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Is Preoperative Administration of Celecoxib and Pregabalin Associated with Decreased Intraoperative and Postoperative Opioid Consumption in Patients Undergoing Total Hip or Knee Arthroplasty?

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IS PREOPERATIVE ADMINISTRATION OF CELECOXIB AND PREGABALIN ASSOCIATED WITH DECREASED INTRAOPERATIVE AND POSTOPERATIVE OPIOID CONSUMPTION IN PATIENTS UNDERGOING TOTAL HIP OR KNEE ARTHROPLASTY?

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EXECTUTIVE SUMMARY

Abstract: The purpose of this study was to determine if a preoperative dose of celecoxib and pregabalin in patients who underwent total hip arthroplasty (THA) or total knee arthroplasty (TKA) was associated with less opioid consumption intraoperatively and postoperatively compared to those who did not receive this regimen.

Introduction: THA and TKA have been associated with a high incidence of postoperative pain. Historically, this pain has been managed with opioids; however, these drugs have negative side effects associated with their use. Consequently, anesthesia providers have begun utilizing multimodal non-opioid analgesics. Recently, a specific combination has been utilized, which includes a nonsteroidal anti-inflammatory drug known as celecoxib (Celebrex) and an anticonvulsant known as pregabalin (Lyrica). While this combination may be a beneficial alternative for opioids, there is no consensus on the timeliness or effectiveness of a single combination dose of these drugs at alleviating perioperative pain.

Methodology: A retrospective cross-sectional study design was utilized for this study that included 200 patients who underwent THA or TKA between May 1, 2008 and May 1, 2018 at Charleston Area Medical Center. A total of 100 patients were included in group one, which consisted of patients who did not receive a preoperative dose of celecoxib and pregabalin or any other preoperative analgesics. Group two consisted of 100 patients who did receive a preoperative dose of both celecoxib and pregabalin. The primary independent variable was the preoperative administration of celecoxib and pregabalin. Secondary independent variables consisted of gender, age, body mass index (BMI), and American Society of Anesthesiologists (ASA) physical classification scores. The dependent variables consisted of intraoperative opioid consumption and total opioid consumption in the postoperative anesthesia care unit (PACU). Control variables consisted of gender, age, BMI and ASA physical classification scores. The research hypotheses were that patient who underwent THA or TKA and received preoperative doses of both celecoxib and pregabalin would have less opioid consumption in the intraoperative period and less opioid consumption in the PACU, compared to those who did not receive the same combination preoperatively.

Results: Comparison of the two groups yielded no differences between mean age, BMI or gender. The mean age and ASA classification between the two groups were statistically different, p=.0001 and p=.017. Group one consisted of 55 females and 45 males, while group two consisted of 52 females and 48 males. The study also revealed there was a statistical significance in terms of PACU opioid consumption (p=.001) between the two groups but no statistical difference in intraoperative opioid consumption (p>.05). Group one received a mean difference of approximately 1.2 morphine equivalents more than group two. There was no statistical significance between PACU opioid consumption and age, gender, BMI, or ASA classification. Analysis showed there was a statistical association between intraoperative opioid consumption and age (p=.022) and gender (p=.025). Further analysis revealed females received a mean of 3.22 morphine equivalents more than males.

Discussion: The study results supported the hypothesis that preoperative celecoxib and pregabalin would be associated with a decrease in PACU opioid consumption in patients undergoing THA or TKA. These results did not support the additional study hypothesis that this combination would also decrease intraoperative opioid consumption.

Implications and Recommendations: The results of this study supported the use of preoperative celecoxib and pregabalin at reducing PACU opioid consumption. Additional

prospective, randomized studies are needed to compare the use of celecoxib and pregabalin independently versus in combination.
Conclusion: In conclusion, this study found an association between the preoperative administration of celecoxib and pregabalin in patients undergoing THA or TKA and decreased PACU opioid consumption; however, no association was found between the preoperative administration of celecoxib and pregabalin and decreased intraoperative opioid consumption in these patients.

Key Words: Arthroplasty, celecoxib, opioid, pregabalin, pain

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INTRODUCTION

Background and Significance of the Problem

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are surgical procedures in which damaged cartilage and bone are removed from the hip or knee area and replaced with prosthetic components (American Academy of Orthopaedic Surgeons, 2015a, 2015b). According to a 2010 report from the National Center for Health Statistics, TKA is the most commonly performed inpatient surgery on patients aged 45 years and older with an approximate 693,400 being performed annually (Williams, Woldford, & Bercovitz, 2015). This number has been predicted to increase to 3.48 million per year by 2030 (Kurtz, Ong, Lau, Mowat, & Halpern, 2007). In comparison, THA surgeries have been predicted to increase from 326,100 annually to 526,000 by 2030 (Kurtz et al., 2007; Woldford, Palso, & Bercovitz, 2015).

The primary indication for THA or TKA is a chronic pain disease known as osteoarthritis, which affects more than 30 million adults in the United States (Centers for Disease Control and Prevention [CDC], 2017; National Institutes of Health, 1994). Osteoarthritis is a chronic pain disease that causes cartilage to breakdown in bones and joints that leads to stiffness and edema (CDC, 2017). While people suffering from osteoarthritis undergo total joint arthroplasty to relieve these symptoms, this type of surgery often leads to chronic postoperative pain (Peterson & Arendt-Nielson, 2016). This chronic pain can lead to prolonged recovery, increased morbidity, chronic opioid use, and increased health care costs (Gan, 2017). Therefore, managing pain during this period for patients undergoing THA or TKA has remained a challenge for anesthesia providers. In the past, opioids have been the mainstay of pain management in these procedures; however, opioids have adverse effects associated with their use such as constipation, nausea and vomiting, respiratory depression, tolerance, and physical dependence

(Benayamin et al., 2008; Golladay, Balch, Dalury, Satpathy, & Jiranek, 2017). To decrease the negative side effects associated with opioids, surgeons and anesthesia providers have begun utilizing multimodal analgesic techniques that include both opioid and non-opioid analgesics (Halawi, Grant, & Bolognesi, 2015). These non-opioid analgesics have included local anesthetics, anticonvulsants such as pregabalin and gabapentin, and nonsteroidal anti-inflammatory drugs (NSAID) such as acetaminophen, ketorolac and celecoxib (Halawi et al., 2015). While some studies have shown that multimodal analgesic techniques can be effective in managing postoperative pain, other studies have indicated that these techniques have demonstrated no superiority to opioids and may actually increase opioid consumption, healthcare costs, and postoperative delirium (Brooks, Freter, Bowles, & Amirault, 2017; Halawi et al., 2015).

Many non-opioid analgesics have not been formulated for intravenous use; therefore, they are administered orally and preoperatively and are considered preemptive analgesics. Preemptive analgesics are pain relieving treatments that are administered before surgical incision that continue to exert their effects throughout the procedure to the initial postoperative period (Kissin, 2000). Preemptive analgesics inhibit central sensitization, which is an altered response to pain that intensifies postoperative pain (Kissin, 2000). Preventing central sensitization can decrease chronic pain, which has been reported to be 12.4% of patients who undergo THA or TKA. (Golladay et al., 2017; Nikolajsen, Brandsborg, Lucht, Jensen, & Kehlet, 2006).

A specific preemptive non-opioid combination that has been utilized during THA and TKA surgeries is celecoxib and pregabalin (Carmichael et al., 2013). Although specific studies have not been conducted to demonstrate if synergistic effects exist between pregabalin and

celecoxib, studies have indicated that when pregabalin is combined with other NSAIDs, such as naproxen, a synergistic relationship exists (Hurley, Chatterjea, Rose Feng, Taylor, & Hammond, 2002). Analgesic drugs are believed to be synergistic if they exhibit a greater pain-relieving effect when used in combination than when either drug is used alone.

Literature Review

NSAIDs such as celecoxib have been used around the world to treat pain and inflammation for over 100 years (Vane, 2000). NSAIDs demonstrate their effects by inhibiting the prostaglandin producing catalytic enzyme prostaglandin H_2 synthase (PGHS), also known as cyclooxygenase (COX) (Vane, 1971). There are two types of cyclooxygenase enzymes: cyclooxygenase type 1 (COX-1) and cyclooxygenase type 2 (COX-2) (Seibert et al., 1994). COX-1 enzymes participate in physiological hemostasis and maintain the integrity of the gastrointestinal and renal system, while COX-2 enzymes are inducible enzymes that are only present at sites of inflammation (Vane, Bakhle, & Botting, 1998).

Pharmacologic agents that interfere with these enzymes have been known to decrease pain and inflammation and are referred to as cyclooxygenase inhibitors (Vane et al., 1998). These drugs work by selectively inhibiting either COX-1 or COX-2, or simultaneously inhibiting both enzymes (Vane et al., 1998). The nonselective forms of these drugs, such as aspirin, naproxen, and ibuprofen have been used to treat pain associated with the inflammation process, but these drugs exhibit other side effects such as decreased platelet functioning and increased gastrointestinal toxicity (Vane et al., 1998).

While nonselective COX inhibiting drugs have proven to be beneficial for specific types of patients, such as those suffering with thrombotic disorders, their use in the perioperative area

can lead unwanted side effects such as increased blood loss during surgery (Connelly & Panush, 1991). These unwanted side effects have limited the use of nonselective NSAIDs in the perioperative period. Consequently, most NSAIDs are stopped days or even weeks before surgery; however, because a selective cyclooxygenase inhibitor such as celecoxib only demonstrates its effects on COX-2 enzymes it does not interfere with normal platelet function (Teerawattananon, Tantayakom, Suwanawiboon, & Katchamart, 2017). Therefore, it does not increase the risk of intraoperative bleeding (Teerawattananon et al., 2017). These beneficial pharmacologic properties have led to an increased use of celecoxib in the perioperative period; however, celecoxib must be administered orally three hours before surgical incision in order to be effective in treating pain (Pfizer INC, 2015).

Currently, celecoxib is the only Food and Drug Administration (FDA) approved selective NSAID available in the United States. Previous COX-2 selective inhibitors such as valdecoxib and rofecoxib have been removed from the market due to an increased risk of adverse cardiovascular effects with their use (U.S Food & Drug Administration, 2018). In order to remain on the market the FDA ordered the manufacturer to complete a cardiovascular safety trial, which is now known as the Prospective Safety Versus Ibuprofen or Naproxen (PRECISION) trial (Nissen et al., 2016). The authors concluded that celecoxib had less risk of gastrointestinal side effects than naproxen and less renal side effects than ibuprofen. The authors also suggested that moderate doses of celecoxib were not associated with an increased risk of cardiovascular events when compared to nonselective NSAIDs such as naproxen and ibuprofen. Due to the findings of this study, as of today, celecoxib remains on the market in the United States for the treatment of pain.

The FDA approved pregabalin 2004 for the treatment of peripheral neuropathy, neuralgia, and seizures. Since then, it has also been approved for the treatment of a chronic pain illness known as fibromyalgia and neuropathic pain (Pfizer Pharmaceuticals LLC, 2011). While pregabalin is a structural analog of the inhibitory neurotransmitter known gamma-aminobutyric acid (GABA), it does not exert its action at GABA receptor sites (Pfizer Pharmaceuticals LLC, 2011). Instead, the drug binds to voltage-gated calcium channel receptors in the central nervous system and decreases the release of neurotransmitters that signal pain (Pfizer Pharmaceuticals LLC, 2011). Although this mechanism of action is not fully understood, it is believed that pregabalin interferes with the pain transmission pathway from the brainstem to the spinal cord that is involved in the formation of chronic pain (Pfizer Pharmaceuticals LLC, 2011).

Various studies have been performed to determine the effectiveness of celecoxib and/or pregabalin during total joint arthroplasty, but most focus on the long-term effectiveness of both preoperative and repeated postoperative doses of these drugs. In 2015, a prospective randomized control trial that consisted of a total of 64 participants who underwent THA showed that patients who received a preoperative 400 milligram (mg) dose of celecoxib and additional scheduled 200 mg doses of celecoxib every 12 hours had decreased pain scores at 12, 24, 48, and 72 hours after surgery (Chen et al., 2015). Additionally, the treatment group had decreased opioid consumption at 6, 12, and 24 hours postoperatively compared to the control group. While the treatment group consisted of both preoperative and postoperative doses of celecoxib, decreased opioid consumption at 6 hours in the treatment group suggested that a single preoperative dose of celecoxib may have been effective in alleviating pain in the immediate postoperative period because repeated doses were not administered until 12 hours after surgery. Additionally, the

incidence of postoperative nausea and vomiting was lower in the treatment group (Chen et al., 2015).

In 2012, a randomized double-blind placebo study that consisted of ninety patients undergoing distal extremity surgery compared the effectiveness of a single preoperative dose of 200 mg of celecoxib versus 320 mg of acetaminophen (Kashefi, Honarmand, & Safavi, 2012). The authors of this study showed that pain scores four hours postoperatively were significantly lower in the celecoxib group compared to the acetaminophen and placebo group. Additionally, this study found that there were no statistically significant differences in pain scores in the three groups four hours after surgery.

In 2015, a prospective, randomized controlled trial that included 120 participants evaluated postoperative pain in patients undergoing TKA (YaDeau et al., 2015). Authors discovered that patients who had received preoperative and postoperative doses of pregabalin in addition to an NSAID did not have decreased pain or opioid consumption compared to those who received the same regimen without pregabalin. The authors also revealed that patients in the pregabalin group had increased sedation on postoperative day one.

In 2011, a randomized placebo-controlled trial that consisted of 50 participants undergoing discectomy showed that the treatment group who received a single 150 mg dose of pregabalin had reduced preoperative anxiety and postoperative pain (Spreng, Dahl, & Raeder, 2011). Although pain scores and morphine consumption did not differ significantly 24 hours postoperatively between the two groups, the authors did reveal that patients in the pregabalin group were able to be discharged from the post anesthesia care unit (PACU) earlier and had significantly lower pains scores at 120 minutes postoperatively. A similar double-blind randomized controlled trial in 2011, that consisted of 32 patients, demonstrated that a single 300

mg dose of pregabalin did not reduce pain intensity in patients undergoing discectomy; however, compared to the placebo, the pregabalin group did have decreased morphine consumption. (Hegarty & Shorten, 2011).

A 2015, a double-blind, randomized, placebo-controlled study that consisted of 184 participants showed that patients undergoing THA, who received a preoperative and postoperative combination of celecoxib and pregabalin, had less morphine consumption 12, 24, and 48 hours postoperative compared to the placebo group who received the same anesthetic regimen without pregabalin (Clarke et al., 2015). The authors also discovered that pain scores were lower 1-7 days after discharge. Another randomized controlled trial conducted in 2012 that consisted of 60 participants compared the analgesic effectiveness of preoperative celecoxib versus pregabalin during open cholecystectomy procedures (Ali & Babar, 2012). The authors concluded that neither drug was superior because there were no significant differences in postoperative pain scores, opioid consumption, or incidence postoperative nausea and vomiting between the two treatment groups (Ali & Babar, 2012). It was also noted in the study that the pregabalin group had a higher frequency of sedation.

Statement of the Problem and Research Purpose

Due to the predicted increase in total joint arthroplasties previously mentioned, the increasing age of the patient population undergoing THA and TKA, and the deleterious side effects of opioids, it is essential for surgeons and anesthesia providers to continue investigating the efficacy of multimodal pain management. While the use of preemptive multimodal combinations such as pregabalin and celecoxib in THA and TKA has been explored, there is no consensus on the effectiveness of single combination doses or the timeliness of this specific drug

combination at alleviating pain in the immediate postoperative period, therefore; further studies are warranted. The purpose of this study was to determine if a preoperative dose of celecoxib and pregabalin in patients who underwent THA or TKA was associated with less opioid consumption intraoperatively and postoperatively compared to those who did not receive this regimen. The importance of this study was to evaluate if orally administered non-opioid analgesics combinations such as these are an effective tool for anesthesia providers to utilize in the perioperative period. The findings of this study could lead to improved evidence based clinical practices and enhanced patient outcomes at Charleston Area Medical Center (CAMC) in Charleston, West Virginia and other facilities that perform THA or TKA.

METHODOLOGY

Research Hypotheses

The specific aim of this study was to evaluate the effectiveness of preemptive non-opioid analgesics in THA and TKA. The main objective of this study was to evaluate the effectiveness of preoperative celecoxib and pregabalin administration at reducing intraoperative and postoperative opioid consumption. There were two proposed hypotheses for this study. The hypotheses were:

1. Patients who underwent THA or TKA and received preoperative doses of both celecoxib and pregabalin will have less opioid consumption in the intraoperative period compared to those who did not receive the same combination preoperatively.
2. Patients who underwent THA or TKA and received preoperative doses of both celecoxib and pregabalin will have less opioid consumption in the PACU compared to those who did not receive the same combination preoperatively.

Research Design/Setting

The study design chosen was a retrospective cross-sectional design. This type of study design allowed for rapid cost efficient data collection for the intended patient population (Jacobsen, 2017). Data was collected from medical records at CAMC in Charleston, WV. CAMC is a non-profit hospital that is made up of 965 beds (Charleston Area Medical Center [CAMC], 2018). CAMC is made up of four divisions: CAMC General Hospital, CAMC Memorial Hospital, CAMC Women and Children's Hospital and CAMC Teays Valley Hospital (CAMC, 2018).

Sample Population and Description of Sample

A retrospective chart review was performed on patients who underwent elective THA or TKA between May 1, 2008 and May 1, 2018 at CAMC. The sample population was divided into two groups for comparison. Group one consisted of 100 patients who underwent THA or TKA that did not receive both celecoxib and pregabalin preoperatively or any other preoperative analgesics. Group two consisted of 100 patients who underwent THA or TKA that did receive pregabalin and celecoxib.

The sample was identified using codes for THA and TKA surgeries from both the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases 10th revision Procedure Coding System (ICD-10-PCS). The ICD-9-CM code for THA is 81.52. The ICD-9-CM code for TKA is 81.54. ICD-10 PCS codes for THA and TKA are listed in Appendix C.

Inclusion criteria:

1. Adult male or female 18 years of age or older
2. Patients who had an American Society of Anesthesiologist (ASA) physical classification I-IV

3. Patients who underwent THA or TKA
4. Patients who received both celecoxib and pregabalin preoperatively

Exclusion criteria:

1. Patients less than 18 years old
2. Patients with allergies to celecoxib or pregabalin
3. Patients who underwent emergent or traumatic THA or TKA
4. Patients who received opioids preoperatively
5. Patients who received spinal anesthesia
6. Patients who received pregabalin or celecoxib in a single dose preoperative and not in combination
7. Patient who received any other analgesics preoperatively
8. Patients who had an American Society of Anesthesiologist (ASA) physical classification V or VI

Procedures/Protocol

A retrospective chart review was performed on patients who underwent elective THA or TKA between May 1, 2008 and May 1, 2018 at CAMC. A sample size of 200 patients was utilized. Patient demographics and clinical information were collected and included: age, gender, body mass index (BMI), ASA classification, the preoperative administration of both celecoxib and pregabalin or lack of, intraoperative opioid consumption, and total opioid consumption while in the PACU. These variables were collected from the Electronic Medical Record (EMR), Medication Administration Record (MAR), PACU record and intraoperative anesthesia record. The primary independent variable was the preoperative administration of a combination of celecoxib and pregabalin. Secondary independent variables consisted of gender, age, BMI, and

ASA physical class scores. The dependent variables were total intraoperative and opioid consumption while in the PACU.

Patient age was calculated on day of surgery. Patient gender was defined as male or female. BMI was determined by extracting patients' height in centimeters (cm) and weight in kilograms (kg). BMI was calculated by dividing the patients weight in kg by their height squared in meters (CDC, 2018). ASA physical classification scores were collected, which is a grading tool used by anesthesia providers to classify a patient's health status. Class I includes healthy patients with no comorbities, Class II includes patients with mild systemic disease, Class III includes patients with severe noncapactitiating systemic disease, Class IV includes patients with incapacitiating systemic disease that threatens life, Class V is reserved for patients that are not expected to live without surgery, and Class VI consists of organ donating patients have been declared brain dead (American Society of Anesthesiologists, 2014). Opioid consumption was recorded from the EMR and anesthesia record and converted to morphine equivalents to permit a standard comparison among various opioids.

Data Collection and Instrumentation

Data was extracted from each patient's EMR and organized using a Microsoft Excel spreadsheet. The EMR for each patient was accessed and data was extracted from the MAR, preoperative evaluation, intraoperative anesthesia record, and PACU record. An anonymous number was assigned to each patient in Data Collection Tool 1 (Appendix A) to maintain confidentiality. Data Collection Tool 2 (Appendix B) was utilized to organize data that was collected and included age, gender, ASA classification, weight, BMI, celecoxib and pregabalin administration or the lack thereof, total intraoperative opioid consumption and total opioid consumption in the PACU.

Statistical Design and Analysis

The main purpose of this study was to determine if there was an association between a preoperative dose of celecoxib and pregabalin and decreased perioperative opioid consumption in patients who underwent THA or TKA. The primary independent variable was the preoperative administration of celecoxib and pregabalin. Secondary independent variables consisted of gender, age, BMI, and ASA physical class scores. The dependent variables consisted of intraoperative and PACU opioid consumption. Independent t-tests were performed to compare if statistical differences existed between age and BMI in the two groups. A chi-squared test was performed to determine if a statistical difference existed between gender and ASA between the two groups. Two step-wise linear regression was used to predict a statistical association between celecoxib and pregabalin administration, age, BMI, gender, ASA classification with intraoperative opioid consumption and opioid consumption in PACU. IBM SPSS statistical software was utilized to analyze data. A p-value of <.05 was considered statistically significant.

Ethical Considerations

This study was approved by the CAMC/West Virginia University Internal Review Board on June 12, 2018 (Appendix D).

RESULTS

Presentation, Analysis, and Interpretation of the Data

The study sample consisted of 200 patients aged 40-90 years of age who underwent THA or TKA at CAMC. The sample was divided into two groups. Group one consisted of 100 patients who underwent THA or TKA and did not receive celecoxib and pregabalin preoperatively or any other preoperative analgesics. Group two consisted of 100 patients who underwent THA or TKA and received a preoperative combination of celecoxib and pregabalin.

Independent t-tests were used to compare differences in mean age and BMI between the two groups. Mean BMI between the two group was not significantly different (p=>.05). The mean age difference between the two groups was statistically different p=.0001. The mean age for group one was 66.50 ± 9.8 years and the mean age for group two was 59.27 ± 8.6 years. Mean BMI for group one was 33.59 ± 7.09 (kg/m^2) and for group two was 32.68 ± 5.9 (kg/m^2). Chi-squared test was performed to compare gender and recoded ASA classification between the two groups. Gender between the two groups was not statistically different, (p>.05). Group one consisted of 55 females and 45 males, while group two consisted of 52 females and 48 males A significant difference existed between the two groups in terms of ASA classification p=.017 (p<.05). Group one had 20 ASA class 1-2 patients and 80 ASA class 3-4 patients. Group two had 35 ASA class 1-2 patients and 65 ASA class 3-4 patients. Each group consisted of 57 patients who underwent TKA and 43 patients who underwent THA, (Table 1).

Table 1: Demographics and Clinical Characteristics of Patients Who Underwent Total Hip or Knee Arthroplasty and Comparisons of Age, BMI, Gender, and ASA Class

Variable	Total Sample	Study Groups		Statistical Value
	Total N=100 Mean (SD)	Did not receive celecoxib and pregabalin N=100 (50%) Mean (SD)	Received celecoxib and pregabalin N=100 (50%) Mean (SD)	p-Value
Age (years)	32.7 (9.2)	66.50 (9.8)	59.27 (8.6)	.0001*
BMI (kg/m2)	33.12 (3.0)	33.59 (7.09)	32.68 (5.90)	(NS)
Gender (F/M) (N) Female Male	F = 107 M = 93	F = 55 M =45	F = 52 M = 48	(NS)

ASA 1-2 N (%) ASA 3-4 N (%)	55 (27.5%) 145 (72.5%)	20 (20%) 80 (80%)	35 (35%) 65 (65%)	.018*
THA TKA	114 (57%) 86 (43%)	57 (57%) 43 (43%)	57 (57%) 43 (43%)	NS

*Indicated significant value (p<.05), NS=Not Significant (p>.05), SD=Standard Deviation, BMI=Body Mass Index, ASA=American Society of Anesthesiologist physical status classification, F=female, M=male.

There was no statistical significance between the two groups when comparing mean intraoperative opioid consumption, (p>.05). Mean intraoperative opioid consumption was 22.56 ± 10.6 morphine equivalents for group 1 and 22.81 ± 9.8 morphine equivalents for group 2. A comparison of the two groups showed statistical significance between the two groups in mean PACU opioid consumption, p=.001. Group one received a mean of 3.59 ± 3.65 morphine equivalents and group two received a mean of 2.15 ± 2.56 morphine equivalents, (Table 2).

Table 2: Comparison of Intraoperative and PACU Opioid Consumption Between Group One and Group Two

Variable	Total Sample	Study Groups		Statistical Value
	Total Sample N=100 Mean (SD)	Did not receive celecoxib and pregabalin N=100 (50%) Mean (SD)	Received celecoxib and pregabalin N=100 (50%) Mean (SD)	p-Value
Intraoperative opioid administration (morphine equivalents)	23.2 (10.2)	22.8 (9.8)	23.6 (10.6)	(NS)
PACU opioid administration (morphine equivalents)	2.9 (2.6)	3.6 (3.7)	2.2 (2.6)	.001*

* Indicated significant value (p<.05), NS=Not significant (p>.05), SD=Standard Deviation, PACU = post-anesthesia care unit.

Linear regression was used to identify statistical association between mean intraoperative opioid consumption and the following independent variables: age, gender, BMI, recoded ASA class, and the preoperative administration of celecoxib and pregabalin or lack thereof. There was no statistical significance between mean intraoperative opioid consumption and BMI, ASA, or celecoxib/pregabalin administration or the lack thereof (p>.05). There was a statistical significance between intraoperative opioid consumption when considering age (p=.022) and gender (p=.025), (Table 3).

Table 3: Linear Regression Analysis Between Age, BMI, ASA, Celecoxib and Pregabalin Use, and Intraoperative Opioid Consumption in Patients Undergoing Total Hip or Knee Arthroplasty

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	31.723	7.394		4.291	.0001
	Age*	-.184	.080	-.179	-2.302	.022*
	Gender:*	3.199	1.414	.157	2.263	.025*
	BMI	.114	.113	.073	1.004	.317
	ASA	-2.403	1.617	-.106	-1.486	.139
	Celecoxib and Pregabalin	-9.32	1.529	-0.46	-.610	.543

*Indicated significant value (p<.05), NS=Not Significant (p>.05), SD=Standard Deviation, BMI=Body Mass Index, ASA=American Society of Anesthesiologist physical status classification, F=female, M=male, Y=yes N=no.

Linear regression was used to identify statistical association between PACU opioid consumption and the following independent variables: age, gender, BMI, recoded ASA class, and the preoperative administration of celecoxib and pregabalin or lack thereof. There was no statistical association between PACU opioid consumption and age, gender, ASA, and BMI.

There was a statistical significance between PACU opioid consumption and the administration of celecoxib or pregabalin or the lack thereof p=.002, (Table 4).

Table 4: Linear Regression Analysis Between Age, BMI, ASA, Celecoxib and Pregabalin Use, and PACU Opioid Consumption in Patients Undergoing Total Hip or Knee Arthroplasty

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	3.325	2.355		1.412	.160
	Age	-.020	.025	-.061	-.780	.437
	Gender:	.713	.450	.110	1.583	.115
	BMI	.023	.036	.046	.637	.525
	ASA	.622	.515	.086	1.207	.229
	Celebrex and Pregabalin	-1.499	.487	-.232	-3.079	.002*

*Indicated significant value (p<.05), NS=Not Significant (p>.05), SD=Standard Deviation, BMI=Body Mass Index, ASA=American Society of Anesthesiologist physical status classification, F=female, M=male, Y=yes N=no.

An independent t-test was used to compare gender with intraoperative and PACU opioids. There was no statistical association between total PACU opioids and gender. There was a statistical significance between total intraoperative opioids and gender (p=.21), (Table 5).

Table 5: Independent t-test Comparing Gender and Intraoperative and PACU Opioid Consumption

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
Total Intraoperative Opioids*	Equal variances assumed	198	.21*	3.3102
	Equal variances not assumed	194.592	.19	3.3102
Total PACU Opioids	Equal variances assumed	198	.588	.2494
	Equal variances not assumed	189.183	.578	.2494

* Indicated significant value (p<.05), NS=Not significant (p>.05), SD=Standard Deviation, PACU = post-anesthesia care unit

An independent t-test was conducted to assess if there was a statistical significance between males or females. In terms of intraoperative opioids, females received a mean 21.68 ± 10.14 morphine equivalents and males received a mean 24.92 ± 9.98 morphine equivalents. These finding were statistically significant p<.05, (Table 6).

Table 6: Independent T-Test Comparing Gender and Intraoperative Opioid Consumption in Patients Undergoing TKA or THA

	Gender: M=1, F = 0	N	Mean	Std. Deviation
Intraoperative Opioids (morphine equivalents)	F	107	21.68	10.1359
	M	93	24.920	9.9768

* Indicated significant value (p<.05), NS=Not significant (p>.05), SD=Standard Deviation, F=female, M=Male.

Independent t-tests were conducted to determine if there was a statistical significance between type of surgery (THA or TKA) and age. Mean age for patients undergoing TKA in the study was 63.96 ± 8.208 and for THA was 61.45 ± 11. 621.There was no statistical significance between type of surgery and age (p>.05), (Table 7).

Table 7: Independent T-Test Comparing Type of Surgery (TKA or THA) and Age

	Surgery: TKA/THA	N	Mean	Std. Deviation	Sig. (2-tailed)
Age (years)	TKA	114	63.96	8.208	.075
	THA	86	61.45	11.621	.075

Indicated significant value (p<.05), NS=Not significant (p>.05), SD=Standard Deviation, TKA=total knee arthroplasty, THA=total hip arthroplasty.

Further analysis was performed to determine if there was a statistical association between type of surgery and gender. There were 65 females and 49 males in the TKA group. There was

42 females and 44 males in the THA group. There was no statistical association between gender and type of surgery (p>.05), (Table 8).

Table 8: Chi-Square Test Comparing Type of Surgery (TKA or THA) and Gender

Gender: F or M	TKA	THA	Total	Sig. (2-tailed)
F	65	42	107	.251
M	49	44	93	.251

Indicated significant value (p<.05), NS=Not significant (p>.05), SD=Standard Deviation, TKA=total knee arthroplasty, THA=total hip arthroplasty.

DISCUSSION

Discussion of Study Results

The purpose of this study was to determine if an association could be made between a preoperative dose of celecoxib and pregabalin in patients undergoing THA or TKA and their intraoperative and PACU opioid consumption. The hypotheses predicted that patients who received a preoperative dose of both celecoxib and pregabalin would consume less opioids intraoperatively and postoperatively. The study revealed there was a statistical significance in terms of PACU opioid consumption between the two groups but no statistical difference in intraoperative opioid consumption. The group that did not receive celecoxib and pregabalin preoperatively (group one) received a mean difference of approximately 1.2 morphine equivalents more than group two.

Independent t-tests and chi-squared tests revealed that mean BMI and gender between the two groups was not statistically significantly different; however, ASA classification and age were statistically significantly different between the two groups. Group one, that did not receive celecoxib and pregabalin, had more patients with ASA 3-4 classifications and were older by a

mean of approximately 7 years. Therefore, based on previous research on this topic, it would be anticipated that group one would have required less opioids due to the mean age of this group being greater (Kanonidou & Karystianou, 2007). However, the results of this study showed that there was an increased amount of opioid consumption in group one which had older aged patients. This could be also be attributed to the increased number of ASA 3-4 class patients in this group. Further research is needed to determine if there are associations between higher ASA classifications and opioid consumption.

Independent t-tests showed that there was a statistical significance between intraoperative opioid consumption and age and gender. Further, independent t-tests revealed that females received less opioids intraoperatively, approximately 21.68 morphine equivalents compared to males receiving 24.9 morphine equivalents. This study is consistent with findings from a 2003 study in which the authors revealed that females are more sensitive than males to the effects of opioids; therefore, they require a lesser amount (Pleym, Spigset, Kharasch, & Dale, 2003).

Further analysis was conducted to examine the association between age and both intraoperative and PACU opioid consumption. Patients were assigned to two groups. Group A consisted of patients aged 40-64 years and group B consisted of patients aged 65-90 years. The analysis showed there was no statistical difference between the groups in terms of PACU opioid consumption. The analysis showed that the older aged group (group B) received approximately 3.3 morphine equivalents less than group A. The older aged group (group B) received a mean of 21.42 ± 11.22 morphine equivalents and the younger aged group (group A) received 24.725 ± 11.22 morphine equivalents. These results are in consensus with the previous research mentioned that found a decreased opioid need in older aged patients (Kanonidou & Karystianou, 2007).

A 2015 study revealed that patients who underwent THA were approximately 65 years old and those who underwent TKA were approximately 67 years old (Fang, Noiseux, Linson, & Cram, 2015). Additional analysis was conducted to determine if there was a statistical association between the type of surgery (TKA or THA) and age in the current study. The mean age for patients undergoing TKA in this study was 63.96 ± 8.208 and for THA was 61.45 ± 11. 621. While the results of the current study do not concur with the results of the previously mentioned study, there was no statistical significance between the two groups in terms of age and types of surgery ($p>.05$). There was also no significant association between type of surgery (THA or TKA) and gender, ($p>0.05$).

Study Limitations

There were numerous limitations to this research. Most influentially was the retrospective nature of the study which did not allow for total control of the variables. Retrospective cross-sectional studies have less control of variables than prospective studies; consequently, this type of study could not prove causation only association.

Numerous cofounding variables could have affected the results such as the administration of NSAIDs as well as the use of local anesthetics. The author was unable to control these variables or convert the doses of those medications into morphine equivalents. Another variable that may have affected the results is the type of surgery since both THA and TKA were included to allow for a larger sample size. Differences in personnel such as surgeons, anesthesia providers, and nursing staff may have influenced the total opioid consumption. Additionally, variations in charting between anesthesia providers and nursing staff could have affected the study. Additional prospective studies are needed in the future to compare the use of celecoxib

and pregabalin when administrated separately compared to when used in combination dose in total joint replacement surgery.

IMPLICATIONS AND RECOMMENDATIONS

The results of this study supported the use of preoperative celecoxib and pregabalin at reducing PACU opioid consumption. In the future, additional prospective, randomized studies are needed to compare the use of celecoxib and pregabalin independently versus in combination. In these studies, variables such as specific type of joint replacement surgery and perioperative administration of an NSAID and any local anesthetic use must be controlled.

CONCLUSION

In conclusion, this study found an association between the preoperative administration of celecoxib and pregabalin in patients undergoing THA or TKA and decreased PACU opioid consumption; however, no association was found between the preoperative administration of celecoxib and pregabalin and decreased intraoperative opioid consumption. The results of this study can improve patient outcomes in patients undergoing TKA or THA at CAMC or similar facilities where these procedures are performed.

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APPENDICES

Appendix A: Data Collection Tool 1

Patient Safety Number	Patient Identification Number
1	
2	
3	
4	
5	
…	
200	

Appendix B: Data Collection Tool 2

Study #	Age (years)	Gender (Male=1 Female=0)	ASA (I-IV)	Weight (kg)	BMI (kg/m^2)	Celecoxib and Pregabalin (Y=1, N=0)	Total Intraoperative Opioids (morphine equivalents)	Total PACU Opioids (morphine equivalents)
1								
2								
3								
4								
5								
…								
200								

Appendix C: ICD-10-PCS THA and TKA CODES

Code	Procedure
0SRB	Replacement of Left Hip Joint
0SRB0	Replacement of Left Hip Joint, Open Approach
0SRB019	Replacement of Left Hip Joint with Metal Synthetic Substitute, Cemented, Open Approach
0SRB01A	Replacement of Left Hip Joint with Metal Synthetic Substitute, Uncemented, Open Approach
0SRB01Z	Replacement of Left Hip Joint with Metal Synthetic Substitute, Open Approach
0SRB029	Replacement of Left Hip Joint with Metal on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SRB02A	Replacement of Left Hip Joint with Metal on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SRB02Z	Replacement of Left Hip Joint with Metal on Polyethylene Synthetic Substitute, Open Approach
0SRB039	Replacement of Left Hip Joint with Ceramic Synthetic Substitute, Cemented, Open Approach
0SRB03A	Replacement of Left Hip Joint with Ceramic Synthetic Substitute, Uncemented, Open Approach
0SRB03Z	Replacement of Left Hip Joint with Ceramic Synthetic Substitute, Open Approach
0SRB049	Replacement of Left Hip Joint with Ceramic on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SRB04A	Replacement of Left Hip Joint with Ceramic on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SRB04Z	Replacement of Left Hip Joint with Ceramic on Polyethylene Synthetic Substitute, Open Approach
0SRB069	Replacement of Left Hip Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Cemented, Open Approach

0SRB06A	Replacement of Left Hip Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SRB06Z	Replacement of Left Hip Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Open Approach
0SRB07Z	Replacement of Left Hip Joint with Autologous Tissue Substitute, Open Approach
0SRB0J9	Replacement of Left Hip Joint with Synthetic Substitute, Cemented, Open Approach
0SRB0JA	Replacement of Left Hip Joint with Synthetic Substitute, Uncemented, Open Approach
0SRB0JZ	Replacement of Left Hip Joint with Synthetic Substitute, Open Approach
0SRB0KZ	Replacement of Left Hip Joint with Nonautologous Tissue Substitute, Open Approach
0SR9	Replacement of Right Hip Joint
0SR90	Replacement of Right Hip Joint, Open Approach
0SR9019	Replacement of Right Hip Joint with Metal Synthetic Substitute, Cemented, Open Approach
0SR901A	Replacement of Right Hip Joint with Metal Synthetic Substitute, Uncemented, Open Approach
0SR901Z	Replacement of Right Hip Joint with Metal Synthetic Substitute, Open Approach
0SR9029	Replacement of Right Hip Joint with Metal on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SR902A	Replacement of Right Hip Joint with Metal on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SR902Z	Replacement of Right Hip Joint with Metal on Polyethylene Synthetic Substitute, Open Approach
0SR9039	Replacement of Right Hip Joint with Ceramic Synthetic Substitute, Cemented, Open Approach
0SR903A	Replacement of Right Hip Joint with Ceramic Synthetic Substitute, Uncemented, Open Approach

0SR903Z	Replacement of Right Hip Joint with Ceramic Synthetic Substitute, Open Approach
0SR9049	Replacement of Right Hip Joint with Ceramic on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SR904A	Replacement of Right Hip Joint with Ceramic on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SR904Z	Replacement of Right Hip Joint with Ceramic on Polyethylene Synthetic Substitute, Open Approach
0SR9069	Replacement of Right Hip Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SR906A	Replacement of Right Hip Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SR906Z	Replacement of Right Hip Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Open Approach
0SR907Z	Replacement of Right Hip Joint with Autologous Tissue Substitute, Open Approach
0SR90J9	Replacement of Right Hip Joint with Synthetic Substitute, Cemented, Open Approach
0SR90JA	Replacement of Right Hip Joint with Synthetic Substitute, Uncemented, Open Approach
0SR90JZ	Replacement of Right Hip Joint with Synthetic Substitute, Open Approach
0SR90KZ	Replacement of Right Hip Joint with Nonautologous Tissue Substitute, Open Approach
0SRE	Replacement of Left Hip Joint
0SRE0	Replacement of Left Hip Joint, Open Approach
0SRE009	Replacement of Left Hip Joint, Acetabular Surface with Polyethylene Synthetic Substitute, Cemented, Open Approach
0SRE00A	Replacement of Left Hip Joint, Acetabular Surface with Polyethylene Synthetic Substitute, Uncemented, Open Approach

0SRE00Z	Replacement of Left Hip Joint, Acetabular Surface with Polyethylene Synthetic Substitute, Open Approach
0SRE019	Replacement of Left Hip Joint, Acetabular Surface with Metal Synthetic Substitute, Cemented, Open Approach
0SRE01A	Replacement of Left Hip Joint, Acetabular Surface with Metal Synthetic Substitute, Uncemented, Open Approach
0SRE01Z	Replacement of Left Hip Joint, Acetabular Surface with Metal Synthetic Substitute, Open Approach
0SRE039	Replacement of Left Hip Joint, Acetabular Surface with Ceramic Synthetic Substitute, Cemented, Open Approach
0SRE03A	Replacement of Left Hip Joint, Acetabular Surface with Ceramic Synthetic Substitute, Uncemented, Open Approach
0SRE03Z	Replacement of Left Hip Joint, Acetabular Surface with Ceramic Synthetic Substitute, Open Approach
0SRE07Z	Replacement of Left Hip Joint, Acetabular Surface with Autologous Tissue Substitute, Open Approach
0SRE0J9	Replacement of Left Hip Joint, Acetabular Surface with Synthetic Substitute, Cemented, Open Approach
0SRE0JA	Replacement of Left Hip Joint, Acetabular Surface with Synthetic Substitute, Uncemented, Open Approach
0SRE0JZ	Replacement of Left Hip Joint, Acetabular Surface with Synthetic Substitute, Open Approach
0SRE0KZ	Replacement of Left Hip Joint, Acetabular Surface with Nonautologous Tissue Substitute, Open Approach
0SRA	Replacement of Right Hip Joint
0SRA0	Replacement of Right Hip Joint, Open Approach
0SRA009	Replacement of Right Hip Joint, Acetabular Surface with Polyethylene Synthetic Substitute, Cemented, Open Approach
0SRA00A	Replacement of Right Hip Joint, Acetabular Surface with Polyethylene Synthetic Substitute, Uncemented, Open Approach

0SRA00Z	Replacement of Right Hip Joint, Acetabular Surface with Polyethylene Synthetic Substitute, Open Approach
0SRA019	Replacement of Right Hip Joint, Acetabular Surface with Metal Synthetic Substitute, Cemented, Open Approach
0SRA01A	Replacement of Right Hip Joint, Acetabular Surface with Metal Synthetic Substitute, Uncemented, Open Approach
0SRA01Z	Replacement of Right Hip Joint, Acetabular Surface with Metal Synthetic Substitute, Open Approach
0SRA039	Replacement of Right Hip Joint, Acetabular Surface with Ceramic Synthetic Substitute, Cemented, Open Approach
0SRA03A	Replacement of Right Hip Joint, Acetabular Surface with Ceramic Synthetic Substitute, Uncemented, Open Approach
0SRA03Z	Replacement of Right Hip Joint, Acetabular Surface with Ceramic Synthetic Substitute, Open Approach
0SRA07Z	Replacement of Right Hip Joint, Acetabular Surface with Autologous Tissue Substitute, Open Approach
0SRA0J9	Replacement of Left Hip Joint, Acetabular Surface with Synthetic Substitute, Cemented, Open Approach
0SRA0JA	Replacement of Right Hip Joint, Acetabular Surface with Synthetic Substitute, Uncemented, Open Approach
0SRA0JZ	Replacement of Right Hip Joint, Acetabular Surface with Synthetic Substitute, Open Approach
0SRA0KZ	Replacement of Right Hip Joint, Acetabular Surface with Nonautologous Tissue Substitute, Open Approach
0SRS	Replacement of Left Hip Joint, Femoral Surface
0SRS0	Replacement of Left Hip Joint, Femoral Surface, Open Approach
0SRS019	Replacement of Left Hip Joint, Femoral Surface with Metal Synthetic Substitute, Cemented, Open Approach
0SRS01A	Replacement of Left Hip Joint, Femoral Surface with Metal Synthetic Substitute, Uncemented, Open Approach

0SRS01Z	Replacement of Left Hip Joint, Femoral Surface with Metal Synthetic Substitute, Open Approach
0SRS039	Replacement of Left Hip Joint, Femoral Surface with Ceramic Synthetic Substitute, Cemented, Open Approach
0SRS03A	Replacement of Left Hip Joint, Femoral Surface with Ceramic Synthetic Substitute, Uncemented, Open Approach
0SRS03Z	Replacement of Left Hip Joint, Femoral Surface with Ceramic Synthetic Substitute, Open Approach
0SRS07Z	Replacement of Left Hip Joint, Femoral Surface with Autologous Tissue Substitute, Open Approach
0SRS0J9	Replacement of Left Hip Joint, Femoral Surface with Synthetic Substitute, Cemented, Open Approach
0SRS0JA	Replacement of Left Hip Joint, Femoral Surface with Synthetic Substitute, Uncemented, Open Approach
0SRS0JZ	Replacement of Left Hip Joint, Femoral Surface with Synthetic Substitute, Open Approach
0SRS0KZ	Replacement of Left Hip Joint, Femoral Surface with Nonautologous Tissue Substitute, Open Approach
0SRR	Replacement of Right Hip Joint, Femoral Surface
0SRR0	Replacement of Right Hip Joint, Femoral Surface, Open Approach
0SRR019	Replacement of Right Hip Joint, Femoral Surface with Metal Synthetic Substitute, Cemented, Open Approach
0SRR01A	Replacement of Right Hip Joint, Femoral Surface with Metal Synthetic Substitute, Uncemented, Open Approach
0SRR01Z	Replacement of Right Hip Joint, Femoral Surface with Metal Synthetic Substitute, Open Approach
0SRR039	Replacement of Right Hip Joint, Femoral Surface with Ceramic Synthetic Substitute, Cemented, Open Approach
0SRR03A	Replacement of Right Hip Joint, Femoral Surface with Ceramic Synthetic Substitute, Uncemented, Open Approach

0SRR03Z	Replacement of Right Hip Joint, Femoral Surface with Ceramic Synthetic Substitute, Open Approach
0SRR07Z	Replacement of Right Hip Joint, Femoral Surface with Autologous Tissue Substitute, Open Approach
0SRR0J9	Replacement of Right Hip Joint, Femoral Surface with Synthetic Substitute, Cemented, Open Approach
0SRR0JA	Replacement of Right Hip Joint, Femoral Surface with Synthetic Substitute, Uncemented, Open Approach
0SRR0JZ	Replacement of Right Hip Joint, Femoral Surface with Synthetic Substitute, Open Approach
0SRR0KZ	Replacement of Right Hip Joint, Femoral Surface with Nonautologous Tissue Substitute, Open Approach
0SRD	Replacement of Left Knee Joint
0SRD0	Replacement of Left Knee Joint, Open Approach
0SRD069	Replacement of Left Knee Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SRD06A	Replacement of Left Knee Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SRD06Z	Replacement of Left Knee Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Open Approach
0SRD07Z	Replacement of Left Knee Joint with Autologous Tissue Substitute, Open Approach
0SRD0J9	Replacement of Left Knee Joint with Synthetic Substitute, Cemented, Open Approach
0SRD0JA	Replacement of Left Knee Joint with Synthetic Substitute, Uncemented, Open Approach
0SRD0JZ	Replacement of Left Knee Joint with Synthetic Substitute, Open Approach
0SRD0KZ	Replacement of Left Knee Joint with Nonautologous Tissue Substitute, Open Approach)

0SRD0L9	Replacement of Left Knee Joint with Unicondylar Synthetic Substitute, Cemented, Open Approach
0SRD0LA	Replacement of Left Knee Joint with Unicondylar Synthetic Substitute, Uncemented, Open Approach
0SRD0LZ	Replacement of Left Knee Joint with Unicondylar Synthetic Substitute, Open Approach
0SRC	Replacement of Right Knee Joint
0SRC0	Replacement of Right Knee Joint, Open Approach
0SRC069	Replacement of Right Knee Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Cemented, Open Approach
0SRC06A	Replacement of Right Knee Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Uncemented, Open Approach
0SRC06Z	Replacement of Right Knee Joint with Oxidized Zirconium on Polyethylene Synthetic Substitute, Open Approach
0SRC07Z	Replacement of Right Knee Joint with Autologous Tissue Substitute, Open Approach
0SRC0J9	Replacement of Right Knee Joint with Synthetic Substitute, Cemented, Open Approach
0SRC0JA	Replacement of Right Knee Joint with Synthetic Substitute, Uncemented, Open Approach
0SRC0JZ	Replacement of Right Knee Joint with Synthetic Substitute, Open Approach
0SRC0KZ	Replacement of Right Knee Joint with Nonautologous Tissue Substitute, Open Approach)
0SRC0L9	Replacement of Right Knee Joint with Unicondylar Synthetic Substitute, Cemented, Open Approach
0SRC0LA	Replacement of Right Knee Joint with Unicondylar Synthetic Substitute, Uncemented, Open Approach

0SRC0LZ	Replacement of Right Knee Joint with Unicondylar Synthetic Substitute, Open Approach
0SRU	Replacement of Left Knee Joint, Femoral Surface
0SRU0	Replacement of Left Knee Joint, Femoral Surface, Open Approach
0SRU07Z	Replacement of Left Knee Joint, Femoral Surface with Autologous Tissue Substitute, Open Approach
0SRU0J9	Replacement of Left Knee Joint, Femoral Surface with Synthetic Substitute, Cemented, Open Approach
0SRU0JA	Replacement of Left Knee Joint, Femoral Surface with Synthetic Substitute, Uncemented, Open Approach
0SRU0JZ	Replacement of Left Knee Joint, Femoral Surface with Synthetic Substitute, Open Approach
0SRU0KZ	Replacement of Left Knee Joint, Femoral Surface with Nonautologous Tissue Substitute, Open Approach
0SRT	Replacement of Right Knee Joint, Femoral Surface
0SRT0	Replacement of Right Knee Joint, Femoral Surface, Open Approach
0SRT07Z	Replacement of Right Knee Joint, Femoral Surface with Autologous Tissue Substitute, Open Approach
0SRT0J9	Replacement of Right Knee Joint, Femoral Surface with Synthetic Substitute, Cemented, Open Approach
0SRT0JA	Replacement of Right Knee Joint, Femoral Surface with Synthetic Substitute, Uncemented, Open Approach
0SRT0JZ	Replacement of Right Knee Joint, Femoral Surface with Synthetic Substitute, Open Approach
0SRT0KZ	Replacement of Right Knee Joint, Femoral Surface with Nonautologous Tissue Substitute, Open Approach
0SRW	Replacement of Left Knee Joint, Tibial Surface

0SRW0	Replacement of Left Knee Joint, Tibial Surface, Open Approach
0SRW07Z	Replacement of Left Knee Joint, Tibial Surface with Autologous Tissue Substitute, Open Approach
0SRW0J9	Replacement of Left Knee Joint, Tibial Surface with Synthetic Substitute, Cemented, Open Approach
0SRW0JA	Replacement of Left Knee Joint, Tibial Surface with Synthetic Substitute, Uncemented, Open Approach
0SRW0JZ	Replacement of Left Knee Joint, Tibial Surface with Synthetic Substitute, Open Approach
0SRW0KZ	Replacement of Left Knee Joint, Tibial Surface with Nonautologous Tissue Substitute, Open Approach
0SRV	Replacement of Right Knee Joint, Tibial Surface
0SRV0	Replacement of Right Knee Joint, Tibial Surface, Open Approach
0SRV07Z	Replacement of Right Knee Joint, Tibial Surface with Autologous Tissue Substitute, Open Approach
0SRV0J9	Replacement of Right Knee Joint, Tibial Surface with Synthetic Substitute, Cemented, Open Approach
0SRV0JA	Replacement of Right Knee Joint, Tibial Surface with Synthetic Substitute, Uncemented, Open Approach
0SRV0JZ	Replacement of Right Knee Joint, Tibial Surface with Synthetic Substitute, Open Approach
0SRV0KZ	Replacement of Right Knee Joint, Tibial Surface with Nonautologous Tissue Substitute, Open Approach

Appendix D: IRB Approval Letter

New study by expedited review: Approved

CAMC INSTITUTE
RESEARCH AND GRANTS ADMINISTRATION

June 12, 2018

Mike Frame, DMP, APRN, CRNA
3110 MacCorkle Avenue S.E.
Room 2040
Charleston, WV 25304

RE: Initial Review Submission Packet 06/07/2018 08:29:31 AM EDT regarding study number 18-450 IS PREOPERATIVE ADMINISTRATION OF CELECOXIB AND PREGABALIN ASSOCIATED WITH DECREASED POSTOPERATIVE PAIN SCORES AND PERIOPERATIVE OPIOID CONSUMPTION IN PATIENTS UNDERGOING TOTAL HIP OR KNEE ARTHROPLASTY?

Initial Approval Date: 06/12/2018 **Expiration Date: 06/11/2019**

Dear Dr. Frame:

Your request for expedited approval of the new study listed above has been reviewed. This type of study qualifies for expedited review under FDA and DHHS (OHRP) regulations.

This is to confirm that your application is approved. The following items are approved:

Submission Components			
Form Name	Version	Outcome	
Study Document			
Title	Version #	Version Date	Outcome
Threadway COI	Version 1.0	06/06/2018	Approved
Frame COI	Version 1.0	06/06/2018	Approved
IRB Protocol_CierraTreadway FINAL	Version 1.0	05/30/2018	Approved

The accrual goal is 200. You must submit a request to the IRB to increase enrollment beyond the approved accrual goal.

You are granted permission to conduct your study as described effective immediately. If any study related activites are to continue beyond the expiration date, a renewal application must be submitted to the IRB and approved before the expiration date. It is your responsibility to submit your protocol for continuing renewal. The study is subject to continuing review on or before **06/11/2019,** unless closed

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before that date.

Please note that any changes to the study as approved must be promptly reported and approved prior to implementation. Some changes may be approved by expedited review; others require full board review.

Also, serious and/or unanticipated adverse events must also be reported as required by law and in accordance with CAMC/WVU Charleston Division IRB policies. Contact CAMC / WVU Charleston Division IRB at (304) 388-9973 or email michael.whitler@camc.org or april.white@camc.org if you have any questions or require further information.

Sincerely,

Chris Terpening, PhD, PharmD
Chair, CAMC/WVU IRB