Preemptive Opioid Sparing Analgesia in Total Hip and Knee Arthroplasty

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Abstract

Background

Total Knee and Total Hip Arthroplasty procedures have been reported to be very painful in the first 48 hours postoperatively. Undermanaged postoperative pain can significantly limit rehabilitation, recovery, increase patient dissatisfaction, increase healthcare costs, and lead to chronic pain.

Local Problem

Although opioids are included in perioperative analgesic management for joint arthroplasty, side effects such as sedation, respiratory depression, nausea, vomiting, ileus, and pruritus remain major issues. A large tertiary hospital in Maryland performs high volumes of procedures performed annually, and with the expectation to continually provide effective postoperative pain management, this facility expressed interest in the need for a clinical practice guideline. Research has shown that a pre-emptive multimodal approach, a combination of non-opioid drugs administered prior to surgical incision, produces synergistic analgesia, while decreasing side effects.

Interventions

The purpose of this quality improvement project was to develop a clinical practice guideline for preemptive opioid sparing analgesia through the use of preoperative administration of Acetaminophen, Gabapentin, and Celebrex for patients undergoing elective lower extremity arthroplasties. The development of the guideline was guided by the Knowledge-to-Action Framework and occurred over three phases. A literature review was completed on multimodal and preemptive analgesia for patients undergoing lower extremity arthroplasty. Three medications were frequently studied; therefore, each group member focused on one drug, and later combined all the literature data to formulate a draft clinical practice guideline. During phase one, a draft clinical practice guideline was introduced to stakeholders. The guideline was then evaluated by stakeholders using the AGREE II tool, a valid and reliable tool was used to assess variability, rigor and transparency of quality of the guideline. In phase three, the Practitioner Feedback Questionnaire was utilized to gain feedback regarding the quality of the guideline from the Anesthesia Department.

Results

The results of the AGREE II tool's domains scores ranged from 71.6 to 100%, with 100% (n=29) of reviewers recommending the guideline for implementation into practice. The results for the Practitioner Feedback Questionnaire were as followed: the majority of respondents were CRNAs (59%), SRNAs (24%), and physician anesthesiologists (17%). Sixteen out of twenty-three items had a response of "strongly agree." One hundred percent of the participants agreed that the rationale for the CBG was clear, and that the methodology, review of literature, and interpretation of evidence were identified to be pertinent and valid.

Conclusions

Inadequate postoperative pain management can significantly limit rehabilitation recovery, decrease patient dissatisfaction, increase healthcare costs, and complications. Traditional analgesics such as opioids are often associated with undesirable side effects. A clinical practice guideline for preemptive opioid sparing analgesia through the use of preoperative administration of Acetaminophen, Gabapentin, and Celebrex have shown to be effective in improving postoperative pain, lowering overall narcotic consumption and side effects, reducing hospital stay, and improving function while minimizing complications.

Introduction

It is estimated that about 80% of patients undergoing surgical procedures experience acute postoperative pain, with about 75% reporting it as moderate to extremely severe (Gan, Habib, Miller, White, & Apfelbaum, 2014). Although acute postoperative pain is a predictable response for the patient undergoing surgery, Chou et al. (2016) stated, less than half of patients report adequate postoperative pain relief. Inadequate relief of postoperative pain may result in severe physiologic and psychological consequences such as increased length of stay, decreased mobility, increased falls, increased risk for infection and chronic pain (Joshi and Ogunnaike, 2005).

Background and Problem

One of the most painful surgeries reported by patients, with a moderate to severe pain level in the first 48 hours postoperatively, are Total Knee Arthroplasty (TKA) and Total Hip Arthroplasty (THA), procedures for severe osteoarthritis (Beswick, Wylde, Gooberman-Hill, Blom, & Dieppe, 2012). Pain after TKA and THA is related to mechanical, thermal, and chemical damage leading to cellular injury and release of cellular mediators such as histamine, prostaglandins, and bradykinins. These releases lead to nociceptor sensitization, which lowers the amount of stimulation needed to trigger a pain response (Golladay, Balch, Dalury, Satpathy, & Jiranek, 2017). Undermanaged postoperative pain can significantly limit rehabilitation, recovery, decrease patient satisfaction, increase healthcare costs, and lead to chronic pain (Golladay et al, 2017). Therefore, pain management following total joint arthroplasty is an important aspect of patient care.

According to the American Joint Replacement Registry (2016), a total of 427,181 joint replacement procedures were performed between 2012 and 2015. Recent studies have examined a variety of pain management protocols. Although opioids are included in perioperative analgesic management for joint arthroplasty, side effects such as sedation, respiratory depression, nausea, vomiting, ileus, and pruritus remain major issues (Parvizi, Miller, & Gandhi, 2011).

Recent data shows multimodal analgesia, which is the administration of non-opioid medications in lieu or in combination with an opioid in an effort to target multiple receptors along the pain pathway, has been shown to reduce the need for postoperative opioids with a resultant decrease in overall side effects. Using this multimodal approach, given preemptively before surgery has been reported to improve postoperative pain and reduce the need for opioid analgesics after surgery (Kissin, 2010, Doleman, Read, Lund, & Williams, 2015). Providing preemptive analgesia may reduce central sensitization resulting from surgical incision. This may provide more effective pain control in the postoperative period compared with the same analgesic given after incision in the absence of preemptive analgesia (Doleman, et al., 2015. The primary non-opioid medications typically administered preemptively include Gabapentin, Celebrex and Acetaminophen. Each student registered nurse anesthetist (SRNA) will focus on one drug; for the purposes of this review I will concentrate on Acetaminophen.

Acetaminophen, a non-steroidal anti-inflammatory drug is often used as part of a multimodal regimen and has been shown to be an effective and safe medication to administer prior to total joint surgery. Although the exact mechanism of action (MAO) is unclear, there is evidence that Acetaminophen acts on a number of central mechanisms which include effects on prostaglandin production, and on serotonergic, opioid, nitric oxide (NO), and cannabinoid pathways (Doleman, et al., 2015). Unlike other NSAIDS, which act on COX-1 and -2, Acetaminophen may act on a discrete COX-1 splice variant (COX- 3). This COX-1 variant is thought to be active in the central nervous system, rather than at the site of injured or inflamed tissue, such that inhibition by Acetaminophen supports its lack of anti- inflammatory and anti-platelet activity, while still an effective analgesic and antipyretic medication (Sharma and Mehta, 2014). Another theory on the MAO of Acetaminophen is via the activation of the descending serotonergic pathways because it has been shown that the anti-nociceptive effects of Acetaminophen can be partially inhibited by co-administration of 5- HT_3- receptor antagonists (Sharma and Mehta, 2014). Finally, Acetaminophen has shown to have indirect activation of cannabinoid CB_1 receptors. In brain and spinal cord, Acetaminophen is conjugated with arachidonic acid to form AM404, an endogenous cannabinoid. This enzyme is an agonist at TRPV1 receptors and an inhibitor of cellular anandamide uptake, which leads to increased levels of endogenous cannabinoids (Bertolini, Ferrari, Ottani, Guerzoni, Tacchi, & Leone, 2006). Acetaminophen is the analgesic of choice for adult patients in whom salicylates or other NSAIDs are contraindicated, such as asthmatics, those with salicylate allergies, and those with a history of peptic ulcer disease (Toms, McQuay, Derry, & Moore, 2017). Therefore, Acetaminophen administered as preemptive or preventive medication is effective and safe (Doleman, et al., 2015).

Purpose

The purpose of this DNP project was to develop and evaluate the feasibility of a clinical practice guideline (CPG) for preemptive opioid sparing analgesia for patients undergoing TKA and THA with the goal of reducing opioids and their potential side effects. The target institution performs more than 1,000 TKA and THA annually. With high volumes of procedures performed annually, and the expectation to continually provide effective postoperative pain management, this facility expressed interest in the need for a CPG. This CPG will provide a standardized pain management approach to anesthesia providers the will result in a significant reduction in the use of opioids and their potential side effects. The medications considered for preoperatively use in this CPG will include Acetaminophen, Celebrex, and Gabapentin. However, as previously stated this project will focus on evidence based practices using Acetaminophen as part of a multimodal analgesic regimen. The focus will be in the preoperative phase with the intent to improve pain in the postoperative phase. Long-term goals include improved patient satisfaction and reduce postoperative pain and complications, and decrease hospital costs.

Theoretical Framework

The theoretical framework utilized to guide this DNP project for preoperative multimodal analgesia for TKA and THA was the Knowledge-to-Action (KTA) Framework by Graham and Tetroe (2010). The framework has two phases: Knowledge Creation and Action Cycle. Knowledge Creation represents the production and synthesis of knowledge. As knowledge moves through steps, it is refined and summarized to be more useful for end-users. This phase includes three steps: 1) knowledge inquiry 2) knowledge synthesis, and 3) the creation of tools and products (Fields, Booth, Ilott, & Gerrish, 2014). The second phase, the Action Cycle includes a range of activities needed for knowledge implementation. There are 7 steps to the Action Cycle: 1) identifying the problem, 2) adapt knowledge to the local context, 3) assess facilitators and barriers to knowledge use, 4) select, tailor and implement intervention, 5) monitor knowledge use, 6) evaluate outcomes, and 7) sustain knowledge use (Field et al., 2014). *Identifying the problem* refers to what is known about a problem, what the current practice is, and whether there is a gap to be addressed. *Adapt knowledge to the local context* refers to knowing the intended audience and assessing the value, usefulness and appropriateness of the particular knowledge, which is critical to the sustained use of a CPG.

Assess facilitators and barriers to knowledge use can be done quantitatively and qualitatively using a variety of instruments for example the AGREE II tool. *Select, tailor and implement intervention* involves planning and carrying out interventions to bring about the intended change. *Monitor knowledge use* occurs after the implementation and via various monitoring methods. *Evaluate outcomes* involves evaluating whether application of the knowledge is actually impacting the desired outcome, and *Sustain knowledge use* includes an ongoing feedback loop cycling back through the seven action phases (Field et al., 2014).

The KTA framework was utilized to guide this DNP project, in the following manner: during the *Knowledge Creation* phase, primary, systematic reviews, and meta-analysis studies were researched and reviewed. Using the knowledge obtained from articles, the development of a CPG that presents an evidence-based practice tailored to the facility's needs was formulated. Moving forward, the knowledge was disseminated through the Action Cycle. The formulated CPG will be presented to stakeholders and assessed for quality, validity, and reliability using the AGREE II tool. The CPG was revised to meet needs of the facility and a final CPG for preemptive multimodal analgesia was presented to the anesthesia department. *Monitoring knowledge* occurred after the presentation of the project to the anesthesia department via a PFQ questionnaire to the providers. Finally, the *Evaluation of outcomes*, and *Sustain knowledge* use will be completed via ongoing qualitative and quantitative methodologies, such as patient satisfaction scores and measured outcomes (Graham & Tetroe, 2010). The outcomes measured included pain scores and incidence of nausea/vomiting in the post-operative period.

Literature Review

To develop a CPG for the use of a preemptive opioid sparing analgesic regimen for the patient undergoing TKA and THA, a literature review was completed on multimodal and preemptive analgesia for patients undergoing lower extremity arthroplasty. Three medications were frequently studied; therefore, each group member focused on one drug, and later combined all the literature data to formulate a draft clinical practice guideline. The following literature review will focus on the use of Acetaminophen, and will begin with an analysis of Acetaminophen as an adjunct in pain management and its benefits in a multimodal analgesia approach if administered preemptively. A comparison of efficacy between routes of administration (intravenous versus PO) will be presented. Finally, the safety and dosing regimens of Acetaminophen will be presented. This discussion will then be followed by a synthesis of similarities and differences among studies supporting the recommended use of Acetaminophen as an adjunct to a preemptive opioid sparing analgesic regimen (Table 1).

Multiple meta-analyses have been conducted evaluating the use of Acetaminophen as an adjunct to multimodal analgesia regimen. Gupta, Abubaker, Demas, and Ahrendtse, 2016) conducted a randomized controlled trial (RCT) (N=74) comparing the safety and efficacy of intravenous (IV) Acetaminophen as an adjunct when given with and without IV ibuprofen..During induction, Group 1 (n=35), received 800 mg of Ibuprofen, plus additional 800 mg every six hours for five days or discharge, whichever occurred first. Group 2 induction (n=39), received 800 mg ibuprofen plus during closure, received Acetaminophen 1,000mg every six hours or until discharge. Outcomes measures included Visual Analog Scale (VAS) pain scores, opioid use, quality of recovery scale (QoR), length of post-anesthesia care unit (PACU) stay, antiemetic consumption, and opioid consumption. As a result, the group 2 had lower visual analog scale (VAS) scores, p < 0.002, less opioid requirements and adverse events, and decrease PACU time by day three. Time to discharge from the PACU was also less in Group 2 (38 minutes in Group 2 versus 55 minutes in Group 1). Limin et al. (2017) performed a meta- analysis of three RCT and one non-RCT evaluating the efficiency of Acetaminophen for pain control following TKA and THA (N= 832). The Experimental Group (n=534) received IV Acetaminophen, and the Control Group (n=331) received normal saline or none. Pain scores, opioid consumption, and length of hospital stay, nausea and vomiting were measured at 24, 28, and 72 hours. Pain scores were significantly less for all intervals in the Experiment Group when compared to the Control Group. The opioid consumption of the Experiment Group was 207 mg versus 252 mg in the Control Group (p<0.05).

Similarly, Lamplot Wagner, & Manning, (2014) conducted a RCT to analyze the effects of a multimodal analgesic regimen versus patient controlled analgesia (PCA) (N=36). Group 1, the multimodal group (n=19) received scheduled Oxycodone 10 mg orally every 12 hrs, Tramadol 50 mg orally every 6 hrs, Ketorolac 15 mg parenterally every 12 hrs, and Hydrocodone 5 mg orally, and Hydromorphone 1 mg parenterally as needed for breakthrough pain. Group 2 (n=17) received Hydromorphone PCA and Hydromorphone 1 mg parenterally as needed for breakthrough pain. Data was collected on post-op day 0, 1, 2, and week 3 between the multimodal groups that received intraoperative periarticular injection, and a controlled postoperative regimen versus the Hydromorphone PCA group. The multimodal management regimen was not only associated with a decreased of VAS scores and opioid consumption, but enhanced functional recovery and improved patient satisfaction scores. The evidence from this study supports the use of Acetaminophen as an effective adjunct in alleviating postoperative pain, reducing the use of opioids, the adverse effects associated with opioids, increases patient satisfaction scores, and decreases length of hospital stay in patients undergoing total joint arthroplasty (Gupta, Abubaker, Demas, &Ahrendtse , 2016; Limin et al., 2017; Lamplot Wagner, & Manning, 2014).

Although several studies have shown that IV Acetaminophen is effective and safe for reducing pain and opioid consumption, evidence from research suggests PO Acetaminophen is equally effective as the IV form (O'Neal et al., 2017; Politi, Davis, and Matrka, 2017; Sun, Zhu, Zou, Li, & Han, 2018). O'Neal et al., (2017) conducted a RCT, double-blinded, placebo- controlled clinical trial (N= 174) to determine the efficacy of IV vs. PO Acetaminophen in patients undergoing unilateral TKA. Patients were randomized into three groups: IV Acetaminophen Group (n=57), PO Acetaminophen Group (n=58), and Placebo Group (n= 59). Outcomes included pain scores measured every 15 minutes during PACU stay, average pain scores, maximum pain score, pain scores before physical therapy, total opiate consumption, time to PACU discharge, time to rescue analgesia, and time to break through pain. No differences were revealed among all three groups in average pain scores, maximum pain score, and pain scores before physical therapy. In addition, there were also no differences revealed in total opiate consumption, time to PACU discharge, time to rescue analgesia, and time to breakthrough pain.

Politi et al., (2017) compared the effectiveness of IV versus PO Acetaminophen as part of a standard multimodal perioperative pain regimen by conducting an RCT (N=120). Group 1 (n=63) received IV Acetaminophen and Group 2 (n=57) received PO Acetaminophen in addition to a standard multimodal perioperative pain regimen. Each group received 1 gram of Acetaminophen preoperatively and then every 6- hours for 24 hours. Total opioid use and visual analog scale (VAS) scores were collected every 4- hours postoperatively. Results revealed no difference in pain benefit. The 24-hour average Hydromorphone equivalents administered revealed no significant differences between groups (3.71 vs. 3.48) at 24 hours, $p<0.76$, or at any of the individual 4-hour intervals. The 24-hour average VAS scores in Group 1 (IV) was 3.00 and in Group 2 (PO) was 3.40, $p<0.06$. Only the 0-4 hour postoperatively interval in the IV Acetaminophen Group was significantly different, $p< 0.03$.

Another meta-analysis of RCTs (N=5762) was done by Toms, McQuay, Derry, & Moore (2017) in which they evaluated the efficacy and safety of a single dose of Acetaminophen as compared to a placebo group. The patients in the Acetaminophen group were given PO doses ranging from 325 mg to 1,000mg. Approximately half of participants treated with Acetaminophen achieved at least 50% pain relief over 4-6 hrs, compared to 20% treated with placebo. There were no reported differences of adverse events following a single dose of the study medication (Toms et al., 2017). This evidence supports the safe administration of Acetaminophen 1,000 mg in patients in the preoperative phase to patients undergoing TKA and THA as part of a multimodal analgesic regimen.

In conclusion, Acetaminophen has been shown to be an effective adjunct in pain management reducing opioid consumptions and lower incidence of side effects. Moreover, preventative analgesia, the administration of Acetaminophen prior to surgical incision may reduce central sensitization, and therefore more pain control in the postoperative period compared to Acetaminophen given after incision. Furthermore, PO Acetaminophen is equally effective as the IV form; IV has no greater benefits over PO for pain control in the perioperative period after TKA (Lamplot Wagner, & Manning, 2014; O'Neal et al., 2017; Politi et al., 2017; Sun et al., 2018). Finally, evidence supports the safe administration of Acetaminophen 1,000 mg in patients in the preoperative phase to patients undergoing TKA and THA as part of a multimodal analgesic regimen.

Implementation

This DNP project was the development and evaluation of a CPG for preemptive opiod sparing analgesia through the use of preoperative administration of Acetaminophen, Gabapentin, and Celebrex for patients undergoing TKA and THA. The project was carried out in a large level II trauma facility in the state of Maryland that performs more than 1,000 TKA and TKA annually. The development of the CPG occurred over three phases. Phase one began February 2018 by recruiting two stakeholders, an anesthesiologist that runs the orthopedic operating rooms and a Certified Registered Nurse Anesthetist (CRNA) with a doctorate degree to assist in the development and implementation of the CPG. Their roles and responsibilities were discussed and confirmed, as well as project goals and objectives. After IRB submission and approval (July 2018), a first meeting was held with stakeholders for presentation of relevant literature review and a CPG draft. The CPG draft was evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool (Appendix

B), which was provided to stakeholders via email and instructions how to access the AGREE II tool online. Revisions to CPG were made based on recommendations and feedback provided by stakeholders. A second meeting was held on August 2018 to present the revise CPG to stakeholders and following the meeting, stakeholders reevaluated the CPG using the AGREE II tool. Phase two began on September 2018: the final CPG was sent to the Chief of Anesthesiology for further revisions and final approval prior to implementation. During phase three (December 2018), the final CPG (Appendix A) was presented to the anesthesia staff during Grand Rounds. An email was sent out to the end-users, which consist of Anesthesiologists and CRNAs, one week prior to meeting that includes time, location, and a copy of the CPG. After implementation of the CPG, a practitioner feedback questionnaire (PFQ) (Appendix C) was distributed to the anesthesia staff. Feedback provided by anesthesia staff based on PFQ results were incorporated for a final and revised CPG.

Data Collection

Data collection included two components. In stage one, the AGREE II tool, a valid and reliable tool was used to assess variability, rigor and transparency in the quality of CPG was used to evaluate the CPG (Brouwers, Graham, Hanna, Cameron, & Browman, 2004; AGREE Next Steps Consortium, 2009). The AGREE II consists of 23 items divided into six distinct domains and an additional section for an overall assessment of the CPG (Appendix B). Items are graded on a 7 point Likert scale ranging from “strongly agree” to “strongly disagree.” (AGREE Next Steps Consortium, 2009). Construct validity of the instrument was established using a systematic analysis and all the mean ratings were found to be in the intended direction (Brouwers et al. 2010b). To report the reliability, Cronbach’s alpha was used and ranged from 0.69 to 0.89. The inter-rater reliability was also reported as adequate and has been recommended as the revised standard for guideline development, reporting, and evaluation. The AGREE II tool was sent electronically to the stakeholders to be completed and returned via email. This allows for measurement of progress of development of CPG prior to submitting the CPG to the Chief Anesthesiologist at a large level II trauma facility in the state of Maryland.

In stage three, the PFQ was utilized to gain feedback regarding the quality of the CPG from the Anesthesia Department after presenting the CPG. The PFQ is a valid and reliable tool created to measure the end users' attitude and acceptance of the CPG among the staff and those adopting the CPG (Brouwers et. al., 2004). The PFQ was distributed in person to each anesthesia staff member prior to the presentation at Grand Rounds via pencil/pen and paper format. This tool contains 23 questions graded via a three point Likert scale ranging from "strongly agree" to "strongly disagree." Demographics data was also collected with the questionnaire include age, gender, title, and years of experience. Data obtained from the PFQ was categorized by the providers' years of experience. Data was collected via pencil and paper questionnaire and saved in a locked box.

Data Analysis

To analyze the data from the AGREE II tool, the domains are scored independently as a percentage; this is done by dividing each item score by its maximum possible score. Once domains are scored independently, quality scores are calculated for each of the six domains which includes scope and purpose, stakeholder participation, thoroughness of development, lucidity of presentation, applicability, and editorial independence (Brouwers et. al., 2004).Overall assessment involves rating the guideline’s overall quality and whether it would be recommended for use in clinical practice.

To analyze the PFQ results, descriptive statistics, in particular, frequency scores were used to analyze demographic data. “Strongly agree” was rated as a three, “unsure” was rated as a two, and “strongly disagree” was rated as a one, except for negative items. Reverse scoring was done for the negative items (i.e., items 10, 13, 14, and 15). The frequency, percentages, minimum, maximum, mean, median, and standard deviation were calculated for all items, since the data is ordinal level.

Protection of Human Subjects

Measures to protect human rights include confidentiality and Institutional Review Board (IRB) approval. Project proposal was submitted for review to the University of Maryland IRB for Non-Human Subjects Research determination (query). Development of this CPG is for quality improvement purposes. This project was not intended to be generalizable to other institutions or settings. In order to protect human rights, limited demographic data was collected and participation was on a voluntary basis. No identifiers were collected from the AGREE II Instrument or PFQ. Data collected was kept in a locked box and destroyed at the conclusion of the project.

Results

The results of the AGREE II tool’s domains ranged from 71.6% to 100 (Appendix D). The highest rated domain was “Editorial Independence” at 100%. Other strongly scored domains included “Scope and Purpose” at 94.4%, “Clarity of presentation” at 83.3% and “Rigour of Development” at 84.7%. The lowest rated domains included “Stakeholder Involvement” at 71.6% and “Applicability” at 80.4%. Overall, 100% of reviewers recommended the guideline for implementation into practice. The results for the PFQ are as followed: the majority of respondents were CRNAs (59%), SRNAs (24%), MD Anesthesiologists (17%) (Appendix E). A total of 29 forms were received (74% return rate). Item 1 was excluded from analysis because it was a yes or no question referring to relevance to providers' practice. Sixteen items = 85-100% response as "strongly agree," including the statements "draft guideline should be approved as a practice guideline and "rationale for developing these guidelines were clear and there is a need for it. Two items= majority response to "strong disagree" including statements "to apply draft guideline will be technically challenging" (Appendix F). One hundred percent of the participants agreed that the rationale for the CBG was clear, and that the methodology, review of literature, and interpretation of evidence were identified to be pertinent and valid. The CPG needed minor revisions since only partial of respondents believed that the implementation of the recommendations would be easy (55%) and not technically and financially challenging (60%), however, most of the providers (96%) recommended the CPG to be accepted. 100% of respondents were comfortable to incorporate and utilize it into their practice and apply it to patients. Key findings observed from the PFQ is that majority of the providers were in acceptance of the adoption of the CPG, not only for the intuition as a policy but also into their practice.

Sustainability

The practices outlined by the CPG will be sustained through continued efforts by the hospital's anesthesia department. The anesthesia department staff was educated on the CPG for identification, evaluation, and administration of preoperative multimodal analgesia for the patient undergoing THA and TKA during grand rounds. To increase the efficiency of ordering medications for patients once they are assessed in the preoperative period, an order set bundle was created in the electronic health record (EHRs) via PowerChart. This process has facilitated communication among anesthesia providers and preoperative registered nurses in ordering and administering the preemptive medications in a timely manner. The preoperative nurse manager also received information and a copy of the CPG to communicate and forward it to staff as the success of this CPG will require collaboration with the preoperative nurses. For new hires, this CPG will also be provided and education will be reinforced during orientation. A copy of the CPG will also be available in the facility's intranet for easy access. Finally, a team of champions will be assigned to take over the task of performing electronic medication administration record audits to assess if anesthesia providers are ordering preoperative multimodal medications in the preoperative period when indicated for the joint arthroplasty population.

Discussions

Opioids have traditionally been the cornerstone for pharmacotherapy in the management of postoperative pain; however, substantial studies have shown the effectiveness of preemptive opioid-sparing multimodal analgesia for improved postoperative pain in the patients undergoing total joint arthroplasty. By initiating an preemptive opioid sparing CPG at the target facility, both short-term and long-term objectives can be met; this include standardizing a regimen for patients undergoing lower extremity total joint arthroplasty that will result in a significant reduction in the use of opioids and their potential side effects, and thus improved patient satisfaction, reduce postoperative pain and complications, and decrease hospital costs.

Significant strides have been made toward understanding pain mechanisms which lead to sensitization of the nervous system and hyperalgesia. These mechanisms are more effectively targeted by analgesics other than opioids, such as nonsteroidal anti-inflammatory agents, cox-2 inhibitor agonists, and gabapentonoids. Several meta-analyses have shown the efficiency of preemptive Acetaminophen and as it possess a generally safe profile except in significant overdose, with few drug interactions. When used as an opioid adjunct, oral or rectal, acetaminophen reduces pain intensity and opioid consumption by up to 30%. Toms et al., (2017) recommend the administration of Acetaminophen 1,000 mg in patients in the preoperative phase to patients undergoing TKA and THA as part of a multimodal analgesic regimen. Furthermore, PO Acetaminophen is equally effective as the IV form; IV has no greater benefits over PO for pain control in the perioperative period after TKA (Lamplot Wagner, & Manning, 2014; O'Neal et al., 2017; Politi et al., 2017; Sun et al., 2018).

The efficacy of Acetaminophen in combination with other non-opioids not only improved postoperative pain, but also other outcomes have been reduced as well. Gupta, et al., 2016; Limin et al., 2017; Lamplot Wagner, & Manning, 2014, demonstrated a reduction of opioid use, length of post-anesthesia care unit stay and antiemetic consumption. Adverse effects are rare and include nausea and vomiting (1% individuals) and skin irritation (e.g., urticaria, erythema,dermatitis) (0.1%), with more serious adverse effects being much rarer (e.g., thrombocytopenia, leucocytosis, agranulocytosis, and liver enlargement) (0.01%) (Toms et al., 2017)

There have been many advances in optimizing management of postoperative analgesia to facilitate enhanced recovery, with multimodal analgesia regimens now the standard practice in Enhanced Recovery after Surgery (ERAS) protocols. ERAS is a model of coordinated care delivery of evidence-based care bundles, aimed at achieving perioperative optimization and reducing the adverse effects of the surgical stress response

(Gadsden, 2017). A number of studies have examined the ERAS pathway care bundles for primary hip and knee replacement surgeries, with a recent review highlighting that such pathways can be applied to a wide variety of patients.

ERAS protocols in total joint arthroplasty have been introduced worldwide in many hospitals with documented success and reduced LOS and morbidity. Thus, with the long term goal of initiating an ERAS protocol at this particular hospital facility, it will be beneficial to incorporate a standardize perioperative anesthesia protocol in order to optimize postoperative pain. Literature supports the administration of PO Acetaminophen, as an adjunct to Gabapentin and Celebrex to improve pain scores.

Assessment of barriers and facilitators to implementation are important to reassess throughout the process for success implementation. Possible facilitators include patient/provider education, encouragement of provider feedback, and accessibility of the CPG. Potential barriers to the implementation of the CPG are cost of education/training, patient refusal to receive preemptive medications, provider resistance to change. To overcome this barrier, an emphasis on educating patients, bedside nurses, and anesthesia providers is crucial. Limitations to the CPG include time constraints between cases. For example, before the first scheduled case, providers have sufficient time to order the preemptive medications, however between cases; it is often difficult for patients to get their medications in the one-hour prior surgery timeframe. The creation of an electronic power- set may facilitate this process.

Since the presentation of the CPG, there have been no known consequences such as unexpected benefits, issues, or costs. The total cost of utilizing the medications mentioned in the CPG would be roughly $6,300 in one year, which can result to a 73% savings when compared to their current practice. Gabapentin 100 mg cap costing five cents each; Tylenol 325 mg cap costing one cent each and Celebrex 100 mg caps at 87 cents each.

Conclusion

In conclusion, inadequate postoperative pain management can significantly limit rehabilitation recovery, decrease patient dissatisfaction, increase healthcare costs, and complications. Traditional analgesics such as opioids are often associated with undesirable side effects. Moreover, opioids may not be effective particularly in the presence of tolerance and hyperalgesia.. In many instances, incorporating select non-opioid analgesics in a multimodal analgesic regimen is associated with better pain control and less opioid side effects. Preemptive multimodal therapy, the introduction of an analgesic regimen before the onset of painful stimuli targets different aspects of the inflammatory response and nociceptive pathway, and may cause sensitization of the nervous system to subsequent stimuli that can amplify pain, thus allowing more effective pain control with fewer side effects.

Therefore, a CPG for preemptive opioid sparing analgesia through the use of preoperative administration of Acetaminophen, Gabapentin, and Celebrex in patients undergoing TKA and THA is effective in improving postoperative pain, lowering overall narcotic consumption and side effects, reducing hospital stay, and improving function while minimizing complications. Current research supports the use of Acetaminophen given prior to surgical incision may reduce central sensitization, and therefore more pain control in the postoperative period compared to Acetaminophen given after incision. The development of this CPG is for patient quality improvement purposes. This project is not intended to be generalized to other institutions or settings. The anesthesia department has identified the need for a CPG that will provide anesthesia providers with a standardize pain management approach which minimizes the use of opioids and their potential side effects, therefore this CPG is intended solely to meet the needs of this institution. The practices outlined by the CPG will be sustained through continued efforts by the hospital's anesthesia department. This CPG will be in alignment with the institution revision of policy. Review of the outcomes and current evidence supporting this CPG will occur at regular intervals by the anesthesia staff.

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Table1: Evidence Review Table and Quality Rating of Preoperative Multimodal Analgesia for Total Hip and Knee Arthroplasty

Author, year	Study objective	Design	Sample (N)	Outcomes studied	Results	*Level and Quality Rating
Doleman, B., Read, D., Lund, J. N., & Williams, J. P. (2015)	To evaluate the role of preventive Acetaminophen compared with postincision Acetaminophen in reducing postoperative pain, opioid consumption and opioid-related side effects.	Systematic Review and Meta-analysis	7 RCTS; N=544 Preventive Group • Acetaminophen given one hour before induction of anesthesia Postincision Group • Acetaminophen given any time between post-incision and within 30 minutes from the end of surgery	• 24-hour opioid consumption • Postoperative pain scores at 1 hour • Time to first analgesic request • Nausea, vomiting and pruritus	• 24-hour opioid consumption less in the preventive group (SMD of -0.52; 95% CI -0.98 to -0.06). • Pain scores lower in the preventive group at 1 hour with a MD of -0.50 (95% CI -0.98 to -0.02). • Preventive group requested their first analgesic 12.48 minutes later (95% CI, 1.3923.58 minutes) than the post-incision group. • Lower incidence of postoperative vomiting (risk ratio, 0.50; 95% CI, 0.31–0.83)	1B

Gupta, Abubaker, Demas, and Ahrendtse (2016)	Compare the safety and efficacy of the perioperative administration of IV ibuprofen with/without IV Acetaminophen on patient undergoing total knee or hip arthroplasty	Randomized controlled trial (RCT)	N=74 Group 1 induction (n=35) • 800 mg of Ibuprofen, plus 800 mg every 6 hrs X5 days or discharge Group 2 induction (n=39) • 800 mg ibuprofen and closure, plus Acetaminophen 1,000 mg plus every 6 hrs or until discharge.	• Visual Analog Scale (VAS) pain scores. • Opioid use • Quality of recovery scale (QoR) • Length of post-anesthesia care unit (PACU) stay • Antiemetic consumption • Opioid consumption • Opioid related adverse events.	• Compared to Group 1, Group 2 had lower VAS scores ($p < 0.002$) by day 3 only. • Compared to Group 1, Group 2 had less opioid requirements and adverse events. • Time to discharge from the PACU: -Group 1: 55 minutes -Group 2: 38 minutes • Length of hospital stay: no significant difference noted between groups ($p = 0.138$).	1B

Lamplot Wagner, & Manning, (2014).	To analyze the effects of a multimodal analgesic regimen versus patient controlled analgesia (PCA)	Prospective Randomized Controlled Trial (RCT)	N= 36 • Group 1 • (multimodal) (n=19) received scheduled oxycodone 10 mg PO q12 h, tramadol 50 mg PO q 6 h, ketorolac 15 mg parenterally q 12 12h, & hydrocodone 5 mg PO PRN and hydromorphone 1 mg parenterally PRN for rescue. • Group 2 (control) (n=17) received hydromorphone PCA and hydromorphone 1 mg parenterally PRN for rescue.	Data collected on postoperative days zero, one, two, and at 3week • Visual Analog Scale (VAS) pain score • narcotic consumption • medication-related adverse effects • time to physical therapy milestones • length of hospitalization • patient satisfaction score.	• Group 1: the multimodal group reported lower VAS scores, adverse effects, narcotic usage, and higher satisfaction scores and earlier times to physical therapy milestones. • Multimodal pain management protocol decreased narcotic usage, improved pain scores, increased satisfaction and enhanced early recovery. • Group 1 has improved outcomes than group 2.	1B

Limin et al., 2017	To evaluate the efficiency and safety of IV Acetaminophen as an adjunct to multimodal analgesia for pain control after total joint arthroplasty.	Meta-analysis of RCT and non-RCTs of patients undergoing total joint arthroplasty.	3 RCTs, 1 non-RCT N= 832 • Acetaminophen group (n=534) • Control group (n= 331)	• Pain scores at: -24 hours -48 hours -72 hours. • Opioid consumption at: -24 hours - 48 hours -72 hours • Length of hospital stay (LOS) • Nausea and vomiting	• Pain scores of all 3 intervals showed significant difference between both groups; lower VAS scores (WMD=_0.926, 95% CI: -1.171 to -0.681, p=.000) • Opioid consumption: difference between both groups (207 mg versus 252 mg, P<0.05) • Length of hospital stay: No difference observed between the 2 groups (WMD=0.037, 95% CI: -0.083 to 0.157, p=.544) • Nausea and vomiting: significant difference found between the 2 groups (RD=_0.107, 95% CI: -0.152 to • -0.062, P=0.000	1A

O'Neal et al., 2017	To determine the efficacy of IV vs.PO Acetaminophen in patients undergoing unilateral TKA.	Randomized, double-blinded, placebo-controlled clinical trial.	N= 174
			3 groups:
			• IV Acetaminophen group (n=57)
			• PO group (n=58)
			• Placebo group (n= 59)
				• Pain scores were obtained every 15 minutes during PACU stay.
				• average pain scores, maximum pain score, and pain scores before physical therapy were compared among the 3 groups.
				• total opiate consumption
				• time to PACU discharge
				• time to rescue analgesia
				• time to break through pain.
					• No differences revealed across the groups:
					  • in time to breakthrough pain, time to rescue.
					  • total opiate consumption within 6 or 24 hours, time to PACU, and discharge time
					• There is no benefit of using Acetaminophen, either IV or orally, for pain control in the perioperative period after TKA when compared with placebo.
						1A

Politi, Davis, and Matrka, (2017)	To compare the effectiveness of IV versus PO Acetaminophen as part of a standard multimodal perioperative pain nregimen.	Randomized Controlled Trial (RCT)	N= 120 patients • Group 1: (n=63) IV Acetaminophen • Group 2: (n=57) PO Acetaminophen	• Total narcotic use • Visual Analog Scale (VAS) scores at every 4 hours intervals postoperatively.	• Narcotic use : No difference between groups at 24 hr =3.71 vs. 3.48 (P = .76) • VAS scores at 24 hrs= 3.00 (IV) and 3.40 (PO) (P = .06) • None of the 4-hour intervals were significantly different except the first interval (0-4 hour postoperatively), the IV group (P = .03), with a one point difference in VAS score.	1A

Sun et al., 2018	To evaluate the efficacy between intravenous and PO Acetaminophen as adjunct to multimodal analgesia regimens for pain management after total knee and hip arthroplasties.	Systemic Review and Meta-Analysis.	Two RCTs; N=236 • Experimental group=: (n= 120) IV Acetaminophen • Control group: (n=116) PO Acetaminophen	• VAS scores at 12, 24, 48 hrs • opioid consumption at 12, 24, 48 hours • length of stay • postoperative complications (nausea, vomiting, purities).	• No differences between groups regarding pain scores at 12, 24, or 48 hours. • No differences were observed in terms of opioid consumption at 12, 24, or 48 hours after arthroplasties. • No difference in length of hospital stay or postoperative complications among both groups.	1A

Toms, McQuay, Derry, & Moore (2017)	To assess the efficacy and adverse effects of single dose PO Acetaminophen for the treatment of acute postoperative pain.	Meta-analysis of RCTs	N=5762 Group 1: (n= 3277) Acetaminophen group • Acetaminophen 500 mg in six studies (n=561) • Acetaminophen 600 or 650 mg in 19 studies (n=1886) • Acetaminophen 975 or 1000 mg in 28 studies (n=3232) • Acetaminophen 325 mg in one study • Acetaminophen 1500 mg in one study Group 2: n=2425) Placebo group	• VAS pain scores • Use of rescue medication	• About half of participants treated with Acetaminophen of all doses achieved at least 50% pain relief over 4-6 hrs, compared with 20% treated with placebo. • About half of participants needed additional analgesia over 4-6 hrs, compared with 70% with placebo. • Reported adverse events were mainly mild and transient, and occurred at similar rates of around 16% in both Acetaminophen and placebo groups.	1A

Rating System for Hierarchy of Evidence

Level of the Evidence	Type of the Evidence
I (1)	Evidence from systematic review, meta-analysis of randomized controlled trails (RCTs), or practice-guidelines based on systematic review of RCTs.
II (2)	Evidence obtained from well-designed RCT
III (3)	Evidence obtained from well-designed controlled trials without
randomization IV (4)	Evidence from well-designed case-control and cohort studies
V (5)	Evidence from systematic reviews of descriptive and qualitative studies
VI (6)	Evidence from a single descriptive or qualitative study
VII (7)	Evidence from the opinion of authorities and/or reports of expert committees

Melnyk, B.M. & Fineout-Overholt, E. (2014). *Evidence-based practice in nursing & healthcare: A guide to best practice* (3rd ed.). New York: Lippincott, Williams & Wilkins.

Rating Scale for Quality of Evidence

A: High – consistent results with sufficient sample, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific literature

B: Good – reasonably consistent results; sufficient sample, some control, with fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence

C: Low/major flaw – Little evidence with inconsistent results; insufficient sample size; conclusions cannot be drawn

Appendix A

Clinical Practice Guideline: Preemptive Opioid-Sparing Analgesia for Total Hip and Knee Arthroplasty

I. Scope and Practice

1. Objective
   - To improve postoperative pain in patients undergoing hip and knee arthroplasties at Sinai Hospital by utilizing pre-emptive opioid-sparing analgesia
2. Health Question Covered by the Guideline
   - Effectiveness of pre-emptive opioid-sparing analgesia in improving postoperative pain in patients undergoing hip and knee arthroplasties. Intervention proposed by administering Acetaminophen, Gabapentin, and Celebrex in the preoperative phase as oppose to standard practice.
3. Population
   - Males/females, ≥ 18 years old, ASA I, II, or III
   - Patient having any elective inpatient or outpatient total knee or hip arthroplasties under general anesthesia or spinal anesthesia.
   - Excluding pediatrics and emergent cases

II. Stakeholder Involvement

1. Individuals/ Professionals Included in the Guideline Development
   - Participants involved the Director of Regional Anesthesia and Acute Pain Medicine, Jason Brookman, MD and Certified Registered Nurse Anesthetist (CRNA), Alex Halstead, DNP. The CPG is intended for Sinai Hospital, a level II trauma facility in Baltimore Maryland. Stakeholders involvement was to review the clinical practice guideline (CPG) using the AGREE II tool. The CPG will be revised according to recommendations provided by stakeholders and presented to the anesthesia providers. The Chief of Anesthesia was also consulted during the final process.

2. Target Population Preferences and views
   - The Practitioner Feedback Questionnaire (PFQ) will be utilized to gain feedback regarding the quality of the CPG from the anesthesia department gathered after initial presentation during grand rounds. All PFQs will be analyzed via descriptive statistics and kept confidential.

3. Target Users
   - The intended guideline is meant to aide Anesthesiologists, Certified Registered Nurse Anesthetists (CRNA), and Student Registered Nurse Anesthetists (SRNA) on providing an opioid sparing analgesia technique.

III. Rigour of Development

3. Search Methods
   - Using University of Maryland Health and Science Library and Cumulative Index to Nursing and Allied Health Literature (CINAHL), an advance search was conducted using the keywords alone and in combination: *multimodal, preemptive analgesia, Tylenol, acetaminophen, Gabapentin, Celebrex, total hip arthroplasty, total knee arthroplasty and postoperative pain*. Electronic databases included Medline, Nursing Academic Edition, Cochrane, and PubMed using the inclusion and exclusion criteria. Results were narrowed to include English language articles published between 2008 and 2018. Abstracts were reviewed, and further data extraction and categorizing identified fourteen studies for the development of this CPG.
4. Evidence Selection Criteria
   - Inclusion criteria included targeted patient population, adult patients undergoing total hip and knee arthroplasty, RCTs, Systematic reviews, meta-analysis, and publication within the last 5 years. Exclusion included editorial publication and articles written in any other language other than English.
5. Strengths and Limitations of the Evidence
   - Utilizing the Johns Hopkins Nursing Evidence-Based Practice Model, the quality of the evidence was rated with the Guideline Evidence Level Rating Guide, and

Quality Rating Guide by Dearholt & Dang. All fourteen studies included in the review were level one and two, with a quality of evidence ranging from A-B. Strengths were found with study sampling to include blind and randomized selection process.

- Furthermore, relevance of primary and secondary outcomes was measure with validity and reliability methods. Limitation across studies were found with varying dose and timing across studies.

6. Formulation of Recommendations
   - The recommendations provided by this CPG were formulated by SRNAs with the guidance of faculty of UMB and stakeholders from the facility the CPG was intended. The recommendations are supported by high quality evidence using the Johns Hopkins Evidence-Based Practice Evaluation Tool and suggestions by the stakeholders and target users were incorporated.
7. Consideration of Benefits and Harms
   - Multiple benefits have been found using a preemptive opioid-sparing analgesia technique to include a reduction in opioid consumptions and opioid related complication that include sedation, respiratory depression, nausea, vomiting, ileus, urinary retention, and pruritus (Golladay et al., 2017). Additionally, providing effective postoperative pain management may contribute to earlier mobilization, which may decrease the incidence of thromboembolism, facilitate return of bowel function, faster recovery and reduced hospital cost (Arumugam, Lau, & Chamberlain, 2016). Acetaminophen contraindicated in patients with active liver disease or elevated liver enzymes, and hypersensitivity to Acetaminophen. A recommendation is to maintain a 4g daily limit.
   - Celebrex contraindicated in patients with hypersensitivity to sulfonamides, active gastrointestinal ulcer, asthma, elevated blood urea nitrogen (BUN) or creatinine levels.
   - ontraindicated to Gabapentin hypersensitivity, precautions with renal impairment, patients greater than 80 years of age.
8. Link Between the Recommendations and Supporting Evidence

- The American Society of Anesthesiologist (ASA) supports the routine use of NSAIDS, COX-2 inhibitors, and acetaminophen, for preemptive analgesia (Austin, 2017).
- The Enhanced Recovery After Surgery (ERAS) Society recommends multimodal analgesia using a combinations of nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol, anticonvulsant agents, and calcium channel blockers to block a variety of pain receptors centrally and peripherally in the pain transmission pathways (Beverly et al., 2017)

9. External Review
    - Prior to conducting an external review, an internal review of the medical facility was conducted identifying a need for the CPG. The purpose and the intent of the external review was to improve quality of care amongst patients undergoing total hip and knee arthroplasties. A systematic review of literature was conducted on each medication recommended for the CPG, Tylenol, Gabapentin, and Celebrex. Each group member was assigned a medication for review. Evidence was then complied from each group member to form the CPG and presentation to stakeholders. Subsequently, collaboration with stakeholders was executed to provide a transparent and high-quality CPG. The initial CPG was evaluated by the Director of Regional Anesthesia and a CRNA using the Appraisal of Guidelines for Research and Evaluation (AGREE) II Tool. This is a 23-item instrument that uses methodological strategies to assess the quality and reporting of the practice guideline to minimize any variability in quality. The AGREE II tool provides an opportunity to address any concerns with the quality of the CPG leading to improvements with revisions provided to stakeholders until all concerns are met.

    - Once the guideline is revised, a presentation to include practice problem, background information, and the proposed guideline will be given to the anesthesia department in a medical facility in Baltimore, MD. All attendees will fill out a PFQ, which consist of 23 questions to assess the likelihood of adoption by the staff into the facility. The PFQ interprets quality, applicability, acceptability and comparative value of the guideline while providing demographic data. The data collected from the PFQ will be reviewed and analyzed using differential and inferential statistical analysis. Concluding the presentation, a copy of the presentation will be e-mailed to the entire anesthesia department for reference.

10. Updating Procedure

- The practices outlined by the CPG will be sustained through continued efforts by the hospital's anesthesia department and updated according to the institution's timeline review. Recommendation to maintain updated review should occur within a three-year time frame. To maintain sustainability, however, assessment of barriers to implementation must be continuously assessed such as new employees, medication availability, support from preoperative assessment staff to carry out medication order on power set. Therefore, it is recommended to monitor sustainability with anesthesia staff on the schedule at which the institution's protocols should be reviewed.

IV. Clarity of Presentation

11. Specific and Unambiguous Recommendations

- Change in standard of care for the target population prior to surgery should consist of administering the medication discussed below to reduce post-operative pain. It is recommended the CPG be continually evaluated for outcomes and edit the CPG as necessary. Additionally, it is prudent to review most recent literature every three years and update the CPG accordingly.

Recommendation

a. Pre-operative Period

One hour before surgical incision

- Acetaminophen 1000 mg PO
- Gabapentin 300 mg PO
- Celebrex 200 mg PO

b. Intra-operative Period

- Hip Arthroplasty: Spinal Anesthesia
- Knee Arthroplasty: Spinal Anesthesia or Adductor Canal Block and General Anesthesia

*Do NOT give Acetaminophen to patients with active liver disease or increased liver enzymes.

**Do NOT give Gabapentin to patients on hemodialysis and age 80 or older. Decrease dose for patients with reduced renal functioning and BMI of <25 kg/m2.

***Do NOT give Celecoxib to patients with allergic-type reactions to sulfonamides.

- Among the different multimodal pain management reviewed, celecoxib, acetaminophen, and pregabalin are the frequently utilized medications to facilitate preemptive analgesia because of their opioid sparing effect (Lamplot et al., 2013).
- Based on the review of the research studies, one major component noted was the utilization of preemptive analgesia. The multimodal pain analgesics included in each study was administered in the preoperative phase. Preemptive administration of analgesics plays a role in postoperative pain (Lee et al., 2015; Michelson et al., 2013; Yi-Li et al., 2017).

V. Health Benefits, Side Effects, and Risks a. Potential Benefits

- Studies have shown that preemptive opioid sparing analgesia has benefits in decreasing post- operative pain depicted by decrease pain scores, decrease intraoperative opioid consumption a lower risk of complication associated with opioid consumption. Additionally, it has been found through research that patient satisfaction has been increased with the use of preemptive opioid sparing analgesia.

Furthermore, it will shorten patient's hospital stay and improve patient's ability to participate in physical therapy (Lamplot et al., 2013).

b. Side effects:

Medication	**Mechanism of actions (MOA)**	**Side effects and contraindications**
Acetaminophen	The exact MOA is still unclear but it is believed to work on the central nervous system by blocking pain receptors in the brain. Potential mechanism of action is that acetaminophen has antipyretic and moderate analgesic properties, but largely lacks anti-inflammatory activity. probably both an isoform nonspecific and partial cyclooxygenase (COX) inhibition (Gupta et al., 2016). antipyretic and moderate analgesic properties, but largely lacks anti-inflammatory activity. While its mechanism of action is	Contraindicated with elevated liver enzymes, active liver disease, and hypersensitivity to Acetaminophen (Gupta et al., 2016).

	not entirely understood, it is probably both an isoform nonspecific and partial cyclooxygenase (COX) inhibition (Gupta et al., 2016).	

Gabapentin	Gabapentin interacts with a high-affinity binding site in brain membranes, which has recently been identified as an auxiliary subunit of voltage-sensitive Ca2+ channels, specifically the α2δ-1 subunit. Inhibits excitatory neurotransmitters and Ca2+ influx in the spinal and supraspinal pathways Gabapentin prevents pain responses and hyperalgesia (Gandhi et al., 2009).	Contraindicated in patients aged 80 or older. Decrease the dose by have for patients with BMI below 25.0 kg/m2. Adverse reactions: double or blurred vision, asthenia, dizziness, or disorientation. Caution should be taken in patient with decreased renal function since is eliminated via the kidneys unchanged (about 90%) (Gandhi & Viscusi, 2009).
Celecoxib	Inhibits the conversion of arachidonic acid to prostaglandins. Does not affect platelet functions as other NSAIDs (Kashefi et al., 2013)	Contraindicated in patients with hypersensitivity to sulfonamides, active gastrointestinal ulcer, asthma, elevated blood urea nitrogen (BUN) or creatinine levels (Kashefi et al., 2013).

VI. Applicability

A. Facilitators to Application

- Principal implementors that will facilitate the progression of this practice change include the following: champions whom are extremely well versed of the current evidence on the practice change, mentors that are skilled in EBP and will serve as part of an expert panel, support from the administrative team such as management staff that encourage receptiveness for transformation. The creation of an expert panel is essential to assist and mentor throughout the development and implementation of the CPG. The expert panel assisted in modifying drafts of the CPG utilizing the Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument prior to presenting the CPG to the anesthesia department
- The facilitators identified in the implementation of the clinical practice guideline include collaborative relationship between healthcare providers and patients; presence of transformational leaders; patient centered practice; and support for evidence-based practice. The chief of anesthesia, the chief orthopedic surgeon, a CRNA, the entire anesthesia providers, and the director of pharmacy had an active role in the process of the guideline development. Having the key stakeholders buy-in earlier in the process may garner support to implement the guideline successfully.

A. Barriers to Application

- One of the possible barriers could be the possibility of delay in administering the medications. To overcome this barrier, patients should be educated about the importance of arriving at the preoperative area on time; and educating pre-operative nurses about the importance of giving the medications as early as possible.

Furthermore, some practitioners may be unaware of the latest evidence-based practice and other providers could resist changing the way they practice. To overcome these, having educational meetings such as workshops, lectures and conferences;

- One of the possible barriers could be the possibility of delay in administering the medications. To overcome this barrier, patients should be educated about the importance of arriving at the preoperative area on time; and educating pre-operative nurses about the importance of giving the medications as early as possible. Furthermore, some practitioners may be unaware of the latest evidence-based practice and other providers could resist changing the way they practice. To overcome these, having educational meetings such as workshops, lectures and conferences; educational material such as booklet and online tool will be helpful to inform the end-users of the current evidence-based practice (National Institute for Health and Clinical Excellence, 2007).

2. How the Recommendations Can Be Implemented
    - Successful implementation will require proper information dissemination and education. Buy-in from the anesthesia and orthopedic surgeons is essential. Pre-operative nurses will be educated about the guideline. This can be done through in-service education and poster presentation to the anesthesia department, orthopedic surgeons, and preoperative nurses during grand rounds.
    - Continuous protocol evaluation and modification should be done every two years based on new evidence-based practice. Flyers containing the summarized guideline recommendations will be distributed to the anesthesia providers, orthopedic surgeons, and nurses.

3. Potential Resource Implications of Applying the Recommendations
    - The total cost of utilizing the medications mentioned in the CPG would be roughly $5,600 in one year, which can result to a 78% savings when compared to their current practice.
4. Monitoring and/or Auditing Criteria
    - Pain level using the visual analog scale should be assessed between emergence and postoperative day one.

VII Identifying Information and Availability

1. Funding Body/ Competing Interests
    - The development of this guideline was developed without external funding. Everyone who is involved in the development of this guideline confirmed that they have no competing interests.
2. Principal Authors
    - Sherilyn Batista, SRNA
    - Linda Bob-Manuel, SRNA
    - Lia A. Pulido, SRNA
3. Key Contributors
    - Michelle Gonzalez, PhD, CRNA
    - Joseph E Pellegrini, PhD, CRNA, FAAN
    - Alex Halstead, DNP, CRNA
    - Jason Brookman, MD

Appendix B: Agree II Tool

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA
DOMAIN 1: SCOPE AND PURPOSE	
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) Expected benefit(s) or outcome(s) Target(s) (e.g., patient population, society)
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	Target population Intervention(s) or exposure(s) Comparisons (if appropriate) Outcome(s) Health care setting or context
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	Target population, sex and age Clinical condition (if relevant) Severity/stage of disease (if relevant) Comorbidities (if relevant) Excluded populations (ifrelevant)
DOMAIN 2: STAKEHOLDER INVOLVEMENT	
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	Name of participant Discipline/content expertise (e.g., neurosurgeon, methodologist) Institution (e.g., St. Peter's hospital) Geographical location (e.g., Seattle, WA) A description of the member's role in the guideline development group
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) Outcomes/information gathered on patient/public information

	How the information gathered was used to inform the guideline development process and/or formation of the recommendations
6. TARGET USERS **Report the target (or intended) users of the guideline.**	The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)
DOMAIN 3: RIGOUR OF DEVELOPMENT	
7. SEARCH METHODS **Report details of the strategy used to search for evidence.**	Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) Time periods searched (e.g., January 1, 2004 to March 31, 2008) Search terms used (e.g., text words, indexing terms, subheadings) Full search strategy included (e.g., possibly located in appendix)
8. EVIDENCE SELECTION CRITERIA Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.	Target population (patient, public, etc.) characteristics Study design Comparisons (if relevant) Outcomes Language (if relevant) Context (if relevant)

9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	Study design(s) included in body of evidence Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) Appropriateness/relevance of primary and secondary outcomes considered Consistency of results across studies Direction of results across studies Magnitude of benefit versus magnitude of harm Applicability to practice context
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)
11. CONSIDERATION OF BENEFITS AND HARMS Report the health benefits, side effects, and risks that were considered when formulating the recommendations.	Supporting data and report of benefits Supporting data and report of harms/side effects/risks Reporting of the balance/trade-off between benefits and harms/side effects/risks Recommendations reflect considerations of both benefits and harms/side effects/risks
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE Describe the explicit link between the recommendations and the evidence on which they are based.	How the guideline development group linked and used the evidence to inform recommendations Link between each recommendation and key evidence (text description and/or reference list) Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline

13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) Methods taken to undertake the external review (e.g., rating scale, open-ended questions) Description of the external reviewers (e.g., number, type of reviewers, affiliations) Outcomes/information gathered from the external review (e.g., summary of key findings) How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	A statement that the guideline will be updated Explicit time interval or explicit criteria to guide decisions about when an update will occur Methodology for the updating procedure
DOMAIN 4: CLARITY OF PRESENTATION	
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	A statement of the recommended action Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) Relevant population (e.g., patients, public) Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline

16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	Description of management options Population or clinical situation most appropriate to each option
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms Specific recommendations grouped together in one section
DOMAIN 5: APPLICABILITY	
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	Types of facilitators and barriers that were considered Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) How the information influenced the guideline development process and/or formation of the recommendations
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	Additional materials to support the implementation of the guideline in practice. For example: Guideline summary documents Links to check lists, algorithms Links to how-to manuals Solutions linked to barrier analysis (see Item 18) Tools to capitalize on guideline facilitators (see Item 18) Outcome of pilot test and lessons learned
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) Information/description of the cost information that emerged from the

	inquiry (e.g., specific drug acquisition costs per treatment course) How the information gathered was used to inform the guideline development process and/or formation of the recommendations
21. MONITORING/ AUDITING CRITERIA Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.	Criteria to assess guideline implementation or adherence to recommendations Criteria for assessing impact of implementing the recommendations Advice on the frequency and interval of measurement Operational definitions of how the criteria should be measured
DOMAIN 6: EDITORIAL INDEPENDENCE	
22. FUNDING BODY **Report the funding body's influence on the content of the guideline.**	The name of the funding body or source of funding (or explicit statement of no funding) A statement that the funding body did not influence the content of the guideline
23. COMPETING INTERESTS **Provide an explicit statement that all group members have declared whether they have any competing interests.**	Types of competing interests considered Methods by which potential competing interests were sought A description of the competing interests How the competing interests influenced the guideline process and development of recommendations

Appendix C: Practitioner Feedback Questionnaire (PFQ)

	Yes	No	Unsure
1. Are you responsible for the care of patients for whom thisdraft guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.	☐	☐	☐
If you answered "*No*" or "*Unsure*", there is no need to answer or return this questionnaire. If you answered "*Yes*", please answer the questions below and return to **[enter expected destination of surveys]**.			
	Strongly y agree	Neither agree or disagree	Strongly disagree
2. The rationale for developing a guideline is clear.	☐	☐	☐
3. There is a need for a guideline on this topic.	☐	☐	☐
4. The literature search is relevant and complete (e.g., no key evidence was missed nor any included that should not have been) in this draft guideline.	☐	☐	☐
5. I agree with the methodology used to summarize the evidence included in this draft guideline.	☐	☐	☐
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.	☐	☐	☐
7. The draft recommendations in this report are clear.	☐	☐	☐
8. I agree with the draft recommendations as stated.	☐	☐	☐
9. The draft recommendations are suitable for the patients for whom they are intended.	☐	☐	☐
10. The draft recommendations are too rigid to apply to individual patients.	☐	☐	☐
11. When applied, the draft recommendations will produce more benefits for patients than harms.	☐	☐	☐
12. The draft guideline presents options that will be acceptable to patients.	☐	☐	☐
13. To apply the draft recommendations will require reorganization of services/care in my practice setting.	☐	☐	☐
14. To apply the draft guideline recommendations will be technically challenging.	☐	☐	☐
15. The draft guideline recommendations are too expensive to apply.	☐	☐	☐
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.	☐	☐	☐

17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.	☐	☐	☐
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☐	☐	☐
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☐	☐	☐
20. I would feel comfortable if my patients received the care recommended in the draft guideline.	☐	☐	☐
21. This draft guideline should be approved as a practice guideline.	☐	☐	☐
22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.	☐	☐	☐
23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.	☐	☐	☐

Appendix D: AGREE 2 Tool Results

	Obtained Score	Domain Score
Domain 1. Scope and Purpose	40	94.4
Domain 2. Stakeholder Involvement	23	71.6
Domain 3. Rigour Of Development	97	84.7
Domain 4. Clarity of Presentation	36	83.3
Domain 5. Applicability	42	80.4
Domain 6. Editorial Independence	28	100 .0

Appendix E: Modified Practitioner's Feedback Questionnaire (PFQ) Demographics Results

Demographic Characteristic (n = 29)

	n	***PCT***
TYPE OF PROVIDER		
MD Anesthesiologist	**5**	**17%**
CRNA	**17**	**59%**
Resident/Fellow	**-**	**0%**
SRNA	**7**	**24%**
YEARS OF EXPERIENCE		
0-5 years	**8**	**38%**
6-10 years	**5**	**24%**
>10 years	**8**	**38%**

Appendix F: Modified Practitioner's Feedback Questionnaire (PFQ) Results:

	Agree %	Neither %	Disagree %
2. The rationale for developing a guideline is clear.	100%	0%	0%
3. There is a need for a guideline on this topic.	85%	15%	0%
4. The literature search is relevant and complete (e.g., no key evidence was missed nor any included that should not have been) in this draft guideline.	100%	0%	0%
5. I agree with the methodology used to summarize the evidence included in this draft guideline.	96%	4%	0%
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.	100%	0%	0%
7. The draft recommendations in this report are clear.	100%	0%	0%
8. I agree with the draft recommendations as stated.	100%	0%	0%
9. The draft recommendations are suitable for the patients for whom they are intended.	100%	0%	0%
10. The draft recommendations are too rigid to apply to individual patients.	33%	33%	33%
11. When applied, the draft recommendations will produce more benefits for patients than harms.	96%	4%	0%
12. The draft guideline presents options that will be	100%	0%	0%

acceptable to patients.			
13. To apply the draft recommendations will require reorganization of services/care in my practice setting.	37%	37%	26%
14. To apply the draft guideline recommendations will be technically challenging.	19%	41%	41%
15. The draft guideline recommendations are too expensive to apply.	15%	37%	48%
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.	85%	7%	7%
17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.	70%	19%	11%
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	89%	11%	0%
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA).	85%	15%	0%
20. I would feel comfortable if my patients received the care recommended in the draft guideline.	96%	0%	4%
21. This draft guideline should be approved as a	100%	0%	0%
22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.	100%	0%	0%

23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.	100%	0%	0%

Adapted from: Brouwers, M.C., Graham, I.D., Hanna, S.E., Cameron, D.A., & Browman, G.P. (2004). Clinicians' assessments of practice guidelines in oncology: The CAPGO survey**.** *International Journal of Technology Assessment in Health Care, 20*(4), 421-6.