient education class for patients and their family members every week at Lutheran Hospital. Approximately 75% of patients having total joint replacement surgeries at Lutheran Hospital attend this class. She will introduce the study at the conclusion of the class, verbally informing potential participants about the study and providing the recruitment flyer to potential participants who attend the class. Participants will not be consented at this time so as to allow potential participants time to consider enrolling in the study. Recruitment flyers will be posted in all patient rooms. Prior to surgery all total knee arthroplasty patients of the three participating surgeons will be screened for inclusion and exclusion criteria by a member of the study team. On the day of surgery, a study team member will approach those patients who meet inclusion criteria in the preoperative unit (4B) to solicit participation. Study team members will review the consent document in the patient's room prior to anesthesia and consent those who choose to participate using the standard signed consent form.

Data Collection

Study team members will gather the following information from those agreeing to participate: recruitment date, name, best time of day to call, best phone number to call, patient's surgeon, age, sex, race/ethnicity, and whether they had a saphenous nerve block performed. This information will be entered into the study database in REDCap. Follow up phone calls will be conducted by a member of the study team beginning on postoperative day four. If the patient does not answer, then a total of two follow up calls can be made up through postoperative day seven. If the patient does not participate by day seven, they will be considered lost to follow up. The phone calls will follow a phone script, which starts with confirming that the participant still wants to answer the follow up questions. The script will be housed in REDCap so as to create a

database of responses as participants answer questions. After completing the survey, if the patient states they have not had a satisfying bowel movement, they will be instructed to increase their fluid and fiber consumption and use a laxative of their choosing or call their primary care physician or surgeon's office to get further direction in resolving their constipation.

Data needed to answer the research questions will come from two primary sources, patient report and abstracted from the electronic health record. All data will be gathered by members of the research team and entered into a REDCap database.

- Patient reported measures:
    - Age
    - Sex
    - Race/ethnicity
    - Bowel movement within first three post-operative days (yes/no)
    - Straining with bowel movement (0-10 numeric rating scale)
    - Discomfort with bowel movement (0-10 numeric rating scale)
    - Laxative use (yes/no)
    - Opioid analgesic use (yes/no)
    - Saphenous nerve long-acting regional block for pain control (yes/no/not sure)
- Electronic health record measures collected by study team members:
    - Surgeon
    - Past medical history diagnoses needed to calculate the Charlson Comorbidity Index Revised, as documented in the admitting problem list
    - Type of anesthesia (general vs. spinal/local) as documented in anesthesia OpTime record
    - Length of surgery calculated in minutes based on anesthesia OpTime record documented as start time of case and end time of case

Data Analysis

Intent-to-treat analysis will be used in this study. Data analyses will be conducted by a statistician from Quantitative Health Sciences using SAS software (version 9.3; Cary, NC) or R software (version 3.1; Vienna, Austria) as appropriate. Demographic characteristics will be reported using descriptive statistics. Categorical data will be summarized using frequencies and percentages, and continuous data described using means, standard deviations, and percentiles of interest (median, quartiles, and range). Pearson chi-square t-tests for nominal factors, Wilcoxon rank sum tests for ordered factors and non-normal continuous measures, and two-sample t-tests for normal continuous measures will be used to compare treatment groups on collected patient and surgical characteristics. Logistic regression models will be used to assess differences in constipation rates between groups while adjusting for patient and surgical characteristics that differ between groups. Linear regression models will be used to compare groups on levels of pain and straining between groups with similar adjustment. Distributional assumptions of the linear mode will be tested, and if they are not met, alternative approaches, such as ordinal regression may be used instead. Rates of laxative and opioid use in the follow-up period will be summarized and, if warranted, sensitivity analyses of the same analyses as above, omitting those who use laxatives or opioids, may be performed.

Feasibility

The participating surgeons at Lutheran Hospital perform on average 57 total knee arthroplasty surgeries every month, thus making it possible to complete data collection in six months. The surgeons and the advanced practice providers caring for this group of patients are supportive of this study. Nursing administration at Lutheran Hospital is supportive of this study. The information gathered from participants during the follow up phone calls is purposely brief so as to be as minimally burdensome to the participants as possible. Study team members are available to make follow up phone calls from Cleveland Clinic devices.

Limitations and Anticipated Problems

The major limitation to this study is the single site and homogeneity that exists within the patient populations served by the three participating surgeons. There is also the potential for social desirability bias as participants respond to questions in the follow up phone call. There are no valid and reliable instruments that measure constipation for this population, so using participant self-report is the best way to quantify postoperative constipation and its symptoms. The primary anticipated problem in this study is losing participants to follow up. Oversampling should account for this loss.

Human Subjects Protection

In order to protect the confidentiality and anonymity of participants, access to the data will be limited to study team members and QHS staff conducting the analysis. A written informed consent document will be used as part of the informed consent process, and completed copies will be kept in a locked file drawer in the PI's office. All data will be stored in REDCap databases accessible only to study team members. Collected protected health information is limited to those items needed to make the follow up phone call and extract data from the electronic medical record. All PHI will be deleted from the final database and replaced with a participant code number prior to analysis. This final database will be maintained electronically as the source of truth for this study.

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