Marian University

Leighton School of Nursing

Doctor of Nursing Practice

Final Project Report for Students Graduating in May 2023

Preoperative Pain Management for Laparoscopic Cholecystectomy to Decrease Immediate Postoperative Pain and Opioid Consumption

Valine C. Nnoruo and Bessem Enoweyere

Chair: Dr. Bradley Stelflug

(Signature)

Project Team Members: Reed Stockman CRNA

(Signature)

Diana Madsen

(Signature)

Date of Submission: November 28, 2022

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Abstract

Inadequate pain management during a laparoscopic cholecystectomy can affect postoperative hemodynamics, impair recovery, and extend hospital stay. The use of opioid medications during and after surgeries can reduce postoperative pain, however, the complications of opioid use such as nausea, vomiting, respiratory depression with the associated cardiovascular implications, and pneumonia can also impair recovery from surgery, cause postoperative discomfort, prolong hospital stay and could potentially cause opioid abuse in some patient population with surgical exposure. Numerous studies have reported the crucial role of administering preoperative or intraoperative non-opioid medications to mitigate postoperative pain. The purpose of this project is to utilize preoperative non-opioid multimodal analgesics to manage postoperative pain and reduce intraoperative and postoperative opioid use. Eight patients were studied in this project to determine the efficacy of preoperative acetaminophen, in combination with gabapentin and ibuprofen to reduce post-operative pain perception and post-operative rescue opioid administration. The study determined that preoperative pain medications, intraoperative pain medications, duration of surgery, gender and age can all influence postoperative pain. Also, among the participants who perceived pain after surgery despite receiving preoperative treatment, pain was more significant among females compared to males, and pain rating was highest within the first 15 minutes and reduced as time progressed. Further studies need to include more variables such as comorbidities, and ethnic differences in how they affect postoperative pain. Also, more studies are needed to ascertain the best combination of preoperative non-opioid treatment regimen that can maximally reduce intraoperative and postoperative pain and opioid use.

Preoperative Pain Management in Laparoscopic Cholecystectomy to Decrease Immediate Postoperative Pain and Opioid Consumption

This project is submitted to the faculty of Marian University Leighton School of Nursing as partial fulfillment of degree requirements for the Doctor of Nursing Practice, Nurse Anesthesiology track. In more than 80% of surgical procedures done today, postoperative pain is inadequately treated with 71% of patients reporting moderate to severe pain (Apfelbaum et al., 2003). Although pain after surgery is a predictable part of the surgical experience, inadequate pain management may lead to profound implications with increasing clinical and surgical stress, morbidity, mortality, and a decrease in the quality of life (Apfelbaum et al., 2003). Also, ineffective postoperative pain management has shown to cause negative clinical outcomes like pulmonary embolism, deep vein thrombosis (DVT), coronary artery ischemia, myocardial infarction (MI), delayed wound healing, pneumonia, demoralization, and insomnia. Effective pain relief and prevention improves clinical outcomes, avoids clinical complications, saves healthcare resources, and improves quality of life for the patient. According to the Joint Commission on Accreditation of Healthcare Organizations, pain management must become part of all patient care activities (Apfelbaum et al., 2003). Due to the advancement in technology and the discovery of new medications, providers are required to stay current and incorporate in their practice new ways to manage and control the patient's pain (Young et al., 2006). The purpose of this project is to evaluate the effectiveness of administering multimodal non-opioid medications (Tylenol, Gabapentin, and Ibuprofen) in the preoperative area to decrease pain and reduce the amount of opioid administered in the immediate post-anesthesia care unit (PACU) after a laparoscopic cholecystectomy (LC). Adequate pain management and limited opioid use not only improve recovery but are also associated with improved patient's satisfaction and comfort.

Background and Problem Statement

Pain has become the primary concern after surgery for most patients as nociceptors are stimulated. Inflammation from injury to the nerve stimulates the buildup of prostanoids at the site of surgery. Numerous signal pathways augment nociceptive sensitivity distal to the site of the injury, which is referred to as peripheral sensitization. Peripheral sensitization causes hyperalgesia and allodynia (Lou & Min, 2017). When a painful stimulus is prolonged, the dorsal horn acts as the site of central sensitization because of repetitive nociceptive stimulation. The brainstem contributes to central sensitization by decreasing inhibitory modulation. A combination of central and peripheral sensitization causes hypersensitivity in the postoperative period due to the increased excitability of spinal nerves and decreased pain threshold in peripheral pain receptors (Lou & Min, 2017). According to Morgan and Mikhail (2008), pain may resolve quickly after the stimulus is removed or it can persist for a long time even after the stimulus is removed. The mainstay of surgical pain management is with opioid analgesics, but they have been shown to cause numerous side effects like nausea, vomiting, pruritus, urinary retention, and respiratory depression.

This project is to evaluate the use of multimodal pain management techniques and to assure patients of the importance of decreased opioid consumption which is beneficial to their health. Apfelbaum et al. (2003) explained that there is an increasing number of ambulatory surgeries done today and decreasing the number of narcotics administered significantly improves the outcome and satisfaction of patients undergoing laparoscopic cholecystectomy. This minimizes opioid related side effects like decreased alertness, hypoventilation, and nausea.

Laparoscopic procedures are the most common surgical procedures in the world, and LC is the prevailing surgical procedure for gallbladder disease. Due to its minimal nature, it has the

advantage of minor pain, short length of hospital stays, minor trauma, and it is better tolerated compared to non-laparoscopic approaches. There are two kinds of laparoscopic surgeries: elective laparoscopic surgery performed as a same-day surgery, or emergency laparoscopic surgery which could be done for acute cholecystitis. The latter can result in prolonged hospital stay averaging about 4.5 days and results in more postoperative complications than the elective.

Several factors contribute to the development of visceral pain following laparoscopic cholecystectomy. Some of these factors include phrenic nerve irritation resulting from pneumoperitoneum, port-size incisions, abdominal distension, trauma associated with gallbladder removal, and the sociocultural status of the patient (Karaca et al., 2019). Inadequate pain control can result in undesirable outcomes if left untreated. Most patients are admitted to PACU after their surgical procedure, and inadequate pain control in this setting can delay recovery (Luo & Min, 2017). About 41% of patients in the PACU report pain from the surgery and emergence from anesthesia, which end up affecting multiple organ systems (Lou & Min, 2017). As stated above, postoperative pain can cause serious side effects or problems due to either insufficient treatment or excessive use of opioid medications to reduce the pain. Complications could lead to cardiac, pulmonary, immune system, and thromboembolic dysfunction. More so, excessive sedation due to increased narcotic use can increase length of stay and impair quality of life. In cases like LC, adequate analgesia can be challenging after a painful stimulus due to hypersensitive receptors and central nervous system hyperexcitability (Karaca et al., 2017).

Approaches which focus on the preoperative period, also known as “preemptive analgesia,” aim to decrease postoperative pain by decreasing the sensitivity of afferent pain receptor neurotransmitters caused by surgical stimulus, and by attenuating the effects of pain

throughout surgery (Karaca et al., 2017). In preemptive analgesia, an analgesic is administered before tissue injury during surgery for better pain relief compared to when an analgesic is administered after the painful stimulus has occurred (Hariharan et al., 2009). Measures to antagonize the nociceptive signals before injury have been shown to prevent central hypersensitization, therefore reducing the intensity of pain after the injury. Medications like Tylenol, Gabapentin and Ibuprofen have been found useful in decreasing the need for postoperative analgesic when given in the preoperative area. Tylenol works on the central nervous system (CNS) by inhibiting prostaglandins via the cyclooxygenase pathway. Gabapentin inhibits gamma-aminobutyric acid (GABA) by preventing the release of neurotransmitters like glutamate, substance P, and noradrenaline that can promote pain transmission. Gabapentin is also effective at treating neuropathic pain. Ibuprofen is a nonsteroid analgesic which has anti-inflammatory, antipyretic and analgesic effects. Though these medications are used routinely, combining them provides an additive or synergistic analgesia (Thybo et al., 2019).

The use of multimodal pain management techniques has demonstrated an improvement in pain control when the patient is in the postoperative area (Hariharan et al., 2009). The fear of pain is significant prior to a surgical experience (Mumm, 2010). Tylenol, Gabapentin, and Ibuprofen may help reduce the intensity of pain, thereby improving the overall satisfaction level and the surgical experience. This project will evaluate outcomes of patients related to pain control after LC.

Needs Assessment and Gap Analysis

The purpose of this project is to facilitate change in the clinical setting as it relates to pain control after laparoscopic gallbladder surgery. To facilitate the effective use of the non-opioids stated above, an understanding of the timing of their administration and action on pain

receptors will help in their preemptive analgesic role. Applying this same concept in reducing postoperative nausea and vomiting (PONV) has proven to be successful. It is believed that when a receptor site for PONV is blocked before a response to nauseous stimuli, it helps to reduce the incidence of nausea and vomiting. At a midwestern hospital in Indiana, a multimodal approach in treating pain preoperatively has not been introduced as an additional approach to pain management and opioid reduction strategy. Though there have been multiple approaches used in the past in treating postoperative pain, this project will focus on evaluating the effectiveness of routine use of Tylenol, Gabapentin and Ibuprofen when given preoperatively to decrease pain opioid consumption in the immediate postoperative period.

Review of Literature

Multimodal approaches to pain management are used to decrease the need for opioid consumption in the intraoperative state and postoperative setting. Acetaminophen, also known as Tylenol, Gabapentin, and Ibuprofen are not concurrently used preoperatively at this midwestern hospital in the state of Indiana. The purpose of this project is to decrease postoperative pain and opioid consumption by administrating Acetaminophen, Gabapentin, and Ibuprofen in the preoperative period before laparoscopic surgery.

Methods

Articles used for this literature review were focused on preemptive or preoperative use of acetaminophen, gabapentin, or ibuprofen for management of post-operative pain in patients undergoing laparoscopic cholecystectomy. The databases searched were Cochrane Library, Ovid MEDLINE, and Google Scholar. The keywords utilized were *laparoscopic cholecystectomy, ibuprofen, gabapentin, acetaminophen, paracetamol, preemptive analgesia, preoperative, premedication, NSAID, and multimodal.* BOOLEAN phrases constructed from the keywords that

were used for these searches include laparoscopic cholecystectomy AND acetaminophen AND preemptive analgesia, laparoscopic cholecystectomy AND acetaminophen AND preoperative, laparoscopic cholecystectomy AND acetaminophen AND premedication, laparoscopic cholecystectomy AND acetaminophen AND multimodal, laparoscopic cholecystectomy AND paracetamol AND preemptive analgesia, laparoscopic cholecystectomy AND paracetamol AND preoperative, laparoscopic cholecystectomy AND paracetamol AND premedication, laparoscopic cholecystectomy AND paracetamol AND multimodal, laparoscopic cholecystectomy AND ibuprofen AND preemptive analgesia, laparoscopic cholecystectomy AND ibuprofen AND preoperative, laparoscopic cholecystectomy AND ibuprofen AND premedication, laparoscopic cholecystectomy AND ibuprofen AND multimodal, laparoscopic cholecystectomy AND gabapentin AND preemptive analgesia, laparoscopic cholecystectomy AND gabapentin AND preoperative, laparoscopic cholecystectomy AND gabapentin AND premedication, laparoscopic cholecystectomy AND gabapentin AND multimodal. These searches were conducted from November 2021 to December 2021.

A total of eleven thousand and fifty-nine articles were found relating to one or more components of this topic. However, 11,039 of these articles were eliminated for not meeting the stipulated inclusion criteria. The inclusion criteria included primary sources and systematic reviewed articles from 2008 to 2021. The reason the literature search went back 13 years is due to the limited number of relevant literatures on this topic within the last decade. Other inclusion criteria are adult patients undergoing laparoscopic cholecystectomy, articles written in English language, and those specifically written about preemptive or preoperative acetaminophen, gabapentin, and ibuprofen (See *Appendix A* for the PRISMA Flow Diagram).

The exclusion criteria are studies done beyond the last 13 years, non-laparoscopic cholecystectomies, and those evaluating medications or preoperative treatment modalities other than the ones being evaluated in this review. After applying the criteria for inclusion, 20 articles were selected for this literature review.

Findings

A considerable number of studies have been done to provide best evidence with the use of these medications in the preoperative phase to manage postoperative pain. 20 articles were reviewed, seven of these articles were focused on acetaminophen (Ekinci et al., 2019; Johnson et al., 2019; Kamali, et al., 2018; Medina et al., 2017; Salihoglu et al., 2009; Sami Mebazaa et al., 2008; Toleska & Dimitrovski, 2019), five of the studies investigated the efficacy of ibuprofen (Ahiskalioglu et al., 2017; Ekinci et al., 2019; Gurusamy et al., 2010; Kamali et al., 2016; Karaca et al., 2019), and nine studies were focused on gabapentin (Abbas & Bashir, 2009; Gilron et al., 2009; Hosseini et al., 2015; Karri et al., 2021; Kochlar et al., 2017; Kotsovolis et al., 2015; Mishra et al., 2016; Nakhli et al., 2018; Srivastava et al., 2010).

Acetaminophen

Multimodal approaches to perioperative pain management are becoming more popular due to the need to reduce opioid use with their associated adverse effects. Acetaminophen has been extensively studied as one of the most favored multimodal approaches to pain management. Acetaminophen, also known as Tylenol or Paracetamol is a derivative of p-aminophenol with analgesic and antipyretic properties. Although the exact mechanism of action is not completely understood, acetaminophen likely inhibits the nitric oxide (NO) pathway for pain generation and transmission through the central and peripheral nervous system. This pathway is mediated through Substance P and N-methyl-D-aspartate (NMDA) receptors leading to increased pain

threshold. The antipyretic effect may result from inhibition of prostaglandin synthesis and release in the central nervous system (CNS) and prostaglandin-mediated effects on the heat-regulating center in the anterior hypothalamus (National Center for Biotechnology Information, 2021).

Acetaminophen is the most common analgesic. It is recommended by the World Health Organization (WHO) as first-line therapy in pain management (National Center for Biotechnology Information, 2021). In addition, its significance in perioperative pain management has been used to improve clinical practice. For the perioperative period, numerous studies have investigated its efficacy in the management of post-operative pain after a laparoscopic cholecystectomy and the role of acetaminophen in multimodal and opioid sparing analgesia when administered preoperatively. Some of the studies compared acetaminophen with nonsteroidal anti-inflammatory drugs (NSAIDs) such as ketorolac, celecoxib, and ibuprofen (Medina et al., 2017; Sami Mebazaa et al., 2008, Ekinci et al, 2019). Despite the variability in the pain scores between acetaminophen and the NSAIDs (ketorolac, celecoxib, and ibuprofen), preoperative administration of acetaminophen reduced postoperative analgesia following laparoscopic cholecystectomy. Additionally, when compared to an alpha- 2 agonist dexmedetomidine, postoperative pain scores were significantly less among the patients who received preemptive acetaminophen. Also, duration of analgesia among this group was longer with a lower postoperative opioid use compared to the group that received dexmedetomidine (Kamali, et al., 2018).

Other supporting studies investigated the efficacy of preoperative acetaminophen in reducing intraoperative and postoperative opioid use (Toleska & Dimitrovski, 2019; Salihoglu et al., 2009). It was found that premedication with acetaminophen (paracetamol) can provide opioid

free analgesia and reduce postoperative opioid use. Most research utilized preoperative intravenous (IV) acetaminophen for this surgical procedure, while some others administered oral acetaminophen to the participants. The common dosage is 1 gram (1000 mg), and both routes of administration reduced postoperative pain scores with no significant difference between the two routes (Johnson et al.,2019).

Ibuprofen

There are limited available studies involving the use of IV ibuprofen in decreasing postoperative opioid consumption, but the available few have shown that ibuprofen plays a beneficial role in the treatment of postoperative pain (Ahiskalioglu et al., 2017). Ibuprofen is a popular over the counter analgesic, antipyretic, and anti-inflammatory drug that has been used for over 40 years in the United States (US). Ibuprofen causes a reversible competitive inhibition of cyclooxygenase-1 (COX - 1), and COX-2 isoenzymes. It is the COX-2 inhibition effect that is responsible for the analgesic, antipyretic and anti-inflammatory responses that occur when it is administered (Ahiskalioglu et al., 2017).

In a randomized double-blind study, 60 patients were selected and divided into two groups. The first group was administered 400mg of IV ibuprofen in 100 milliliters(mL) of saline preemptively, and the control group received 100 mL of saline 30 minutes before surgery (Ahiskalioghu et al., 2017). In another randomized double-blind study, Kamali et al. (2016), divided 55 patients into two groups. The experimental group, comprising of 28 patients received 800mg of ibuprofen within 10 minutes of anesthesia induction, and the control group made of 27 patients received 250 mL bag as a placebo. In another study, the efficacy of ibuprofen was compared with pregabalin. In this study, 58 patients were divided into two groups: Group P and Group PI, each group comprising of 29 patients. The former group received 150mg of

pregabalin, while the latter received the same dose of pregabalin in addition to 400mg of Ibuprofen before surgery (Karaca et al., 2019). In the three studies above, the Visual Analog Scale (VAS) and 40-item Quality of Recovery questionnaire were used to assess pain scores after LC. The studies showed that the preemptive use of IV ibuprofen in LC reduced postoperative opioid consumptions in the first 24 hours. The study conducted by Ahiskalioglu et al. (2017) showed that there was a 45% decrease in opioid consumption while the other two showed that there was significant decline in pain and discomfort in the patients who received IV ibuprofen.

In another study, Ekinci et al. (2019) evaluated and compared the influence of IV forms of Ibuprofen and acetaminophen on pain management and opioid consumption on patients undergoing LC surgery. The VAS score was used to evaluate opioid use and pain intensity in the postoperative period. Pain scores in both the ibuprofen and acetaminophen groups at all time periods were shown to be lower than those in group C who received neither medication. Those patients in group C had a significant increase in opioid consumption than those in the other groups. The result showed that IV ibuprofen reduced pain scores and opioid use more than acetaminophen in the postoperative period after LC surgery. Furthermore, Gurusamy et al. (2010) evaluated pharmacological intervention for prevention and treatment of postoperative pain in patients undergoing LC. Non-steroidal anti-inflammatory drugs like Ibuprofen was one of the pharmacological adjuncts used in the preoperative settings in decreasing the inflammatory response and peripheral nociception. Gabapentin was also used as a multimodal approach to analgesia.

Gabapentin

Gabapentin is a structural analogue of gamma aminobutyric acid (GABA) which was introduced in 1993 as an adjunct for treating partial seizures. For decades now it has been used in

treating chronic neuropathic pain conditions (Srivastava et al., 2010). Recently, numerous studies have demonstrated a beneficial effect of gabapentin on postoperative opioid reduction and pain scores in a variety of procedures including LC (Srivastava et al., 2010). It works by having a high affinity for binding sites throughout the brain in the presence of voltage gated calcium channels which inhibits the release of excitatory neurotransmitters in the presynaptic area.

Mishra et al. (2016) did a comparative study to evaluate postoperative analgesic benefit and efficacy in patients administered oral gabapentin or pregabalin as premedication for LC. In this study, 90 patients were placed into three groups A, B and C. Group A received vitamin B complex, group B received 900mg gabapentin each, and group C received 150mg pregabalin. All medications were given one hour prior to induction of anesthesia. The VAS was used to measure postoperative pain scores, total analgesic requirements, and side effects. Patients in groups B and C had lower VAS scores, prolonged timing of first rescue analgesic and less opioid consumption compared to group A.

Kotsovolis et al., (2014) conducted a study to test whether the combination of gabapentin 600mg, ketamine 0.3mg/kg, lornoxicam 8mg and local ropivacaine 5ml 7.5% which is to be used at the insertion sites to provide superior analgesia in the first 24 hours after LC. This was a randomized controlled study done with a sample size of forty-eight patients assigned to 6 groups consisting of 28 patients each. Although the findings showed that gabapentin reduced postoperative pain, the combination of gabapentin, ketamine, lernoxicam and local ropivacaine was shown not to have a better analgesic action after LC, however, the incident of postoperative nausea and vomiting was reduced with this combination.

In a randomized double blind control trial, Gilron et al, (2009) examined the preoperative effectiveness of gabapentin, and meloxicam in decreasing pain during the postoperative period.

Postoperative pain intensity at rest and with movement was assessed using the numerical pain rating scale (NPRS). Based on the NPRS, the intensity of pain at rest was significantly lower with gabapentin alone versus meloxicam alone. There was a small difference in pain when a combination of meloxicam and gabapentin was used.

Karri et al. (2021) in their randomized double-blind study found that patients who received 600mg of gabapentin before surgery had a lower numerical rating scale (NRS) scores at 15 minutes and 1 hour postoperatively when compared to memantine. Gabapentin was a preferable adjuvant analgesic for LC compared to memantine when given as a single preoperative dose.

Srivastava et al. (2010) evaluated the efficacy of a single dose of 600mg gabapentin given preoperatively for reducing postoperative pain and opioid consumption after a mini-lap open cholecystectomy. 120 patients were randomly selected with the gabapentin group receiving 600mg and the controlled group receiving an identical looking capsule 2 hours before surgery. The Visual Analog Scale (VAS) measured that pain at rest and during movement was less in the gabapentin group than the placebo group. The number of opioids used in the first 24 hours after surgery was very low in the patients who received gabapentin compared to the placebo group.

Abbas & Bashir (2019) evaluated how effective a preoperative use of gabapentin can be in reducing postoperative pain after LC. The VAS was used to measure pain after surgery with 0 being no pain and 10 being the worst imaginable pain. The result showed that 600mg of gabapentin was effective in reducing pain and analgesic use after LC. Abbas & Bashir (2019) found gabapentin to be a safe and well tolerated treatment modality allowing for fast postoperative recovery in patients following LC.

Hosseini et al. (2015) evaluated if melatonin, clonidine, and gabapentin can reduce postoperative pain in patients undergoing LC. Pain intensity was measured using the VAS criteria for the first postoperative 24 hours. The highest score was noted in the placebo group while the intervention groups had less pain. Opioid consumption was also increased in the placebo group compared to the intervention group. The intensity of pain was significantly decreased, and pain reduction trend was different between the groups. In the different time periods, pain score was lowest with clonidine.

One of the side effects after LC is postoperative pain which can be around the scapular. Although the mechanism is multifactorial, the prevailing theory is the presence of persistent carbon dioxide in the right diaphragm and hepatic dome (Nakhli et al., 2018). Gabapentin and pregabalin belong to the gabapentinoid family. In a study carried out by Nakhli et al. (2018), 90 patients undergoing LC were enrolled and divided into 3 groups of 30: a gabapentin group, a pregabalin group and the control group. The VAS was used to assess postoperative pain ranging from 0 to 10. The incidence of shoulder pain was significantly less in the gabapentinoids group compared to the control, and no significant difference was found in the intensity of postoperative shoulder pain between the two gabapentinoid drugs. Therefore, preemptive gabapentin or pregabalin can effectively reduce pain intensity and improve ambulatory practices after LC (Nakhli et al., 2018).

Discussion

In this review, the efficacies of preoperative acetaminophen, gabapentin and ibuprofen were investigated to determine their ability to reduce postoperative pain and opioid consumption following a laparoscopic cholecystectomy. When used preoperatively, the studies reviewed show that acetaminophen 1g (1000 mg) can decrease postoperative pain score and reduce

postoperative opioid use. Ibuprofen as a potent NSAID also significantly reduced postoperative pain and opioid use following a laparoscopic cholecystectomy. Aside from producing favorable results in the outcomes mentioned, gabapentin as a single regime or in combination with other drugs also decreases postoperative nausea and vomiting (PONV), which is an added benefit to this medication (Nakhli et al., 2018; Abbas, & Bashir, 2019; Srivastava et al., 2010; Gilron et al., 2009; Kotsovolis et al., 2015). Same positive results were extrapolated for Ibuprofen. Premedication with PO or IV ibuprofen was associated with reduced stress response and inflammation, decreased postoperative pain and opioids used after LC (Karaca et al., 2019; Ahiskalioglu et al., 2017; Kamali et al., 2016; Ekinci et al., 2019). These findings provide a well understood, yet unique lens into a practice that can not only mitigate postoperative pain, but also reduce opioid use that has negatively impacted patients' outcome both in the hospitals and communities. Furthermore, this practice can reduce healthcare costs and improve patient satisfaction after a surgical journey. Provided that each patient is unique, the efficacy of this practice is promising, and patients that meet the criteria for use should be assessed for how this practice can benefit them.

Implication for Future Practice

The findings from this literature review inform the different opioid free approaches to pain management following laparoscopic cholecystectomy. Although most of the studies looked at each drug regimen individually, the combination of the three drugs would likely have an additive effect (Hannam et al., 2018; Yoon & Yaksh,1999), and provide adequate postoperative pain management and reduction in the amount of opioid that is used in the postoperative area.

Study Limitations

This study provided some of the most common preoperative approaches that can be used to reduce postoperative pain and opioid use. However, it did not investigate the postoperative findings of the three medications that were looked at. Furthermore, most of the studies reviewed were based on monotherapy with each of the medications or in comparison with other adjuvant non-opioid analgesics. No available literature combined the three medications being used in this study for the preoperative management of postoperative pain. Another limitation is that 20 studies were reviewed that were carried out within the last 13 years, which may be an underrepresentation of all the available relevant information on this matter. Also, all the conclusions made in this review relied on the results that were presented by the original authors of the reviewed studies, and there was no way to validate the data.

Future Research

Further research can be done with a focus on the possible side effects of combining the three-medication regimen preoperatively. Also, although it might appear obvious that improving postoperative pain management and reducing opioid use with these medications will result in healthcare savings, more studies can be carried out to provide a more objective and numerical value of the healthcare cost when compared to opioid driven analgesia.

Conclusion

Although pain rates vary based on type of surgery, type of anesthetic and analgesics used, and the intraoperative and postoperative duration, studies have shown that postoperative pain is inadequately managed in over 80% of the US patient population (Gan, 2017). Inadequate postoperative pain management is directly correlated with increased morbidity, impaired quality of life and functionality, delayed recovery time, prolonged duration of opioid use, and increased

cost of healthcare due to longer hospital stay and other pain related complications. Furthermore, the presence and intensity of acute postoperative pain is a prediction factor for the development of chronic pain (Gan, 2017). Progress has been made to recognize postoperative pain as a public health concern. Given the complexity of pain pathways, recent efforts have focused on multifaceted approaches to pain management. Multimodal pain management employs the use of different medications and approaches with varying mechanisms of action to prevent and mitigate pain.

The idea of preoperative and preemptive analgesia with multimodal approach is to arrest tissue sensitization and pain transmission prior to initiating painful stimuli. As a monotherapy, numerous studies have investigated acetaminophen, ibuprofen, and gabapentin and found them to be efficacious in the management of postoperative pain and reduced amount of opioid administered in the recovery unit. The combined use of these medications is intended to provide postoperative pain management more effectively. This will further prevent the harmful effects of poorly controlled pain, reduce the incidence of chronic pain, and mitigate the adverse effects of opioid use.

Theoretical Framework

Nursing theories help to improve nursing care by providing the foundation for practice and evidence-based improvement. The theoretical framework that guides this project is Kolcaba's nursing theory of comfort. It is a middle range theory which has been used to improve institutional outcomes and change (Kolcaba & Wilson, 2002). This theory describes comfort as an immediate desirable outcome of nursing care (Nursing Theory, 2019). It is pertinent to the peri-anesthesia setting because patient comfort and safety are established goals in this care environment. Comfort according to this theory is a state of being strengthened by having needs

for relief, ease, and transcendence met in four contexts of experience (physical, psychospiritual, sociocultural and environmental) (Kolcab & Wilson, 2002).

Relief describes having one's severe discomfort alleviated. Ease describes an absence of specific discomfort. Patients experience ease when the provider proactively minimizes the predisposing factors that can lead to discomfort. Finally, transcendence in the context of this theory is the capacity to surpass the discomfort in instances when they cannot be mitigated or avoided (Kolcaba & Wilson, 2002). Pain is a common cause of discomfort and preemptive pain management is intended to promote comfort preoperatively and post-operatively. Prior to surgical procedures, nurse anesthetists carry out this process by including patient comfort as an integral aspect of the preoperative planning. This plan should include preemptive analgesia which has been shown to effectively reduce postoperative pain. A good comfort measure in this stage will reduce complications in subsequent stages (Kolcaba & Wilson, 2002). Once comfort is achieved, it provides ease to the patient and improves their optimism towards recovery. Pain scales, physical assessment, and most importantly patient feedback are necessary indicators used daily to address pain and guide practice. Using Kolcaba's theory supports the anesthetist's ability to promote transcendence by educating the patients about surgical pain, and the need to control and manage pain to help patients adapt postoperatively.

Project Aim and Objective

The purpose of this project is to delineate a multimodal preoperative pain management to reduce pain and the amount of narcotic consumption in the postoperative period. This project aims to utilize preemptive analgesia preoperatively to mitigate immediate post-operative pain by antagonizing pain receptors before they are stimulated. This will also decrease post-operative opioid use in the recovery area. The objectives include oral administration of one gram of

acetaminophen, 300 milligrams of gabapentin and 600 milligrams of ibuprofen a minimum of an hour before the scheduled procedure. Upon return to the recovery area, the patient's postoperative pain level, and the need for further pain management will be assessed.

SWOT Analysis

The SWOT analysis is a visual display of the strengths, weaknesses, opportunities, and threats that are related to project planning (See *Appendix B*). For this project, some of the identified strengths include a previous experience with preemptive/preoperative pain management and a good grasp of the benefits of multimodal pain management to the patient and healthcare in general. Other identified strengths include the constant support provided by facility stakeholders towards this project, and the availability of computerized patient data which makes it possible to easily access patient information remotely. One of the noteworthy weaknesses surrounding this project includes a limited patient population that meets the inclusive criteria for this study. Other identified weaknesses are the financial burden that might be incurred, as well as limited staff training on the importance and process of preemptive analgesia.

This project provides an opportunity to provide education to the staff, especially the preoperative and recovery nurses regarding preemptive analgesia, because these nurses will be involved in preoperative medication administration and postoperative pain assessment, respectively. With the projected shift away from opioid use because of nationwide opioid epidemic and their related adverse effects, this project provides an opportunity to implement an evidence-based multimodal opioid free pain management at this facility, which will improve pain management and reduce the number of opioids patients receive in the recovery area.

Quality improvement projects can encounter certain levels of environmental threat. Some of the threats that are associated with this project include potential resistance by some of the staff

members, the distance it takes to get to the project site, limited number of literatures on the project topic, and the length of time it takes to acquire Institutional Review Boards (IRB) (See *Appendix E*) approval which can delay the progression of this project.

Project Design / Methods

This is a practice intervention and process improvement DNP project. It will be a quantitative prospective nonrandomized study with historical control group. The reason for using historical controls is due to the limited number of patients available for this study.

Project Site and Population

This prospective trial will be conducted at a 58 bed, level 4, private hospital in the Midwest between March 2022 and October 2022. The project group will include 20 patients having elective laparoscopic cholecystectomy and the control group will be 20 patients with previous laparoscopic cholecystectomy. Inclusion criteria are age between 18 and 80 years, American Society of Anesthesiologists (ASA) physical status classification I or II, and a diagnosis of cholecystitis or any gallbladder diseases requiring an elective laparoscopic cholecystectomy. Criteria for exclusion include liver failure, renal dysfunction, chronic pain, opioid dependence, inability to accurately provide information due to neurological disease or intellectual disability, and patients with history of adverse reaction to ibuprofen, acetaminophen, or gabapentin.

Prior to surgery, each patient will be informed of this study and its relevance. An Eligibility Survey (See *Appendix F*) will be used to determine patients who can participate in the project study. Before medication administration, patient's signed informed consent to the study will be obtained and each patient will be educated on the numerical pain rating scale (NPRS)

(See *Appendix G* for the NPRS). The NPRS will be used because it is an easy-to-use scale for adults with no cognitive impairment and data obtained can be easily measured.

All 20 participants in the study group will receive PO one gram of acetaminophen, 600 mg of Ibuprofen, and 300mg of gabapentin at least one hour prior to the procedure but not administered more than two hours before the procedure. The dosages and duration of administration are based on current clinical practice.

Data Collection Procedure

Following extubation in the operating room, data such as surgery duration, intra-operative complications, and intra-operative analgesics will be recorded in the Intraoperative Patient Form (IP Form) (See *Appendix H* for the IP Form). Once in the post anesthesia recovery unit (PARU), patients will be evaluated at the bedside for postoperative pain using the NPRS at 15 minutes, 30 minutes, and 45 minutes. The NPRS uses a pain scale of 0 to 10. The number 0 indicates no pain and 10 corresponds to the worst possible pain. Fentanyl in increments of 25 micrograms will be used as the rescue analgesic for postoperative pain, unless if contraindicated. All postoperative pain data will be entered into the NPRS form. The amount of fentanyl used in the PACU, other analgesia requirements, and length of stay in the recovery unit will also be recorded.

Ethical Considerations and Protection of Human Subjects

Internal Review Board (IRB) approval was obtained prior to initiating this DNP project. All participants were provided a written informed consent and are protected by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) which protects the privacy of all patients' medical records. Ethical approval was also obtained from the Marian Internal Review Board (MIRB). There is no risk to participation in this study other than receiving regular

perioperative care and assessment. In addition, all relevant data were carefully collected, recorded with unique patient identifiers without identifiable patient information and stored in a password encrypted device that can only be accessed by authorized users for the period of the study.

Project Evaluation Plan

At the completion of the study, Statistical Package for the Social Sciences (SPSS) will be used to input and analyze the data which will be shown as mean and standard deviation (SD). The postoperative pain scores at 15 minutes, 30 minutes, 45 minutes will be calculated and analyzed with one-way ANOVA. Additionally, the total dose of fentanyl administered in the recovery unit for each group will be compared with the use of unpaired t tests. A P value <0.05 will be considered statistically significant. In an event that no control is obtained, the sample size is smaller than projected or does not fit a normal curve, then non-parametric equivalent to the above tests will be used to reduce statistical flaw.

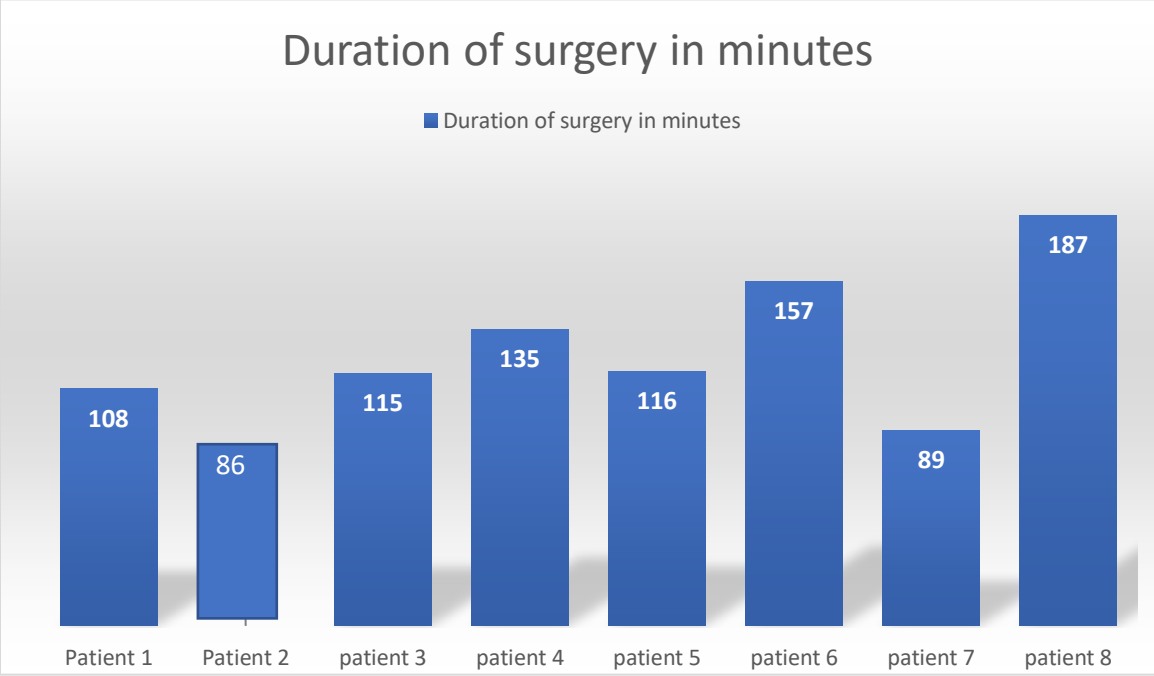
Results

A total of eight patients participated in the project. There were no controls. The participants were aged between 18 and 72 years, and half were male. All the participants received Tylenol, Ibuprofen, and Gabapentin within one hour prior to surgery. No other pre-operative medications were administered.

Intraoperatively, five of the patients received Toradol 30 mg (two males and 3 female participants), one male patient received Toradol 15 mg in addition to fentanyl 100 mcg. One female participant received fentanyl 100 mcg and one male participant received fentanyl 75 mcg. One of the male patients who received Toradol 30 mg also received fentanyl 250 mcg, and one of the female participants who received Toradol 30 mg received an additional dose of

dexmedetomidine 92 mcg. The mean duration of surgery is 124 minutes, with a standard deviation of 34.488. The chart below depicts the duration of surgery for each patient.

Chart 1: Duration of the Laparoscopic Cholecystectomy for each patient.



Postoperatively, for the first 15 minutes, four of the male patients and one of the female patients experienced no pain, while the remaining three female patients rated their pain at 9,8, and 7 respectively. The second 15 minutes recorded decreased pain for the three female participants that reported pain, with zero pain for the other five participants. The last 15 minutes recorded a further decrease in pain for the three participants with existing pain. Also, at this time, four of the five patients with zero pain maintained a score of zero, while one (male participant) reported a pain score of 3. The mean postoperative pain perception is 6.7 for all the patients, which is categorized as moderate pain. Fentanyl, Vicodin, and meperidine were used as rescue analgesics for the three female patients with recorded pain scores.

Data Analysis

All the participants received intraoperative pain medications. The standard deviation (SD) for intraoperative medications is 1.959, with a mean of 2.88. One-way ANOVA was used to analyze the post-operative pain perceived within the first 45 minutes in 15 minutes intervals and the intraoperative medications administered. The table below depicts the results of the one-way ANOVA.

Table 1: One-way ANOVA results

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
postop_pain_zero_to_fiftheen	Between Groups	73.333	5	14.667	.603	.720
	Within Groups	48.667	2	24.333		
	Total	122.000	7			
post0p_pain_fiftheen_to_thirty	Between Groups	43.500	5	8.700	.725	.667
	Within Groups	24.000	2	12.000		
	Total	67.500	7			
postop_pain_thirty_to_fortyfive	Between Groups	37.333	5	7.467	22.400	.043
	Within Groups	.667	2	.333		
	Total	38.000	7			

The results were statistically insignificant, probably based on the small sample size in the study. The Independent T-test p-value of the total dose of fentanyl administered in the recovery unit for the study group was 0.444, which was statistically insignificant. The statistics show that the null hypothesis is maintained, and the alternative hypothesis is rejected. The insignificant p-value confirms that the medications administered do not help reduce post-operative pain. This is

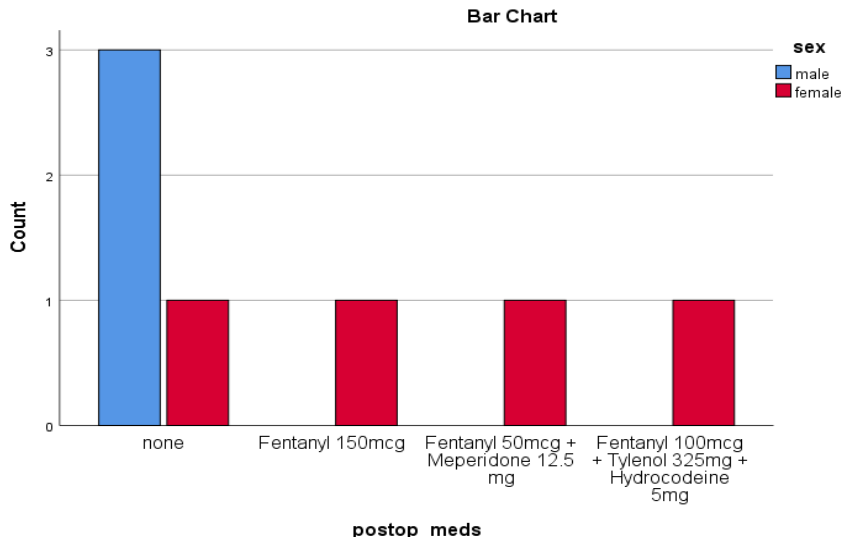
likely due to the sample size and lack of control. In addition, due to the small sample size, lack of a control group and because data obtained do not meet the assumptions about the population sample, a non-parametric Mann-Whitney test was used to analyze postoperative pain scores between male and female participants at the different time intervals. At 15 minutes postoperative, the Mann-Whitney score is 2.000 with p-value of 0.047, indicating a significance in postoperative pain between males and females. At 30 minutes the Mann-Whitney test score is 2.000 with a p-value of 0.040, indicating a significance in the postoperative pain score between both genders. At 45 minutes postoperatively, there is no significant difference in the pain scores between both genders (p-value 0.122). Also, the participants were grouped into three different age groups. Group 1 (18-28 years), group 2 (51-61 years), and group 3 (62-72 years). Using the Krustal- Wallis test for analysis, there was no significant difference in the postoperative pain perceived between the three groups at 15 minutes (p-value 0.292), 30 minutes (p-value 0.195), and at 45 minutes (p-value 0. 084). Finally, participants were grouped based on the duration of surgery in minutes. Using the Krustal-Wallis non-parametric test, there was no significant difference in postoperative pain between surgeries that lasted 90 minutes or less, 91 to 120 minutes and surgeries that lasted over 120 minutes at 15 minutes (p-value 0.388), 30 minutes (p-value 0.364), and at 45 minutes (p-value 0.354) postoperative intervals.

Discussion

The results of the data analyzed indicated that the preoperative medications did not significantly decrease post operative pain and opioids administered largely due to the small sample size and the lack of control participants. However, the study found that male patients experienced less postoperative pain within the first 30 minutes after surgery compared to the female patients. This is in line with previous studies indicating that pain perception is largely

influenced by gender differences, as reported by (Logan & Rose, 2004). More pain medications were administered to the female participants in the PACU within the first 15 to 30 minutes, which might account for the lack of significant difference in pain scores between both genders at 45 minutes PACU time. None of the male participants received any medication in the PACU. Also, Fentanyl was the most common postoperative rescue analgesic administered, likely due to its quick onset and short duration of action.

Chart 2: Post-operative medications administered by gender.

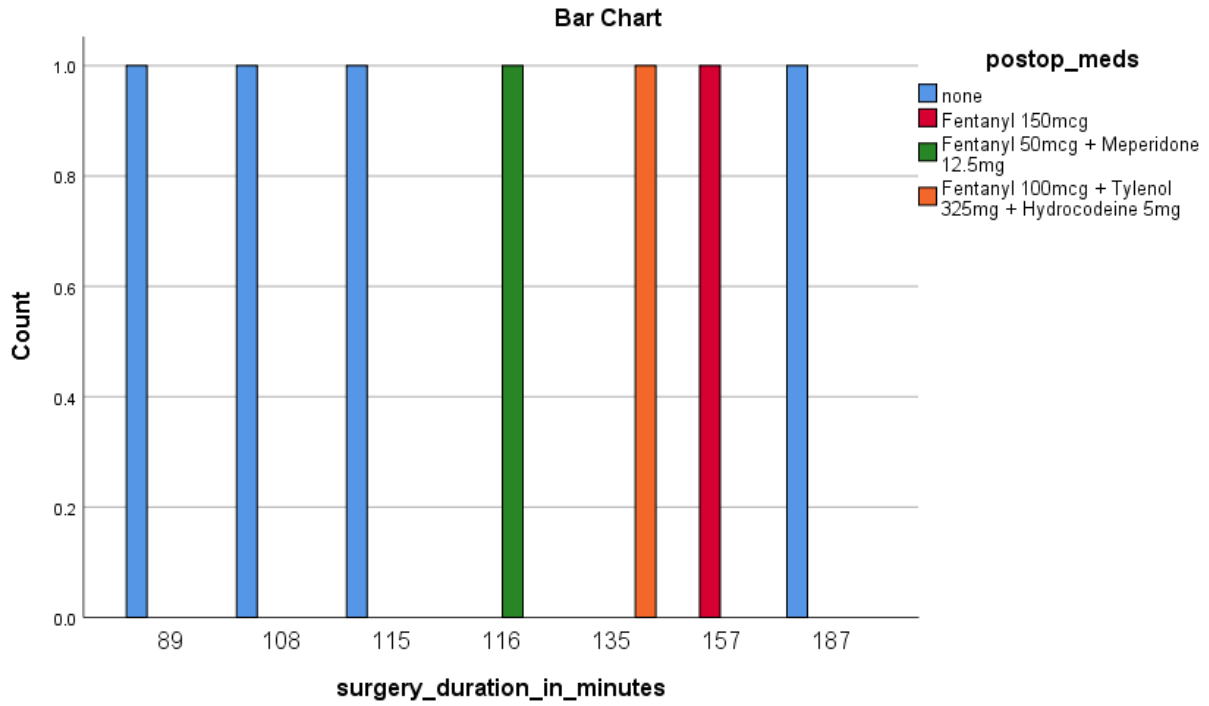


The data analysis obtained showed no predictive relationship between age and the severity of postoperative pain. This can be attributed to the small sample size of eight. Also, the participants were further grouped into three different age groups which further diluted the sample size. On the contrary, Gustafsson et al. (2020) reported a significant correlation between extremes of age and postoperative pain compared to middle-aged adults.

Studies have shown that a longer duration of surgery is a risk factor for postoperative pain and opioid use. According to Hah et al. (2018), laparoscopic surgeries with longer intraoperative operations were associated with more postoperative pain that impaired timely recovery. However, this study analysis showed that surgery duration did not significantly impact

postoperative pain or opioids used. This can also be attributed to the small sample size. More so, the participants were split into three groups based on the duration of surgery, thereby further reducing the sample size. Toradol and Fentanyl were the most frequently administered intraoperative pain medications.

Chart 3: Post-operative pain medications administered by surgery duration.



Project Limitations

The study lacked a control group which became a major setback, making it impossible to show the effectiveness of the preoperative pain medications in reducing postoperative pain and opioid use. Also, the small sample size was a major limitation. A study with an adequate sample size has a high level of evidence. Studies with a low sample size would have most variables statistically non-significant. This DNP project only had eight participants, making it a very low level of evidence.

Considerations and Future Recommendations

The study found that postoperative pain scores were highest during the first 15 to 30 minutes in the PACU. Therefore, more clinical trials are necessary to determine the correct mix of multimodal pain relief medications to be administered preoperatively to alleviate perioperative pain among surgical patients. Studies should focus on drugs with longer half-lives and fewer side effect profiles to ensure optimum pain control throughout the immediate postoperative period. According to Barazanchi et al. (2018), few clinical trials have adequately reported on multimodal pain management and effectively tested desirable drugs to efficiently control postoperative pain without regular dosing. To further complement the enhanced postoperative pain reduction, the role of extended-release single non-opioid agents should be investigated as they provide superior pain management properties. Adequate studies would inform policymaking to optimize postoperative pain control.

The study had a limited number of patients to study the objectives in depth. Furthermore, a proper control group is needed to provide adequate evidence as to the desirable effects of the study. Although expensive, more high-quality studies with sufficient participants and control would provide a high level of evidence.

As observed in the study, there is a significant variation in pain threshold influenced by factors like age and gender. Future clinical trials would consider such differences, including other variables like race, ethnicity, and comorbidities to provide a more detailed conclusion regarding their implication in postoperative pain management.

Conclusion

The complexity of pain after a laparoscopic cholecystectomy possesses a snowballing challenge to recovery after surgery. The management of perioperative pain requires the administration of desired analgesics to optimize patient outcomes and mitigate extended postoperative stay. Opioids are commonly used to alleviate such postoperative pain, but they possess undesirable properties in the form of side effects. Additionally, their short half-lives make regular dosing a necessity. To reduce opioid use while still maintaining optimal pain control, multimodal pain management in the preoperative period using Ibuprofen, Gabapentin, and Tylenol can be implemented. More studies using these preoperative medications are recommended. Furthermore, the influence of gender, age, ethnicity, and comorbidities on preoperative management of postoperative pain using the above non-opioids need to be ascertained. Analyzing the role of these variables, as well as identifying the correct dosing of these preoperative medications can provide a better management of postoperative pain with minimal opioid administration.

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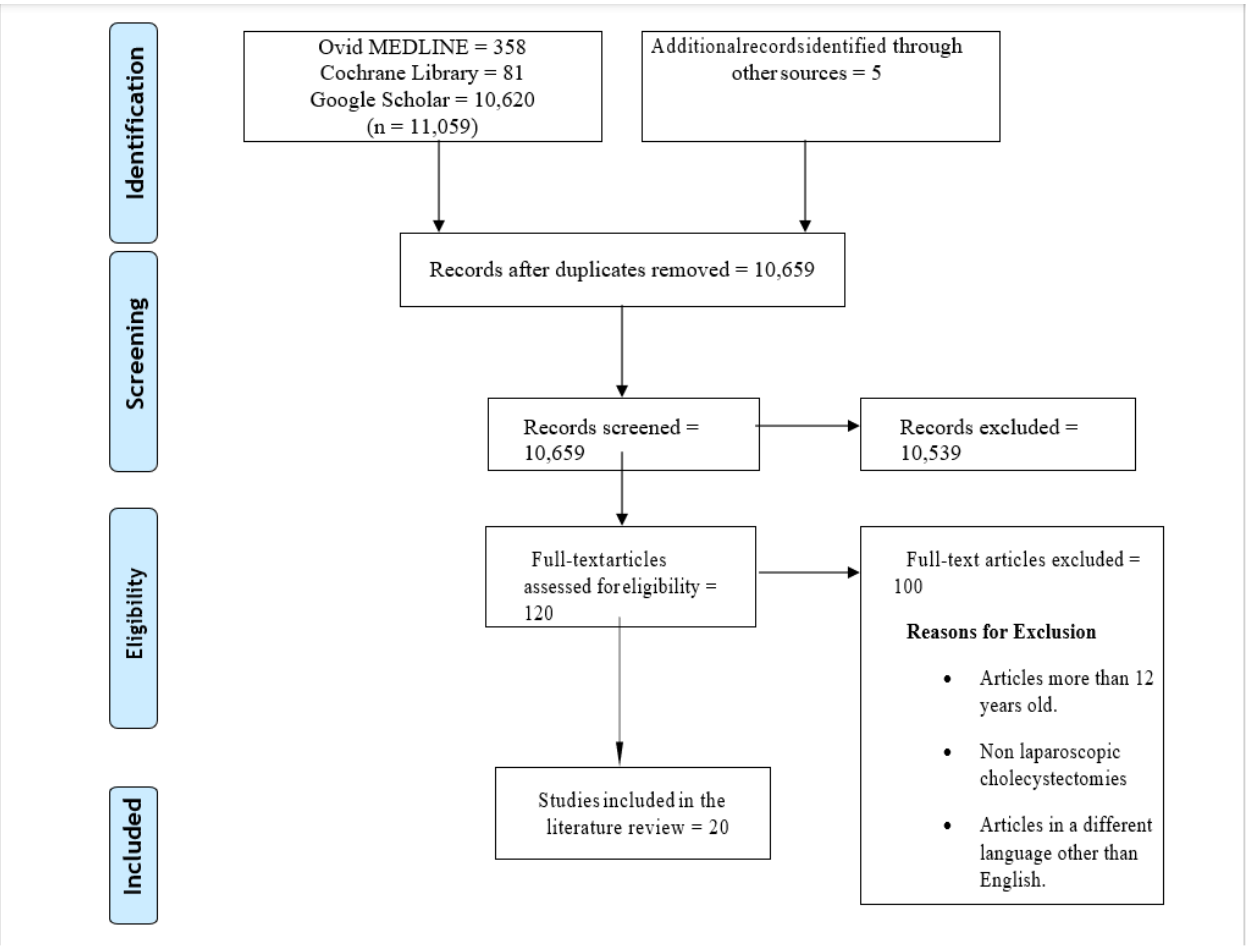
Appendix A

PRISMA Flow Diagram

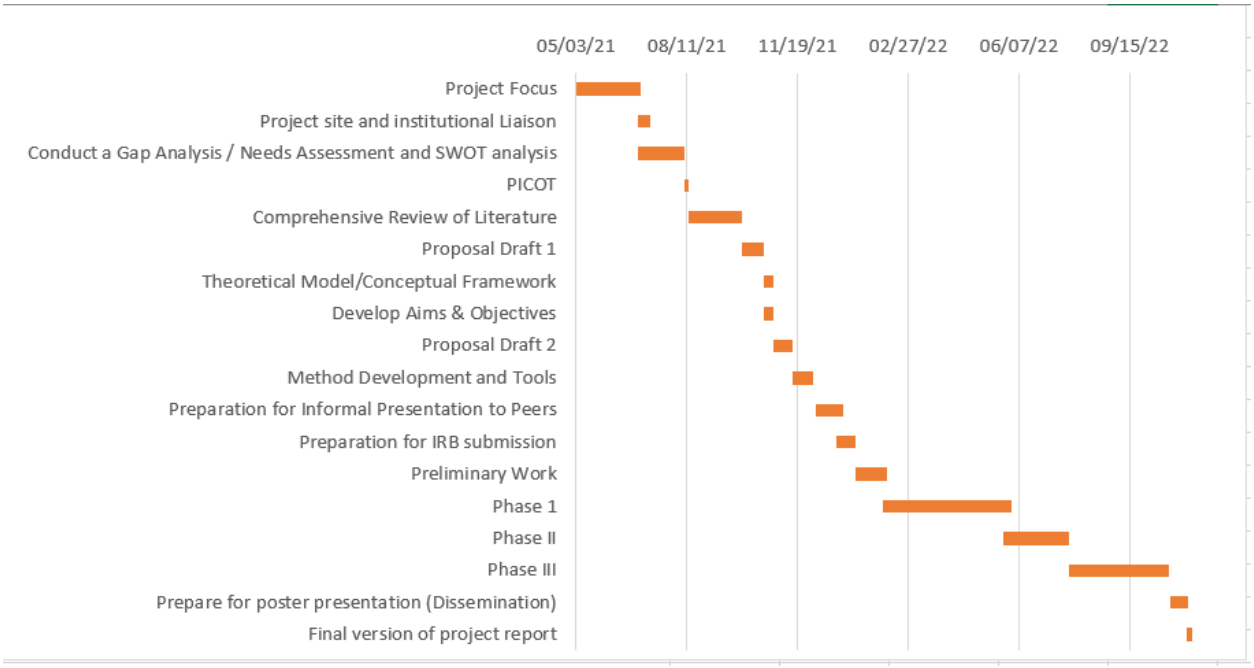


Appendix B

SWOT Analysis

Appendix C

GANTT Chart



Appendix D

Literature Review Matrix

Reference	Research Design & Level of Evidence	Population / Sample n=x	Variables	Instruments / Data collection	Results
Ahiskalioglu, E. O., Ahiskalioglu, A., Aydin, P., Yayik, A. M., & Temiz, A. (2017). Effects of single-dose preemptive intravenous ibuprofen on postoperative opioid consumption and acute pain after laparoscopic cholecystectomy. *Medicine*, *96*(8), e6200. https://doi.org/10.1097/MD.0000000000006200	Prospective, randomized, double-blinded study.	Patients aged 18 to 65, American Society of Anesthesiology (ASA) I-II and scheduled for laparoscopic cholecystectomy. n=60	Ibuprofen, postoperative pain, twenty-four-hour postoperative fentanyl consumption, any additional analgesia.	Visual analogue pain scale (VAS) with active and passive movements.	VAS scores in the IV ibuprofen group were statistically lower at postoperative 30 minutes and 1, 2, 4, 8, 12, and 24 hours. Twenty-four-hour opioid consumption was statistically significantly higher in the control group compared to the ibuprofen group. Additional analgesia use was statistically significantly higher in the control group than in the ibuprofen group,
Ekinci, M., Ciftci, B., Celik, E. C., Köse, E. A., Karakaya, M. A., & Ozdenkaya, Y. (2019). A randomized, placebo-controlled, double-blind study that evaluates efficacy of intravenous ibuprofen and acetaminophen for postoperative pain treatment following laparoscopic cholecystectomy surgery. *Journal of Gastrointestinal Surgery*, *24*(4), 780–785. https://doi.org/10.1007/s11605-019-04220-1	Randomized doubke-blind control study	n=30 for ibuprofen, n=30 for control group, n=30 for accetaminophen	Acetaminophen, ibuprofen, reduced postoperative pain	Visual analog scale	Pain scores in group 1 and group a were lower at all times than those in group C. group C had a significantly higher consumption than other groups.
Gilron, I., Orr, E., Tu, D., Mercer, C. D., & Bond, D. (2009). A randomized, double-blind, controlled trial of perioperative administration of gabapentin, meloxicam and their combination for spontaneous and movement-evoked pain after ambulatory laparoscopic cholecystectomy. *Anesthesia and analgesia*, *108*(2), 623–630. https://doi.org/10.1213/ane.0b013e318193cd1b	Randomized, double-blind trial.	18 yr or older with a body mass index <36 kg/m^2 that fit an ASA I or II classification before elective laparoscopic cholecystectom. N=	meloxicam, gabapentin, a combination of the two, day of surgery spontaneous and movement-evoked pain. Pain on Days 1, 2, and 30, adverse effects, opioid consumption,	Numerical rating scale,	On the day of surgery, 60-min rest pain was significantly lower with gabapentin alone versus meloxicam alone. Observed pain differences between the combination and

			spirometry, pain-related interference, hospital discharge time, return to work time, and patient satisfaction.		gabapentin alone were fairly small in favor of gabapentin alone.
Gurusamy, K. S., Vaughan, J., Toon, C. D., & Davidson, B. R. (2014). Pharmacological interventions for prevention or treatment of postoperative pain in people undergoing laparoscopic cholecystectomy. *The Cochrane database of systematic reviews*, (3), CD008261. https://doi.org/10.1002/14651858.CD008261.pub2	Systematic review of randomized clinical trials, and comparative non-randomized studies.	Low anesthetic risk people undergoing elective laparoscopic cholecystectomy. n=2505	Non-steroidal anti-inflammatory drugs, opioids, and anticonvulsant analgesics, post-operative pain	Review Manager 5 analysis. Visual analogue scale.	The pain at 4 to 8 hours was generally reduced by about 1 to 2 cm on the visual analogue scale of 1 to 10 cm in the comparisons involving the different pharmacological agents and inactive controls. The pain at 9 to 24 hours was generally reduced by about 0.5 cm (a modest reduction) on the visual analogue scale of 1 to 10 cm in the comparisons involving the different pharmacological agents and inactive controls.
Johnson, R. J., Nguyen, D. K., Acosta, J. M., O'Brien, A. L., Doyle, P. D., & Medina-Rivera, G. (2019). Intravenous Versus Oral Acetaminophen in Ambulatory Surgical Center Laparoscopic Cholecystectomies: A Retrospective Analysis. *P & T: a peer-reviewed journal for formulary management*, *44*(6), 359–363.	Retrospective analysis	1,000 mg IV APAP intraoperatively (n = 319) or 1,000 mg PO APAP preoperatively (n = 260).	IV tylenol, oral tylenol, postoperative opiod reduction	Electroninc medical records	Median pain scores were similar for both analgesic methods. PO APAP's non-inferiority to IV APAP can be statistically concluded
Kamali, A., Ashrafi, T. H., Rakei, S., Noori, G., & Norouzi, A. (2018). A comparative study on the prophylactic effects of paracetamol and dexmedetomidine for controlling	A comparative study	Patients aged 18 to 70 years and from both genders, who	Dexmedetomidine, Paracetamol, postoperative pain,	Visual analog scale,	Pain score in the paracetamol group was significantly

hemodynamics during surgery and postoperative pain in patients with laparoscopic cholecystectomy. *Medicine*, *97*(51), e13330. https://doi.org/10.1097/MD.0000000000013330		were candidates for emergency cholecystectomy or elective surgery. n=132	arterial blood pressure, heart rate		lower than that in the dexmedetomidine group. No group differences in the mean scores of pain during these hours. The median opioid use in 24 hours after operation in the paracetamol group was lower when compared with that in the dexmedetomidine group, and the mean duration of analgesia in the paracetamol group was higher when comparing with dexmedetomidine group
Karaca, O., Pınar, H. U., Turk, E., Dogan, R., Ahiskalioglu, A., & Solak, S. K. (2019). Effects of Single-Dose Preemptive Pregabalin and Intravenous Ibuprofen on Postoperative Opioid Consumption and Acute Pain after Laparoscopic Cholecystectomy. *Journal of investigative surgery: the official journal of the Academy of Surgical Research*, *32*(3), 189–195. https://doi.org/10.1080/08941939.2017.1386738	Prospective, randomized, double-blinded study	Patients undergoing laparoscopic cholecystectomy. n=58	pregabalin, pregabalin plus ibuprofen, Postoperative fentanyl consumption, additional analgesia requirements and PACU stay.	VAS	VAS scores in the group PI were statistically lower at PACU, 1and 2 hours at rest, at PACU, 1, 2, 4, 12 and 24 hours on movement compared to the group P. Opioid consumption was statistically significantly higher in the group P compared to the group PI. Rescue analgesia usage was statistically significantly higher in the group P than in the group PI. Four patients in the group PI did not need any opioid drug. Besides, PACU stay was

					shorter in the group PI than the group P.
Karri, S. R., Jayaram, K., Kumar, A., & Durga, P. (2021). Comparison of efficacy of gabapentin and memantine premedication in laparoscopic cholecystectomies for postoperative pain relief - A randomized placebo-controlled trial. *Indian journal of anaesthesia*, *65*(7), 539–544. https://doi.org/10.4103/ija.IJA_140_21	Randomized controlled study	Patients posted for laparoscopic cholecystectomy. n=66	Gabapentin, memantine, Preoperative assessment, the baseline threshold, tolerance values of pain, pain scores reassessed, Ramsay sedation scores	Numerical Rating Scale, Ramsey Sedation score, analgesiometer.	Gabapentin group had lower Numerical Rating Scale scores at 15 min and 1 h postoperatively when compared to the other two groups. Memantine group had a longer time for the first request for rescue analgesia (50.53 min) compared to gabapentin and placebo. Ramsay sedation scores were higher in the gabapentin group compared to the other two. The objective assessment of pain with algesiometer showed no statistical significance between the groups for both threshold and tolerance values
Kochhar, A., Chouhan, K., Panjiar, P., & Vajifdar, H. (2017). Gabapentinoids as a Part of Multi-modal Drug Regime for Pain Relief following Laproscopic Cholecystectomy: A Randomized Study. *Anesthesia, essays and research*, *11*(3), 676–680. https://doi.org/10.4103/0259-1162.204208	Randomized, single-blind study	Patients undergoing laparoscopic cholecystectomy under general anesthesia. n=50	Pregabalin, Gabapentin, Severity of postoperative pain, postoperative fentanyl requirement and incidence, and severity of side effects.	Visual analog scale [VAS]), Ramsay sedation score	A single preoperative dose of pregabalin (150 mg) or gabapentin (300 mg) are equally efficacious in providing pain relief following laparoscopic cholecystectomy as a part of multimodal regime without any side effects.

Salihoglu, Z., Yildirim, M., Demiroluk, S., Kaya, G., Karatas, A., Ertem, M., & Aytac, E. (2009). Evaluation of intravenous paracetamol administration on postoperative pain and recovery characteristics in patients undergoing laparoscopic cholecystectomy. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques*, *19*(4), 321–323. https://doi.org/10.1097/sle.0b013e3181b13933	Randomized study	Patients were divided into equal groups with random number generator to receive either paracetamol (group 1; n = 20) or not (group 2; n = 20)	Paracetamol, analgesia, postoperative pain	Verbal and visual pain scores	Verbal and visual pain scores of the paracetamol group were significantly lower than control group (P<0.05). First morphine requirement and total administered morphine dose and duration of staying in recovery room were significantly decreased in the paracetamol group (P<0.05)
Sami Mebazaa, M., Frikha, N., Ben Hammouda, N., Mestiri, T., Mestiri, H., Khalfallah, T., & Ben Ammar, M. S. (2008). Analgesie postoperatoire pour cholecystectomie sous coelioscopie: comparaison de l'administration preoperatoire du celecoxib et du paracetamol [Postoperative analgesia after laparoscopic cholecystectomy: comparison of the preoperative administration of celecoxib with paracetamol?]. *La Tunisie medicale*, *86*(10), 869–873.	Randomized prospective study	Patients undergoing laparoscopic cholecystectomy. n=75	Paracetamol, celecoxib, VAS scores, hemodynamic parameters, adverse effects,	The VAS at rest and effort (T(30mn) to T(h24), Hemodynamic parameters, Ramsay score and the adverse effects.	VAS scores show a significant difference between the groups P and T with the effort of cough at t24h and between the groups C and T at postoperative T 4h. Group C consumed to a significant degree less morphine 5.44 +/- 3.00 Mg against 7.83 +/- 4.00 Mg for the group P and 8.04 +/- 3.00 Mg for the group T
Srivastava, U., Kumar, A., Saxena, S., Mishra, A. R., Saraswat, N., & Mishra, S. (2010). Effect of preoperative gabapentin on postoperative pain and tramadol consumption after minilap open cholecystectomy: a randomized double-blind, placebo-controlled trial. *European journal of anaesthesiology*, *27*(4), 331–335. https://doi.org/10.1097/EJA.0b013e328334de85	A randomized double-blind, placebo-controlled trial	Adult patients of either sex undergoing minilap open cholecystectomy. n=120	Gabapentin, Post op pain assessment at 0, 2, 4, 8, 12, 24 and 48 hrs, verbal analogue pain scores at rest and at movement. Consumption of tramadol on first and second postoperative days and any adverse effects.	Verbal analogue pain scores at rest and at movement	Verbal analogue pain scores were significantly lower on first postoperative day at all times of observation both at rest and at movement in gabapentin group than in placebo group. Tramadol consumption was also reduced by 33%

					in gabapentin group. But pain scores and tramadol consumption were similar in two groups on second postoperative day.
Toleska, M., & Dimitrovski, A. (2019). Is Opioid-Free General Anesthesia More Superior for Postoperative Pain Versus Opioid General Anesthesia in Laparoscopic Cholecystectomy? *Prilozi (Makedonska akademija na naukite i umetnostite. Oddelenie za medicinski nauki), 40*(2), 81–87. https://doi.org/10.2478/prilozi-2019-0018	Randomized, single-blind clinical study	Patients scheduled for elective laparoscopic cholecystectomy. n=60	Opioid-free anesthesia, fentanyl, post-operative pain scores at rest and on coughing, total opioid requirement	VAS pain score	Patients in the fentanyl group (FG) have higher pain scores at rest and on coughing in all analyzed timeframes compared to patients from the OFA group. In the OFA group 24 hours after surgery none of the patients reported pain at rest and when coughing number 7, 8, 9 and 10 according to the VAS pain score. The total opioid requirement in the postoperative period was significantly higher in the fentanyl group (FG) at rest and when coughing, compared to the OFA group.
Kamali, A., Le, V., Kurnutala, L., SchianodiCola, J., Ahmed, K., Yarmush, J., Daniel Eloy, J., Shapiro, M., Haile, M., & Bekker, A. (2016). Premedication with Intravenous Ibuprofen Improves Recovery Characteristics and Stress Response in Adults Undergoing Laparoscopic Cholecystectomy: A Randomized Controlled Trial. *Pain medicine (Malden, Mass.), 17*(6), 1163–1173. https://doi.org/10.1093/pm/pnv113	Randomized control double blind trial	N=55 in two groups. Group A received a placebo and group B received 800mg of IV ibuprofen	Anti-inflammatory, NSAIDs, cognitive function	40-item Quality of Recovery questionnaire, 9-item modified Fatigue Severity Scale, 15-item Geriatric Depression Scale.	Ibuprofen attenuated the release of proinflammatory processes like interleukin-10

Kotsovolis, G., Karakoulas, K., Grosomanidis, V., & Tziris, N. (2015). Comparison between the combination of gabapentin, ketamine, lornoxicam, and local ropivacaine and each of these drugs alone for pain after laparoscopic cholecystectomy: a randomized trial. *Pain practice : the official journal of World Institute of Pain*, *15*(4), 355–363. https://doi.org/10.1111/papr.12183	Randomized placebo-controlled trial	N=148 patients, between 18 and 70 years of age, were randomly assigned to 6 groups (28 in each group) with the use of computer software	24hour morphine consumption, opioid related side effects, gabapentin	Computer software	Only groups A (6.4 mg), B (9.46 mg), and D (9.36 mg) had lower morphine consumption than control group (20.29 mg) and. Group A was not different from B and D
Mishra, R., Tripathi, M., & Chandola, H. C. (2016). Comparative clinical study of gabapentin and pregabalin for postoperative analgesia in laparoscopic cholecystectomy. *Anesthesia, essays and research*, *10*(2), 201–206. https://doi.org/10.4103/0259-1162.176409	Randomized study	N=90 divided in Group A (placebo), B(gabapentin), and C(pregabalin). 30 patients in each group.	Pain scores, sedation scores	Data was recorded in a standard Performa. Test for analysis among three groups was done by analysis of variance (ANOVA), Visual analog scale (VAS) was used to record pain and sedation scores.	In our study, we had used a single oral dose of 900 mg gabapentin and 150 mg pregabalin, which was administered 1 h prior to the procedure. Pregabalin and gabapentin group had lower visual analog scale (VAS) score prolonged timing of first rescue analgesic min, and less opioid
Nakhli, M. S., Kahloul, M., Jebali, C., Frigui, W., & Naija, W. (2018). Effects of gabapentinoids premedication on shoulder pain and rehabilitation quality after laparoscopic cholecystectomy: pregabalin versus gabapentin. *Pain Research and Management, 2018.*	Randomized double-blind clinical trial	N=90 3 groups of 30 each. Patients of group 1 received 150 mg of pregabalin (2 capsules of 75 mg), those of group 2 received 600 mg of gabapentin (2 capsules of 300 mg), and those of group 3 received 2 capsules of placebo	Gabapentin, lyrica, postoperative pain, postoperative nausea and vomiting	Visual Analog Scale (VAS), Spiegel Scale	Preemptive premedication with 600 mg of gabapentin or 150 mg of pregabalin improves several parameters of postoperative rehabilitation after laparoscopic cholecystectomy. It reduces significantly the intensity of postoperative shoulder pain, decreases the incidence of PONV, improves the quality of sleep during the first night, and

					shortens the time to first standing position
Abbas, Z., & Bashir, A. (2019). Effects of Gabapentin on Postoperative Pain and Total Analgesic Requirement After Laparoscopic Cholecystectomy. *Biomedical and Pharmacology Journal*, *12*(2), 925-929.	Randomized placebo-controlled study	Sixty adult patients listed for laparoscopic cholecystectomy were randomly allocated to two groups of 30 each to receive gabapentin 600 mg p.o. or a matching placebo 2 hours before surgery.	Gabapentin, postoperative pain	Visual Analog Scale (VAS: 0 = no pain; 10 = most severe pain). The software used was Statistical Package for Social Sciences (SPSS) and Microsoft Excel.	Postoperative pain scores and total analgesic requirement was significantly less in gabapentin group compared to placebo group. A single 600 mg dose of gabapentin given preoperatively decreased postoperative pain and total analgesic requirement following laparoscopic cholecystectomy
Hosseini, V. S., Yekta, R. A., Marashi, S., & Marashi, S. M. (2015). The efficacy of melatonin, Clonidine and Gabapentin in reducing preoperative anxiety and postoperative pain in patients undergoing laparoscopic Cholecystectomy: a randomized clinical trial. *Archives of Anesthesiology and Critical Care*, *1*(4), 120-125	Randomized clinical trial	total number of 88 patients were categorized into four groups to receive melatonin, clonidine, gabapentin and placebo (22 patients per group)	Gabapentin, clonidine and melatonin	State-Train Anxiety Inventory (STAI), VAS (Visual Analog Scale)	The intensity of pain was significantly decreased by the time and depending on the assigned group, the pain reduction trend was different among treatment groups
Medina-Vera, A. J., & Novoa, L. M. (2017). Reduced anaesthetic requirements and postoperative analgesics in patients undergoing laparoscopic cholecystectomy: premedication with intravenous paracetamol versus ketorolac, a double blind and randomised clinical trial. *Revista espanola de anestesiologia y reanimacion*, *64*(2), 64–70. https://doi.org/10.1016/j.redar.2016.05.007	Randomized double-blind clinical trial	100 patients randomized into 2 groups. Group 1: pre-medicated with paracetamol 1g, and Group 2: with ketorolac 30mg (both administered intravenously 30minutes prior to surgery).	Paracetamol 1g, ketorolac 30mg	Visual Analog Scale (VAS)	Paracetamol 1g IV placed preoperatively decreased anesthetic requirements and the need for postoperative analgesics, like preoperative administration of ketorolac 30 mg IV.

Appendix E

IRB Approval Letter

SAINT JOSEPH
HEALTH SYSTEM
A Member of Trinity Health

June 15, 2022

Valine Nnoruo RN, BSN, PHN, CCRN, SRNA
Bessem Enoweyere RN, BSN, CCRN, SRNA
Reed Stockman CRNA
Diana Madsen CRNA

RE: 22-002 Preoperative Pain Management for Laparoscopic Cholecystectomy to Decrease Postoperative Pain and Opioid Use.

Approval Date: June 2, 2022
Expiration Date: June 2, 2023

Your request for review of the protocol noted above was reviewed in the Saint Joseph Regional Medical Center Institutional Review Board meeting on June 2, 2022

The board approved and granted permission to proceed with your protocol with one condition, that the consent form has been modified or formatted in a way to allow a patient label to be affixed. This is necessary for health information purposes to allow scanning of the patients consent to their account.

The protocol is next subject to continuing review on or around June 2, 2023 unless closed before that date. When the study is closed, the IRB would like a copy of the protocol findings. In addition, any changes to the study must be promptly reported and approved to continue. Contact me if you have any questions or require further information.

Sincerely,

Amy Crimmins
IRB Program Coordinator
crimmina@sjrmc.com
574-335-6181

Medical Centers

Mishawaka Medical Center
5215 Holy Cross Pkwy.
Mishawaka, IN 46545
574.335.5000

Plymouth Medical Center
1915 Lake Ave.
Plymouth, IN 46563
574.948.4000

Senior Services

Holy Cross
17475 Dugdale Dr.
South Bend, IN 46635
574.247.7500

Saint Joseph PACE
250 E. Day Rd.
Mishawaka, IN 46545
574.247.8700

St. Paul's
3602 S. Ironwood Dr.
South Bend, IN 46614
574.284.9000

Trinity Tower
316 S. Dr. Martin Luther King Jr. Blvd.
South Bend, IN 46601 574.335.1900

VNA Home Care
3838 N. Main St., Ste. 100
Mishawaka, IN 46545
574.335.8600

Community-Based Programs

The Foundation
707 E. Cedar St., Ste. 100
South Bend, IN 46617
574.335.4540

Health Insurance Services
5215 Holy Cross Pkwy.
Mishawaka, IN 46545
1.855.88.SJMED (1.855.887.5633)

Community Health & Well-Being
707 E. Cedar St., Ste. 100 South Bend, IN 46617 574.335.4685

Saint Joseph Medical Group 707 E. Cedar St., Ste. 220 South Bend, IN 46617 574.335.8758

sjmed.com

Appendix F

Eligibility Survey

DNP Project Participant Eligibility Questionnaire

Location: St Joseph Medical Center, Plymouth Indiana

DNP Student names: Valine Nnoruo and Bessem Enoweyere

Date:

Questionnaire (*Please Circle the Correct Response*)

Are you LESS than 18 years old?	YES	NO
Are you undergoing any procedure other than laparoscopic cholecystectomy?	YES	NO
Do you have allergies to?		
Acetaminophen	YES	NO
Ibuprofen	YES	NO
Gabapentin	YES	NO
Fentanyl	YES	NO
Do you have:		
Liver Failure	YES	NO
Kidney Failure	YES	NO
Current GI Bleed	YES	NO
Chronic Pain Synd	YES	NO
Opioid Dependence	YES	NO

Note: Answering YES to any of the questions screens the participant out of the DNP Project

For Use in the Preoperative Area

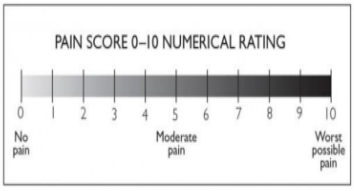
Appendix G

Numerical Pain Rating Scale

NUMERICAL PAIN RATING SCALE

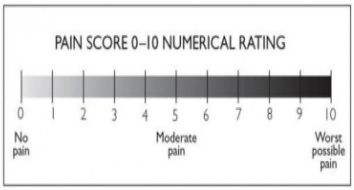
(For pain assessment and re-assessment in the PACU)

Within 15 mins *(please circle)*



Additional Pain Medication	Dose	Time
Fentanyl		
Hydromorphone		
Morphine		
Other		

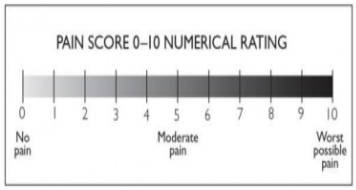
After 15 minutes within 30 minutes *(please circle)*



Additional Pain Medication	Dose	Time
Fentanyl		
Hydromorphone		
Morphine		
Other		

1

After 30 minutes within 45 minutes *(please circle)*



Additional Pain Medication	Dose	Time
Fentanyl		
Hydromorphone		
Morphine		
Other		

This Numerical Pain Scale is for the DNP project Use Only

2

Appendix H

Intraoperative Patient Form

DNP Project Intraoperative Patient Form

Date: _____

Surgery Start Time:_____

Intraoperative Analgesia	Dose	Time
Fentanyl		
Hydromorphone		
Morphine		
Other		

Significant Intraoperative Events: Yes_____ No_____

Comment (*If Applicable*):

Surgery End Time: _____

Provider: _____

For Intraoperative Use Only