Using Esmolol as an Adjunct to Prevent Postoperative Pain: An Educational Module

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Abstract

Background: Poorly managed postoperative pain can severely impact patient recovery and quality of life, potentially leading to prolonged opioid use and chronic pain. Effective multimodal pain management, including esmolol infusions, can mitigate these issues by reducing opioid dependence and recovery time. This project aims to educate anesthesia providers on using esmolol as a nonopioid adjunct for the management of postoperative pain, emphasizing its benefits over traditional opioid use. Esmolol has been shown to have antinociceptive properties reducing postoperative pain, opioid consumption, and related adverse effects without significantly altering hemodynamics. This project also explores the comparison between esmolol and dexmedetomidine, a well-known nonopioid adjunct, highlighting the need for future research on their efficacy in preventing postoperative pain. Addressing these knowledge gaps and incorporating esmolol into pain management strategies can improve patient outcomes, reduce opioid use, and enhance patient satisfaction.

Methods: Participant recruitment occurred via email, emphasizing voluntary participation and anonymity. Accessible on any smart device, the module begins with a pre-module assessment to gauge baseline knowledge and attitudes toward nonopioid adjuncts. Participants then viewed a voiceover PowerPoint on multimodal analgesia and esmolol's effectiveness, followed by a post-module assessment to measure knowledge gained and willingness to adopt new practices. Data from pre- and post-module assessments was stored securely in a password-protected Qualtrics account, anonymized for privacy, and manually entered into Microsoft. Comparative analysis determined statistical significance. The project is approved by the Institutional Review Board (IRB) of Florida International University.

Results: Provider knowledge and attitudes on incorporating esmolol into multimodal pain management strategies increased after viewing the educational module. Overall, there was an increase in knowledge from pre-test to post-test among all questions. There was a shift in provider attitude both away from the use of opioids and towards the implementation of esmolol into their practice.

Discussion: This project aimed to educate anesthesia providers on using esmolol as a nonopioid adjunct to prevent postoperative acute pain. The implementation site's strength lies in its potential to extend the project's impact through preceptorship. However, project limitations included a small sample size (n=11), single-center focus, and narrow distribution. Expanding to a multi-center study with a longer duration and diverse delivery methods could improve participation and reduce biases. The project's educational module, accessible online, included pre- and post-module assessments to evaluate provider knowledge and attitudes towards nonopioid adjuncts and opioid use. Although esmolol's nociceptive mechanism remains unknown, the project increased provider willingness to modify practices and adopt multimodal analgesia strategies. Advanced practice nursing requires continuous learning, continuously applying evidence-based practice to improve practice. Esmolol's cardioprotective properties and known side effects underscore the importance of up-to-date research, especially for the aging population. The project's focus on reducing opioid use aligns with the theory of unpleasant symptoms, aiming to prevent discomfort and long-term effects of acute pain, including chronic pain.

Keywords: Acute pain, chronic pain, opioid-related adverse effects, multimodal analgesia

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Introduction

Purpose

Postoperative pain can severely debilitate a patient. If not appropriately managed, acute postoperative pain can decrease a patient's quality of life and increase recovery time. Along with a delayed recovery time, these patients can face prolonged opioid usage and incur increased healthcare costs.[1] If pain is not appropriately managed and the patient requires hospital admission, this increases the burden on the healthcare system. Acute pain after surgery is a predictor of the development of chronic pain.[1] With more effective multimodal pain management, the incidence of prolonged acute pain and the progression toward chronic pain can be reduced. Incorporating esmolol infusions into multimodal pain management strategies is an effective cardioprotective and antinociceptive measure. Doing so reduces the need for postoperative opioids and reduces recovery time, increasing patient satisfaction.

The primary goal of this DNP project is to educate anesthesia providers about using esmolol as a nonopioid adjunct to prevent postoperative pain. These personnel will be educated about the negative effects of opioids, nonopioid adjunct options, and why esmolol can be a suitable option.

Problem Statement and Identification

Postoperative acute pain is not often managed in a way that optimizes each patient. Proper management is patient-specific and must aim to enhance patient recovery. Aside from numerous adverse effects, opioids can prolong a patient's recovery, decreasing patient satisfaction. Using multimodal analgesia by incorporating esmolol will decrease opioid-related adverse events, reduce postoperative pain, and increase patient satisfaction.

Background

Though there are many proposed mechanisms by which esmolol acts as an adjunct, research has shown that esmolol has antinociceptive properties.[2,3] Using esmolol perioperatively has been shown to reduce postoperative pain, opioid consumption, and postoperative nausea and vomiting.[4,5,6,7,8,9] Esmolol is not incorporated into Enhanced Recovery After Surgery (ERAS) protocols in numerous institutions. Rather than incorporate esmolol into an ERAS protocol, it would be prudent to create a protocol for orthopedic surgeries that integrates esmolol into its perioperative pain management strategies. Orthopedic surgery patients, specifically joint replacement patients, are often optimized for surgery as these are usually elective procedures. Though research also shows that esmolol does not dramatically alter hemodynamics when used as part of a multimodal pain regimen, the joint replacement patient is an ideal patient in which to incorporate esmolol due to many surgeons having a preference for permissive hypotension during these procedures.[10]

An area of potential improvement and further investigation in anesthesia is the comparison of esmolol and dexmedetomidine in preventing postoperative pain. Esmolol, a short-acting cardioselective beta-blocker, and dexmedetomidine, a selective alpha-2 agonist, have been utilized for various purposes in the perioperative period. Both medications affect hemodynamics and both must be used with caution.[11,12] Dexmedetomidine, unlike esmolol, has antisialogue effects and may lead to patient discomfort, though it is useful for intubation.[13] Though dexmedetomidine does not have strong analgesic properties, it is a useful adjunct.[13,14,15] Both drugs aid in providing stable hemodynamics throughout the perioperative period.

PICO

The efficacy of both esmolol and dexmedetomidine in preventing postoperative pain and their comparative effectiveness in this context would benefit from further exploration. To further investigate and evaluate this topic, the following PICO question is addressed: (P) In anesthesia providers, (I) does an educational module on the use of esmolol in multimodal pain management strategies to prevent postoperative pain, (C) compared to no educational module, (O) improve the knowledge and attitude regarding opioid-free pain management strategies? The population involved in this educational module includes patients undergoing elective joint replacement surgeries, as these patients are optimized for surgery and often require postoperative pain management.

Scope of the Problem

Postoperative pain management is a critical aspect of patient care, yet it is inadequately controlled in more than 80% of patients around the United States. This not only leads to increased morbidity and decreased quality of life but also prolonged opioid use and higher healthcare costs. Complications from poorly treated postoperative pain include an increased risk of developing postoperative complications ranging from infections to thromboembolic events. Inadequate pain control can lead to increased and prolonged opioid use. This increases a patient's risk for dependence, misuse, and addiction. Patients with poorly managed postoperative pain are at risk for prolonged hospitalizations and higher readmission rates, both of which incur higher healthcare costs.

Poorly managed postoperative pain is a significant problem that must be further investigated, as it is a predictor of the development of chronic pain.[1] Given these consequences, there is a need for ongoing research and improvement in postoperative pain management

strategies. This includes exploring multimodal approaches to pain control and minimizing opioid reliance. Addressing this issue can improve patient outcomes, reduce the burden of chronic pain, and lower healthcare costs associated with poor pain management strategies.

Addressing the comparative efficacy of esmolol and dexmedetomidine in preventing postoperative pain in joint replacement patients will lend insight into pain adjunct strategies. Decreasing the amount of opioids used will not only benefit patients but also anesthesia practice. This comparison has the potential to improve pain management strategies, optimize patient outcomes, and contribute to the advancement of evidence-based anesthesia care.

Consequences of the Problem

Failing to address postoperative pain and appropriate adjuncts can result in numerous negative consequences. When pain is not properly managed, patients often experience significant discomfort, which can contribute to heightened anxiety and emotional distress. This discomfort not only affects a patient's immediate well-being but can also diminish their overall satisfaction with their surgical experience. As a result, patients may develop increased anxiety or fear of subsequent surgeries or procedures.

Physiologically, inadequate pain control can impede a patient's recovery in several ways. Inadequate pain control can delay ambulation, which can lead to a higher risk of postoperative complications including deep vein thrombosis. Inadequate pain management can also impair respiratory function, increasing the risk of pulmonary complications such as pneumonia, atelectasis, and hypoxemia. Furthermore, poorly managed acute pain is linked to prolonged hospital stays and a higher incidence of postoperative cardiac events, particularly in vulnerable populations.

Insufficient pain control affects patients beyond the immediate postoperative period. Long-term consequences include the development of chronic pain, which can significantly reduce a patient's quality of life. The progression from acute to chronic pain can result in ongoing physical and psychological distress, emphasizing the importance of adequate postoperative pain control.

Knowledge Gaps

The exact mechanism by which esmolol provides antinociceptive effects is not entirely known. One group of researchers found that esmolol modulates inhibitory transmitter release in the substantia gelatinosa of the spinal trigeminal nucleus.[16] Other researchers researching esmolol and its impact on postoperative pain state that there is an unknown mechanism. Interestingly, Chia et al. compare postoperative pain and post-traumatic stress disorder (PTSD), stating that both are acute stress reactions. PTSD and acute-to-chronic stress reactions lead to increased epinephrine and norepinephrine secretion, increasing heart rate and blood pressure, a symptomatology they claim is similar to acute postoperative pain.[17]

Proposal Solution and Summary

Postoperative pain, if not properly managed, can severely affect a patient's quality of life, prolong recovery, and increase the risk of developing chronic pain. Poor pain control can also lead to prolonged opioid use, resulting in higher healthcare costs and an increased burden on the healthcare system. Effective multimodal pain management is essential to reduce the incidence of prolonged acute pain and its progression to chronic pain. One potential addition to these strategies is the use of esmolol infusions, which offer both cardioprotective and antinociceptive benefits. Esmolol has been shown to reduce opioid use, improve recovery times, and enhance patient satisfaction. The primary goal of this DNP project is to educate anesthesia providers

about the use of esmolol as a nonopioid adjunct for postoperative pain management, highlighting its benefits over traditional opioid-based approaches. The project aims to increase awareness about the negative effects of opioids and offer esmolol as an effective alternative.

Despite esmolol's benefits, it is not widely incorporated into ERAS protocols. However, joint replacement patients, often undergoing elective procedures and optimized for surgery, could particularly benefit from its use in perioperative pain management strategies. Incorporating esmolol into multimodal pain management strategies could further optimize patient outcomes, reduce opioid-related adverse events, and enhance recovery. By doing so, anesthesia providers can contribute to evidence-based practices that improve postoperative pain control and patient satisfaction while reducing the reliance on opioids.

Summary of the Literature

Literature Search Process

Research studies were gathered by inputting the below Boolean search phrases into PubMed, Embase, and CINAHL as the primary search engines. These search engines were chosen due to the abundance of scholarly articles available. Articles applicable to the clinical problem were then summarized in a table (Appendix 1).

Boolean search phrase 1: Esmolol[title/abstract]) AND (opioid OR pain) AND (anesth* OR anaesth* [Title/Abstract])

Boolean search phrase 2: Dexmedetomidine[title/abstract]) AND (opioid OR pain) AND (anesth* OR anaesth* [Title/Abstract])

Filters applied: Full free text, Full text, Randomized Controlled Trial, in the last 5 years

Inclusion and Exclusion Criteria

Inclusion criteria featured randomized controlled trials published in the last 5 years, written or translated in the English language. The included studies feature either dexmedetomidine or esmolol as an anesthetic adjunct. Important inclusion aspects are that either dexmedetomidine or esmolol are used as either an adjunct to prevent postoperative pain or other negative postoperative outcomes. Studies that did not highlight the potential effectiveness, or ineffectiveness, of these medications as adjuncts were excluded. Other included studies are those that defined postoperative pain and the mechanisms of both dexmedetomidine and esmolol.

Literature Appraisal and Literature Matrix

Appendix 1 features a literature matrix, reviewing eleven individual studies. These studies describe the effects of both dexmedetomidine and esmolol on postoperative pain and other negative postoperative events including postoperative nausea and vomiting (PONV). Nine of the studies are level II evidence (randomized controlled trials [RCT]), 1 is level I evidence (systematic review), and 1 is an animal study. Of the RCTs, 7 compare esmolol to a control, and 3 compare dexmedetomidine to a control.

Characteristics of the Included Studies

Song et al. conducted a single center, prospective, randomized controlled clinical trial testing the effects different esmolol concentrations have on both perioperative hemodynamics and analgesia in colectomy patients.[9] 125 patients undergoing a colectomy, aged 20-70, American Society of Anesthesiologists (ASA) physical status scores I-III, were placed into 3 groups. Group S, the control group, received saline at 0.75 mL/kg/hr 5 minutes before anesthesia induction, followed by a maintenance infusion of 0.25 mL/kg/hr. Two test groups, group E1 and group E2 received esmolol. E1 received 0.5 mg/kg esmolol 5 minutes before induction followed

by a 0.5 mg/kg/hr maintenance, and group E2 received 1.0 mg/kg esmolol 5 minutes before induction followed by a 2.0 mg/kg/hr maintenance.

This level II evidence study found that group S had both the highest number of intubation responses and the highest usage of nitroglycerin for blood pressure control. Group E2 showed less extubation response than both groups S and E1. Both E1 and E2 used less intraoperative opioids than group S. There was not a statistically significant difference between the opioid administration and pain scale after 48 hours in any group. From these results, authors concluded that esmolol administration before intubation inhibits the intubation response and that E2 reduces extubation responses. Esmolol decreases intraoperative opioid use without an increased risk of adverse reactions.

Authors of this study did highlight numerous limitations. Patients received nerve blocks prior to surgery, which may not have been equally effective in each patient. Gastrointestinal recovery (time to first flatus/ bowel movement) was not measured, and fluctuations in timing for intubation and extubation responses were not recorded and thus, may not have been reliable. Lastly, it would have been beneficial to monitor both mean arterial pressure (MAP) and heart rate (HR) every 5 minutes, rather than plotted hourly. One strength of this study is that the researchers tested 2 different esmolol concentrations. Because esmolol does not increase the incidence of persistent hypotension and bradycardia due to its half-life, there is no harm in reciprocating this study, as long as patients remain stable and medicated for any pain, as appropriate.

Lee et al. conducted a prospective, observer-blinded, randomized controlled study researching the effects of intraoperative esmolol and ketamine infusions on acute postoperative pain post a remifentanil-based anesthetic in laparoscopic cholecystectomy patients.[3] This study is

level II evidence. 60 patients, aged 20-70, ASA I-II, were randomly assigned to 3 groups: remifentanil + esmolol (esmolol group), remifentanil + ketamine (ketamine group), and remifentanil + normal saline (control group). Patients in the esmolol group received 0.5 mg/kg during induction with a 10 mcg/kg/min continuous infusion throughout the procedure. The ketamine group received 0.3 mg/kg during induction with a 3 mcg/kg/min continuous infusion throughout the procedure. Patients in the control group received normal saline during induction with a normal saline intraoperative infusion.

Researchers found that patients in the esmolol group took longer to awaken, post sevoflurane inhalation, than both the ketamine and control groups. There was, however, no difference in MAP, HR, and oxygen saturation among the groups. Both the esmolol and ketamine groups showed reduced pain scores and fentanyl requirements compared to the control group in the first 15 minutes post-operation, with no difference between both groups. The total amount of fentanyl administered during the first postoperative hour is lower in the ketamine and esmolol groups, with no difference between groups. Pain scores 1-6 hours postoperatively, along with analgesic use 1 hour post-operation, were not different among groups. None of the groups experienced nausea, vomiting, or lethargy. Intraoperative esmolol infusion during remifentanil-based anesthesia reduces pain scores and fentanyl requirements immediately postoperatively. There was not a statistically significant difference between outcomes in the esmolol and ketamine groups. Limitations of this study include a lack of differentiation between what kind of pain each patient may experience, along with the choice of only using 1 drug concentration for each group.

Watts et al. wrote a thorough systematic review/ meta-analysis utilizing OVID MEDLINE, OVID EMBASE, EBSCO, CINAHL, and the Cochrane Register of Controlled

Trials to find RCTs comparing esmolol with a placebo in adults receiving general anesthesia.[6] The purpose of this review was to determine the effect of perioperative esmolol on early postoperative pain. This review is level I evidence and identifies 338 studies, including 19 RCTs which feature 936 participants.

This review found that esmolol does not have an effect on emergence time, though it does reduce post-anesthesia care unit (PACU) pain scores. The postoperative morphine equivalent dose was reduced by 5.1 mg in those receiving esmolol, and esmolol reduced rescue opioid usage by 69%. Using esmolol as an adjunct can reduce postoperative pain and opioid consumption, along with reducing PONV. This review features an extensive search, rationales for future research, and a thorough explanation of what is currently understood. Researchers also found that the included trials have a high risk of bias and may have poorly reported adverse effects. Another limitation is that the timing and dose range for esmolol varied widely among studies.

de Morais et al. conducted a double-blind, placebo-controlled study researching the analgesic effects of intraoperative esmolol for laparoscopic gastroplasty patients.[7] This study is level II evidence. Forty patients, ages 18-50, ASA II-III, undergoing gastric bypass surgery were divided into 2 groups. Patients in group 1 received a 0.5 mg/kg esmolol bolus in 30 mL of saline before anesthesia induction, followed by a 15 mcg/kg/min infusion until the end of the procedure. Patients in group 2 received a 30 mL saline bolus, followed by a saline infusion. Both groups received a similar anesthetic, consisting of fentanyl, propofol, rocuronium, and sevoflurane. Remifentanil was given, if required.

Researchers found that pain scores were lower in the esmolol group, except at T0 after extubation and 12 hours postoperatively. Additionally, patients in the esmolol group required

less remifentanil supplementation, had a shorter recovery time, and required less postoperative morphine supplementation. There were no differences between groups in side effects or the time to the first analgesic request. From these results, researchers state that intraoperative esmolol is an effective drug for multimodal analgesia in gastroplasty patients without adverse effects, as it helped reduce both pain intensity and analgesic supplementation. Researchers describe a prophylactic antiemetic, which may have impacted medication-specific adverse effects. This prophylactic reduction of PONV is a limitation of this study.

Beloeil et al. conducted a prospective, multicenter, parallel-group, single-blind randomized control trial comparing pain control and postoperative opioid consumption with dexmedetomidine versus a balanced anesthetic with remifentanil.[12] This study is level II evidence and features patients older than 18 years old who are receiving major or intermediate noncardiac scheduled surgery. This trial took place in 10 centers in France. Patients were randomized into 2 groups, each containing 156 participants. Patients in the remifentanil group received intraoperative remifentanil and morphine, while patients in the dexmedetomidine group received an opioid-free anesthetic. Every patient received a similar anesthetic throughout the case, including both ketamine and lidocaine infusions, a nerve block, and a patient-controlled morphine infusion.

This study aimed to investigate numerous postoperative opioid-related adverse events that typically occur within 48 hours after extubation. Unfortunately, this study ended early due to 5 cases of severe bradycardia in the dexmedetomidine group. Even so, researchers found that 78% of the dexmedetomidine and 67% of the remifentanil group experienced postoperative opioid-related adverse events. 71% of the dexmedetomidine and 61% of the remifentanil group experienced hypoxia. There was no difference in either cognitive dysfunction or ileus between

groups. Lastly, the dexmedetomidine group experienced more incidences of delayed extubation and prolonged PACU stays. Researchers concluded that patients in the opioid-free anesthetic group were more commonly experiencing postoperative opioid-related adverse events.

This study features many limitations. Because the optimal dexmedetomidine dosing in general anesthesia is unknown, dexmedetomidine dosing was decided based on patient heart rate. Due to this, dosages varied, and that is a confounding variable in this study. Additionally, because postoperative hypoxemia is not explicitly defined, it is hard to determine whether or not all cases of postoperative hypoxemia are included due to the author-designed threshold.

Ye et al. conducted a prospective, randomized, double-blind single-center clinical trial studying the effects of dexmedetomidine on intraoperative hemodynamics, recovery profile, and postoperative pain in patients undergoing laparoscopic cholecystectomies.[14] This study is level II evidence and features 120 patients, divided into 4 groups. Three dexmedetomidine groups, D1, D2, and D3, received 0.4, 0.6, and 0.8 mcg/kg dexmedetomidine, respectively. The normal saline group received a similar amount of normal saline. Primary conditions that were measured included heart rate, blood pressure and cough incidence.

Researchers found that heart rate and blood pressure fluctuate less in groups D2 and D3 than in both D1 and the normal saline group. Groups D2 and D3 had less incidence of cough, lower pain scores, and lower tramadol requirements, than the normal saline group. Group D3 required more time until patients were ready for extubation. Researchers concluded that 0.6 mg/kg of dexmedetomidine was the optimal pre-induction infusion dose to maintain hemodynamic stability, decrease the incidence of coughing during emergence, and decrease postoperative pain.

This study's sample size was calculated by the incidence of coughing, which is considered a limitation. Additionally, other confounding variables, such as the other anesthetic agents used, could interact with dexmedetomidine dosing. Lastly, the tramadol dosage in groups D2 and D3 was less than D1 and the normal saline group.

Dereli et al. conducted a prospective study analyzing the effect of an intraoperative esmolol infusion on PONV, analgesic and anesthetic requirements in laparoscopic cholecystectomy patients.[5] This study is level II evidence. Sixty patients, 18-60 years old, were divided into 4 groups: group 1, esmolol infusion added to maintenance anesthesia, which consists of propofol and remifentanil; group 2, only propofol and remifentanil during maintenance anesthesia; group 3, esmolol infusion added to maintenance anesthesia, consisting of desflurane and remifentanil; group 4, only desflurane and remifentanil used during maintenance.

Researchers found that pain scores and PONV incidence were significantly lower in group I. PONV was lower in group III than IV. Though heart rates were lower in esmolol groups compared to both control groups, blood pressure was similar in all groups. From these results, researchers concluded that using esmolol during anesthesia maintenance decreases PONV, postoperative pain, and analgesic requirements. Though there is more research needed on this topic, Dereli et al. found that 3 other researchers found that there is not a significant difference between propofol, sevoflurane, and desflurane for postoperative pain prevention.

Bajracharva et al. conducted a prospective, randomized, double-blind, non-inferiority, randomized controlled clinical trial testing the effects of intraoperative lidocaine versus esmolol on postoperative analgesia in patients scheduled for laparoscopic cholecystectomy.[8] This study is level II evidence. 90 female patients scheduled for elective laparoscopic cholecystectomy were

divided into 2 groups: group 1 received a lidocaine bolus at 1.5 mg/kg at induction, followed by an infusion at 1.5 mg/kg/hr; group 2 received an esmolol bolus at 0.5 mg/kg at induction, plus an infusion of 5-15 mcg/kg/min until surgery stop.

Though median pain scores were similar between groups, researchers found that the postoperative mean morphine equivalent in patients receiving esmolol was 1 mg, while the mean equivalent in the lidocaine group was 1.5 mg. Additionally, there was a higher incidence of sedation in the PACU in patients receiving lidocaine. From these results, researchers concluded that an esmolol infusion is not inferior to lidocaine as an opioid-free analgesia adjunct. Esmolol is an effective adjunct to reduce opioid requirements and pain severity in the first 24 hours postoperative. Limitations include the sample, as only females were included, and sex could be a confounding factor. Additionally, there was no placebo group to control against. Lastly, intraoperative hemodynamics were not compared.

Chia et al. investigated esmolol's analgesic properties for managing postoperative pain in patients undergoing a hysterectomy by conducting a prospective, randomized, double-blind trial.[17] This study is level II evidence, and it enrolled 97 patients, ASA I-II, who were undergoing an abdominal total hysterectomy. These patients were randomly divided into 2 groups: the esmolol group, receiving a loading dose of 0.5 mg/kg followed by an infusion of 0.05 mg/kg/min and the normal saline group, who received a similar volume of normal saline. After the procedure, all patients were on a programmed patient-controlled analgesia (PCA) morphine pump for 3 days.

Patients in the esmolol group required less sevoflurane and fentanyl during the procedure. Additionally, these patients displayed a lower heart rate and blood pressure during intubation, incision, and extubation. Patients in the esmolol group required less postoperative morphine than

patients in the control group, though both groups reportedly had similar pain intensities and medication side effects. These results show that perioperative esmolol reduces patient requirements for inhalational anesthetics and fentanyl, decreases hemodynamic responses to stimulation, and reduces postoperative morphine consumption. Researchers state limitations as the lack of knowledge about esmolol's impact on opioid pharmacokinetics, as well as the healthy patient population possibly masking any possible cardiac events.

Rekatsina et al. conducted a double-blind randomized controlled trial investigating how both dexmedetomidine and lidocaine affect postoperative pain, opioid consumption, and functional recovery after abdominal gynecological surgery.[11] This study level II evidence. 91 women, aged 30-70 years old, who were undergoing either an abdominal hysterectomy or myomectomy, were randomized into 3 groups: dexmedetomidine, lidocaine, or placebo. Each group received a loading dose of 0.9 mL/kg/hr before anesthesia induction, which was followed by a 0.15 mL/kg/hr infusion until the procedure's end. Patients in the dexmedetomidine group received a bolus of 0.6 mcg/kg, followed by an infusion of 0.6 mcg/kg/hr. Patients in the lidocaine group received a bolus of 1.5 mg/kg, followed by a 1.5 mg/kg/hr infusion.

Researchers found that the lidocaine group required less morphine than patients in the control group and the dexmedetomidine group had fewer incidences of nausea than the control group. The dexmedetomidine group required less vasoconstrictors than the lidocaine group, which required less than the control group. Both lidocaine and dexmedetomidine are useful analgesia adjuncts after abdominal surgery. Both agents, specifically dexmedetomidine, required vasopressors for drug-induced hypotension. Lidocaine reduced postoperative opioid consumption more significantly, and dexmedetomidine prevented early postoperative nausea.

Study limitations included researchers not trialing different medication dosages and each drug solely being administered pre- and intraoperatively.

Nonopioid Adjuncts Reduce Opioid-Related Adverse Effects

Numerous nonopioid adjuncts are currently used in anesthesia practice to not only reduce postoperative pain but also to reduce the incidence of opioid-related adverse effects. Aside from potentially delaying discharge time, opioid side effects include respiratory depression, tolerance, physical dependence, constipation, nausea and vomiting, and sedation.[18] Several studies prove that esmolol, dexmedetomidine, and lidocaine are useful nonopioid adjuncts. These pharmacological agents, by decreasing opioid usage, decrease opioid-related adverse effects. A study conducted by Beloeil et al. did find that dexmedetomidine caused increased postoperative opioid-related adverse effects, but this was not a commonly found result.[12] Both esmolol and dexmedetomidine are useful in reducing the incidence of PONV.[5,6,11] Esmolol has varying effects on anesthesia recovery time, as Lee et al. determined that esmolol slows anesthesia wakeup and de Morais et al. found it hastens recovery time.[3,7] Watts et al. conducted a thorough systematic review and found that esmolol does not affect emergence time compared to a placebo.[6]

Using Nonopioid Adjuncts to Prevent Perioperative Pain

Nonopioid adjuncts not only prevent postoperative pain but also decrease anesthetic requirements intraoperatively. Esmolol decreases intraoperative fentanyl, remifentanil, morphine and sevoflurane requirements.[5,7,9,17] Watts et al. found that patients who received esmolol intraoperatively reported lower pain scores in PACU and required less rescue opioid administration.[6] de Morais et al. agreed, stating that patients receiving esmolol required less postoperative morphine compared to patients receiving a placebo.[7] Dereli et al. found the ideal

anesthetic for laparoscopic cholecystectomies is a total intravenous anesthetic (TIVA) consisting of esmolol, propofol, and remifentanil.[5] These patients reported less incidence of PONV and lower pain scores.[5]

An animal study conducted on Wistar rats found that esmolol modulates inhibitor transmitter release in the substantial gelatinous of the caudal part of the spinal trigeminal nucleus (sp5c). This occurs through a mechanism involving calcium entry in a $beta_1$ adrenoreceptor-independent manner.[16] Though this animal study explains that esmolol facilitates the release of inhibitory transmitters in the central nociceptive network, its mechanism in humans is not entirely understood. Lee et al. found that esmolol and ketamine both equally lowered pain scores and fentanyl requirements.[3] Bajracharya et al. determined that esmolol and lidocaine are both equally efficacious as nonopioid adjuncts.[8] Though esmolol's mechanism of action is unclear, it is proven to work as effectively as other nonopioid analgesic drugs. Besides esmolol, dexmedetomidine has proven to be a useful nonopioid adjunct.

Ye et al. trialed numerous dexmedetomidine doses, determining that 0.6 mcg/kg dexmedetomidine is ideal for decreasing postoperative pain.[14] Rekatsina et al. conducted a study comparing dexmedetomidine, lidocaine, and a placebo and found that both dexmedetomidine and lidocaine are useful nonopioid adjuncts.[11] Additionally, Rekatsina et al. found that lidocaine reduced postoperative opioid requirements.[11] Dexmedetomidine usage is not without fault, as numerous studies have found that there are negative hemodynamic consequences of its use.[11,12]

Hemodynamic Consequences of Various Adjuncts

Tracheal intubation, surgical stimulation, and tracheal extubation can cause a hemodynamic response in patients. Esmolol is a pharmacologic agent that decreases a patient's hemodynamic response to these stimuli.[17] Though esmolol is a drug that works on beta-

adrenergic receptors to decrease heart rate, it does not affect hemodynamics significantly when used as part of a balanced anesthetic.[3]

Dexmedetomidine is an appropriate nonopioid adjunct to prevent postoperative pain, but its use can result in hemodynamic instability. Beloeil et al. found that dexmedetomidine caused severe bradycardia, thus ending their study prematurely.[12] Ye et al. found that 0.6 mcg/kg was the ideal dexmedetomidine dose to not only decrease postoperative pain but to also maintain hemodynamic stability.[14] Rekatsina et al. did not trial numerous dexmedetomidine doses, though they stated that generally, patients receiving dexmedetomidine require vasopressors to maintain their blood pressure.[11]

Definition of Terms

Acute surgical pain describes pain following surgery-associated tissue injury. This pain should resolve while the patient heals in up to 3 months.[19]

Chronic pain/persistent pain is pain that lasts longer than 3 months.[19]

Opioid-related adverse effects include medication adverse effects post-opioid administration. These include respiratory depression, tolerance, physical dependence, constipation, nausea and vomiting, and sedation.[18]

Multimodal analgesia is the use of more than 2 analgesics or techniques, targeting different mechanisms and pathways.[20] Combining numerous drugs allows for lower doses of each drug, preserving the individual drug's efficacy and reducing side effects. The goal of multimodal analgesia is to improve analgesia, enhance a patient's functional recovery, and reduce opioid use and side effects.

Summary

Though the exact mechanism of action by which esmolol acts to reduce postoperative pain is unclear, numerous studies show that it is an effective nonopioid alternative. Of course, there are quite a few nonopioid options, and esmolol may not be a perfect option for every patient. Due to decreased opioid-related adverse effects and a limited impact on hemodynamics, it is an exceptional choice to prevent postoperative pain, added to a balanced anesthetic plan.

Objectives

The quality improvement project uses a pre- and post-module assessment and a PowerPoint presentation. Participants are deidentified and voluntarily participate after giving informed consent.

Primary DNP Project Goal

The primary goal of this DNP project is to educate anesthesia providers about using esmolol as a nonopioid adjunct to prevent postoperative pain. These personnel will be educated about the negative effects of opioids, nonopioid adjunct options, and why esmolol can be a suitable option. As this project will include a pre- and post-implementation assessment, increased provider knowledge about esmolol as a nonopioid adjunct and acceptance towards implementing a new practice are primary targets.

As postoperative pain is a well-known issue, more and more providers appear to use opioids as an analgesic of choice, neglecting to incorporate nonopioid adjuncts. Opioids are excellent for pain control, but provide a slew of negative outcomes. Numerous nonopioid adjuncts are currently used in anesthesia practice to not only reduce postoperative pain but also to reduce the incidence of opioid-related adverse effects. Aside from potentially delaying

discharge time, opioid side effects include respiratory depression, tolerance, physical dependence, constipation, nausea and vomiting, and sedation.[18]

Practitioners at this site often administer medications for pain management pre-, intra-, and postoperatively. Of note, acetaminophen and gabapentin are commonly given preoperatively, fentanyl and ketamine intraoperatively, and hydromorphone and Ofirmev postoperatively, as needed. Nonopioid adjuncts are not used more commonly for "bread and butter" cases, though patients receiving cardiac and gastrointestinal surgeries are often placed on an enhanced recovery after surgery (ERAS) protocol. Incorporating nonopioid adjuncts, such as esmolol, into more standard cases, as appropriate, will likely reduce opioid need and increase patient satisfaction.

SMART Objectives

For the purposes of this DNP quality improvement project, the following SMART objectives were identified:

- Assess baseline understanding of anesthesia providers on nonopioid adjuncts in treating postoperative pain before viewing the educational module
- Educate anesthesia providers on the benefits of using nonopioid adjuncts to decrease opioid usage within 3 months of starting the quality improvement project
- Ensure participants complete post-assessment within 30 days of viewing the educational module to measure understanding and willingness to adopt new practices

Framework

Conceptual Underpinning and Theoretical Framework

Nursing theories and theoretical frameworks are useful in organizing thoughts and determining the basis of ideas. Associating evidence-based practice with nursing theories helps

to ensure practices are complete, sound, and practical to carry out. This project most closely relates to Lenz, Suppe, Gift, Pugh, and Milligan's theory of unpleasant symptoms.[21]

Theory Overview

The theory of unpleasant symptoms (TOUS) implies that 1 symptom will contribute to the experience and management of others. Symptoms interact and influence one another, possibly in additive or multiplicative manners. The TOUS explains that the management of 1 symptom will aid in the management of others, terming these related symptoms "symptom clusters."[21] Management can focus on either 1 symptom or multiple symptoms. This theory applies to a large patient population, including the elderly.

According to the TOUS, symptoms have antecedent factors. These factors are physiological, psychological, and situational/environmental, interactive and reciprocal with each other and the patient's symptoms. The TOUS defines symptoms to have measurable characteristics. Symptom intensity, or severity, is determined by the patient using a pain scale or other descriptive measure. Timing includes the frequency, duration, and relation of the symptom to precipitating events. Distress describes the person's reaction to the symptom. Symptom quality describes the symptom and its location.[21] The TOUS hypothesizes that symptoms affect a person's performance, both functional and cognitive. This includes a person's ability to perform activities of daily living, solve problems, and think. Research shows that there is a relationship between cognition and symptom level.[21] According to the TOUS, symptoms and performance both affect one another.

The TOUS describes an individual's experience with an unpleasant symptom and any sequalae the symptom may cause. Numerous factors interrelate to generate a person's experience including the symptom, physiological, psychological and environmental variables, and physical,

cognitive and consequences of said symptom. Symptoms or symptom clusters have variable but measurable components.[21]

Theory Clinical Fit

Pain leads to numerous sequelae, including nausea and vomiting, respiratory depression, delayed functional recovery, and psychological distress. Postoperative acute pain has been shown to negatively affect a patient's recovery. As the TOUS focuses on an individual's experience with unpleasant symptoms, it is in the patient's best interest to receive a multimodal pain management strategy that aims to reduce unpleasant symptoms. These unpleasant symptoms include postoperative pain and opioid-related adverse effects.

Antecedent factors to postoperative acute pain include numerous situational factors, such as poor intraoperative pain management and surgical stimulus. Situational factors, as they are external to the patient, must be mitigated by the provider. A negative experience, which includes postoperative acute pain, can lead to emotional and psychological distress. A decline in functional and cognitive performance due to pain can lead to delayed recovery and readmissions.

Implementation Site

An Overview of the Implementation Site

The chosen implementation site is a large private, independent, not-for-profit teaching hospital in Florida. This large center contains more than 600 beds, 26 operating suites, and staff leaders in numerous fields. This site states its mission is to provide high-quality health care to a diverse community, enhanced through teaching, research, charity care, and financial responsibility.[22] This institution is the sole hospital on Miami Beach and has affiliate sites throughout Miami-Dade, Broward, and Monroe Counties. It emphasizes excellence in research

and in medical and surgical care, proving it to be an excellent candidate for implementing new evidence-based practices.

Description of the Program Structure

Miami-Dade County is still battling this country's opioid epidemic. Since 2000, death rates from opioid overdoses have increased by 200%. Opioid-related overdoses (OOD) are increasing especially with the rise of fentanyl use.[23] Because of this, and the vulnerable populations treated at this medical center, it is of great benefit to reduce the amount of opioids used perioperatively. This institution has a higher average length of stay and 15-day overall readmission rate for its patients.[24] Though the exact reasons are not published, it is known that using opioids can cause complications that lead to increased length of stay and hospital readmissions.[1] This center performs more than 100 hip replacements and more than 60 knee replacements a year.[24] Patients undergoing these elective procedures are generally healthy and low risk. Many of these patients receive nerve blocks and/or spinal anesthesia, but beginning to use nonopioid adjuncts in patients who do not qualify for regional and neuraxial anesthesia is a good first step to decreasing hospital-wide opioid use.

Organizational SWOT Analysis

Acknowledging the strengths, weaknesses, opportunities, and threats within an institution is integral to adopting new evidence-based practices. To successfully translate evidence into practice, the below qualities are addressed:

Strengths

This institution employs a private anesthesia group. This affords the group the privilege to make decisions within itself, without the politics and delays of a larger corporation. This

group truly cares about providing patients with the best outcomes. On top of this, this group also tries to keep up with current literature and ensure that best practices are being followed.

Weaknesses

As with anyone who has been in practice for a considerable amount of time, there is a trend of a reluctance to modify practice. When practitioners find something that they are comfortable with and that works for them, they are less likely to modify their practice. This institution forces production pressure on the operating room staff. Production pressure, aside from increasing workload and decreasing employee well-being, causes an increase in negative outcomes and errors.[25] With production pressure, anesthesia staff are rushed to set up rooms and may not have the time to do anything aside from their standard practices. Lastly, there is not a surplus of anesthesia staff at this institution, and there are no designated personnel to spend time on research and discovering new best practices.

Opportunities

Fortunately, this anesthesia group employs numerous anesthesia providers who are new to practice. Studies have shown that patients treated by older physicians, except those who treat a high volume of patients, have higher mortality than patients treated by younger physicians.[26] A newer class of anesthesia staff may be more likely to keep up to date on research and try incorporating more new evidence-based practices.

Threats

Threats to this organization incorporating new evidence-based practices include the cost of trying something new, along with the possibility of patient and surgeon dissatisfaction. Additionally, production pressure and the institutional culture of using opioids threaten a practitioner's individuality in using nonopioid adjuncts.

Methodology

Project Sponsor and Participants

Alexander Fukes, DNP, CRNA has been a selected project sponsor to aid in the implementation of this quality improvement project. Dr. Fukes is currently employed as a certified registered nurse anesthetist (CRNA) at the implementation site, adding valuable feedback and insight into the hospital's operations and current practices. Additional personnel important in this project's implementation include physician anesthesiologists, anesthesia residents, CRNAs, and student registered nurse anesthetists (SRNAs). These personnel will be educated on the administration of nonopioid adjuncts and current best practices.

Project participants will include CRNAs. The project will include 11 participants who will be educated on the negative impact of opioids and the use of esmolol as a nonopioid adjunct. This sample is integral to the goals of the project, as these practitioners are administering medications to treat postoperative pain regularly.

Participant Recruitment

Participants will be recruited by email. The recruitment email will emphasize voluntary participation and anonymity. Participants will receive a link to the quality improvement project, which includes a pre-module survey, a PowerPoint presentation, and a post-module survey. The quality improvement project was distributed to 35 practitioners, with 11 participating in the quality improvement project.

Implementation and Methods

The goals of this project are accomplished using a pre-/post-intervention design. The objective of the educational module is to educate anesthesia practitioners on the use of nonopioid

adjuncts, specifically esmolol, to prevent postoperative pain. The entirety of the educational module, including the pre- and post-module assessments, can be accessed on any smart device.

The first stage of this project includes a pre-module assessment, which will survey the participant's baseline knowledge on using nonopioid adjuncts, specifically esmolol, to prevent postoperative pain. The pre-module assessment will also ask questions related to the provider's attitude and willingness to adopt new multimodal strategies. This baseline assessment will be compared with the post-module assessment, allowing researchers to evaluate the impact of the educational module on the provider's knowledge and attitude on using esmolol as a nonopioid adjunct.

After completing the pre-module assessment, participants will access a voiceover PowerPoint presentation that discusses multimodal analgesia, current trends, and the use of esmolol as a nonopioid adjunct. The primary learning objective of the educational module is esmolol's effectiveness as a nonopioid adjunct. Participants will learn that esmolol is as effective as other adjuncts and that its use has few adverse effects. Through this module, participants will learn new techniques to increase patient satisfaction, comfort, and positive outcomes.

The last stage of this project includes a post-module assessment, which is identical to the pre-module assessment. This assessment aims to evaluate provider knowledge after viewing the PowerPoint. Aggregate scores will be compared between both, ascertaining provider willingness to adopt new multimodal analgesia practices. This pre-/post-assessment comparison provides data on the effectiveness of the educational module.

Data Collection and Management

Data is collected from pre- and post-module assessments. The data collected was stored in a password-protected Qualtrics account in a secure laptop, solely accessible by the project

team. Participants were deidentified and data was entered anonymously, preserving participant identity and study integrity. Results from the pre- and post-module surveys were manually input into Microsoft Excel using a double data entry method to ensure data was accurate and complete. A comparative analysis was performed on both sets of results, allowing the research team to determine statistical significance of the project.

Data Analysis

To ensure complete disclosure and thoroughness, descriptive statistics are used to summarize the demographics of participants. Participants were asked basic demographic questions including gender, age, ethnicity, position/title, level of education, and years of experience. These demographics provide a clear profile of the sample and allow for a better understanding of the sample. To compare data from both assessments, percent increase and sample number increase between data sets will be compared. This comparison shows change over time. Responses to all survey questions were reported, ensuring that no results were undisclosed, maintaining transparency in the presentation of findings. Analysis was both comprehensive and unbiased.

Protection of Human Subjects

Prior to any contact with participants, the Institutional Review Board (IRB) of Florida International University will approve the project. Participation in this quality improvement project requires the informed consent of each participant. Participation is voluntary, and withdrawing does not incur a penalty. Participation will be through an anonymous link and participant identifiers are not included. Though this project has no associated risks, aside from potential physical discomfort from positioning, it asks for 15-20 minutes of participants' time.

Results

Participant Demographics

Prior to viewing the educational module and completing the survey, participants responded to a set of questions related to participant demographics. This survey had a 100% completion rate from participants, and pre- and post-test demographics are identical. Results are summarized below in Table 1.

Table 1. Participant Demographics

Demographic	*n* (%)
Total Participants	11 (100%)
Gender	
Male	5 (45%)
Female	6 (55%)
Age	
30-39	5 (45%)
40-49	5 (45%)
50-59	0 (0%)
60-69	1 (9%)
>70	0 (0%)
Ethnicity	
Hispanic	7 (64%)
Caucasian	3 (27%)
African American	1 (9%)
Asian	0 (0%)
Other	0 (0%)
Position/ Title	
CRNA	11 (100%)
Level of Education	
Masters	1 (9%)
DNP	10 (91%)
Years of Experience	
>10	3 (27%)
5-10	2 (18%)
2-5	3 (27%)
1-2	2 (18%)
0-1	1 (9%)

Participants answered 6 questions before completing the survey. There were 11 (*n=11*) participants in this study, inclusive of 5 (*n=5*, 45%) males and 6 (*n=6*, 55%) females. Participant ages were 30-39 (*n=5*, 45%), 40-49 (*n=5*, 45%), and 60-69 (*n=1*, 9%). Participant ethnicities vary, with participants identifying as Hispanic (*n=7*, 64%), Caucasian (*n=3*, 27%), and African American (*n=1*, 9%). All participants were certified registered nurse anesthetists (CRNAs) (*n=11*, 100%) with either a doctoral (*n=10*, 91%) or masters (*n=1*, 9%) level of education. Lastly, participants were asked about their years of experience, with a range of experience represented: >10 years (*n=3*, 27%), 5-10 years (*n=2*, 18%), 2-5 years (*n=3*, 27%), 1-2 years (*n=2*, 18%), and 0-1 years (*n=1*, 9%).

Pre-Test Knowledge on Postoperative Pain

This set of 3 questions tested each participant's knowledge of the prevalence and effects of acute postoperative pain. Only 2 (*n=2*, 18%) participants were aware that postoperative pain is poorly controlled in 80% of patients in the United States. 82% of participants believed postoperative pain to be poorly controlled in 60% (*n=6*, 55%), 40% (*n=2*, 18%), or 25% (*n=1*, 9%) of the population, thus underestimating the problem at hand.

Next, participants were questioned on their knowledge of the effects of acute pain. A majority of participants (*n=7*, 64%) were correct in understanding that infection is not an effect of acute pain. The other participants (*n*=4, 36%) believed that delayed recovery is not an effect of acute pain. Lastly, participants were asked what other condition shares a similar symptomatology with acute pain. Most participants (*n=5*, 45%) were correct in choosing post-traumatic stress disorder, while other participants chose generalized anxiety disorder (*n=4*, 36%), primary hypertension (*n=1*, 9%), or chronic pain (*n=1*, 9%).

Pre-Test Knowledge on Esmolol's Use as a Nonopioid Adjunct

The next set of 5 questions tested participants' knowledge of using esmolol as a nonopioid adjunct. First, participants were asked which 3 drug requirements would decrease when esmolol is administered. 64% of participants (*n=7*) correctly chose fentanyl, remifentanil, and sevoflurane. 4 participants (36%) incorrectly chose a combination of other drugs. Selection options included fentanyl, remifentanil, Decadron, sevoflurane, and glycopyrrolate. Participants were next asked a true/false question about whether using esmolol decreases PONV. The majority of respondents (*n=8,* 73%) were correct in affirming that the statement was correct, while the other respondents (*n=3*, 27%) incorrectly selected "false."

Next, participant knowledge was tested on one of esmolol's proposed mechanisms of action. Specifically, this question asked about the mechanism by which esmolol acts as an antinociceptive drug. The majority of respondents (*n=6,* 55%) were correct in choosing that esmolol modulates inhibitory transmitter release in the substantia gelatinosa of the spinal trigeminal nucleus. Other responses included that esmolol works by slowing down the heart rate, thus slowing blood flow to the liver, allowing for a slower metabolism of pain medications (*n=1*, 9%), esmolol decreases bradykinin and histamine release, thus decreasing sensitivity to pain, edema and vasodilation (*n=2,* 18%), and esmolol interacts with first order neurons and modulates substance P release (*n=2,* 18%).

When esmolol is used as a non-opioid adjunct, the majority of respondents (*n=6*, 55%) were correct in stating that there is not a significant hemodynamic effect, as opposed to the 45% (*n-5)* who believed there is a significant hemodynamic effect. Lastly, participants were asked if esmolol produces inferior pain management to fentanyl. The majority of respondents (*n=7,* 64%)

were incorrect in stating that esmolol produces inferior pain management to fentanyl, while 36% (*n=4*) respondents were correct in that it does not.

Pre-Test Attitude on Incorporating Esmolol into Pain Management Strategies

The final 2 questions in the survey's pre- and post-test assessed provider attitude and willingness to both use less opioids and to incorporate esmolol into current pain management strategies. The first question assessed the participants' willingness to incorporate less opioids into their pain management strategies, with responses ranging from extremely unlikely (*n=1*, 9%), somewhat unlikely (*n=4*, 36%), somewhat likely (*n=2*, 18%), and extremely likely (*n=4*, 36%). Next, participant willingness to incorporate esmolol into their pain management was questioned. Responses ranged from extremely unlikely (*n=1*, 9%), somewhat unlikely (*n=2*, 18%), somewhat likely (*n=6*, 55%), and extremely likely (*n=2*, 18%).

Post-Test Knowledge on Postoperative Pain

After viewing the educational module, participants were presented with a post-test to test the effectiveness of the educational module. This post-test contained the same set of questions that participants answered in the pre-test. Provider knowledge increased from pre- to post-test in all domains. After viewing the educational module, 64% (*n=7*) of participants were correct in that postoperative pain is poorly controlled in 80% of patients in the United States. 36% (*n=4*) of participants selected that 60% of patients have poorly controlled postoperative pain. The majority (*n=9*, 82%) of participants were correct in stating that infection is not an effect of postoperative acute pain, while a small amount (*n=2*, 18%) incorrectly selected that delayed recovery is not an effect of acute pain. Lastly, all participants but 1 (*n=10*, 91%) agreed that acute postoperative pain and post-traumatic stress disorder share symptomatology. One

participant (9%) selected chronic pain. Table 2 below shows the overall increase in provider knowledge on postoperative pain.

Table 2. Provider Knowledge on Postoperative Pain

Question	Correct in Pre-Test (*n=11*)	Correct in Post-Test (*n=11*)	Difference
Postoperative pain is poorly controlled in what percentage of patients in the United States?	2	7	+250%
Which of the following is NOT an effect of acute pain?	7	9	+28.6%
Acute postoperative pain shares similar symptomology with which other condition?	5	10	+100%

Post-Test Knowledge on Esmolol's Use as a Nonopioid Adjunct

Provider knowledge was assessed after viewing the educational module, and scores increased on all 5 questions in this section. Participants (*n*=9, 82%) were correct in stating that using esmolol decreases patient requirements of fentanyl, remifentanil, and sevoflurane. 100% of participants agreed that using esmolol decreases PONV. This is a 37.5% improvement from pre-test results. 100% of participants additionally agreed on the mechanism of action by which esmolol acts as an antinociceptive drug. 83.33% more participants selected that this mechanism is by modulating inhibitory transmitter release in the substantia gelatinosa of the spinal trigeminal nucleus.

In the post-test, 82% (*n=9*) of participants were correct in stating that using esmolol as a non-opioid adjunct does not show significant hemodynamic effects and 73% (*n=8*) of participants agreed that esmolol does not produce inferior pain management to fentanyl. Table 3 below shows the overall increase in provider knowledge on esmolol's use as a nonopioid adjunct.

Table 3. Provider Knowledge on Esmolol's Use as a Nonopioid Adjunct

Question	Correct in Pre-Test (*n=11*)	Correct in Post-Test (*n=11*)	Difference
Using esmolol intraoperatively decreases patient requirements of which drugs?	7	9	+28.6%
True/false, using esmolol decreases PONV?	8	11	+37.5%
One proposed mechanism of action by which esmolol acts as an antinociceptive drug is:	6	11	+83.33%
True/false, using esmolol as a non-opioid adjunct has shown significant hemodynamic effects?	6	9	+50%
True/false, esmolol produces inferior pain management to fentanyl	4	8	+100%

Post-Test Attitude on Incorporating Esmolol into Pain Management Strategies

After completing the educational module, provider attitude towards pain management strategies changed. After viewing the educational module, 0% of providers selected that they were both extremely unlikely or somewhat unlikely to incorporate less opioids into pain management strategies. All providers chose that they were somewhat or extremely likely to incorporate less opioids into their practice. When asked about incorporating esmolol into pain management strategies, 0 providers, as opposed to 1 provider on the pre-test, were extremely unlikely to incorporate esmolol into pain management strategies. 1 provider was somewhat unlikely, with 10 providers either somewhat likely or extremely likely. Charts 1 and 2 provide a visual representation of the shift between attitudes, pre- and post-test. Table 4 summarizes provider attitudes on pain management strategies.

Table 4. Attitude on Incorporating Esmolol into Pain Management Strategies

Question	Pre-Test Response (*n=11*)	Post-Test Response (*n=11*)	Difference
How likely are you to incorporate less opioids into your pain management strategies?			
Extremely unlikely	1	0	-100%
Somewhat unlikely	4	0	-100%
Somewhat likely	2	5	+150%
Extremely likely	4	6	+50%
How likely are you to incorporate esmolol into your pain management strategies?			
Extremely unlikely	1	0	-100%
Somewhat unlikely	2	1	-50%
Somewhat likely	6	6	0%
Extremely likely	2	4	+100%

Figure 1. Pre- and Post-Test Comparison: Provider Attitude on Personal Opioid Incorporation

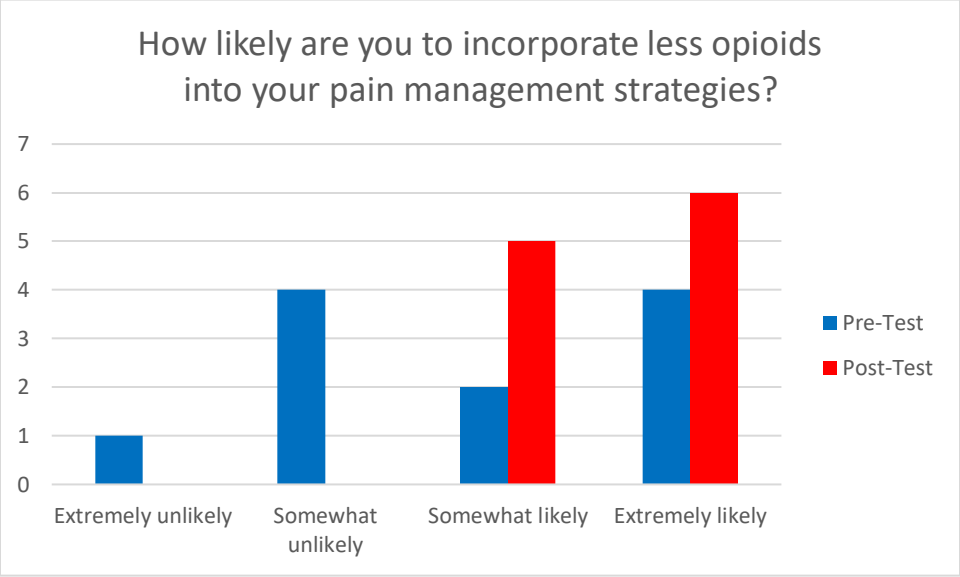
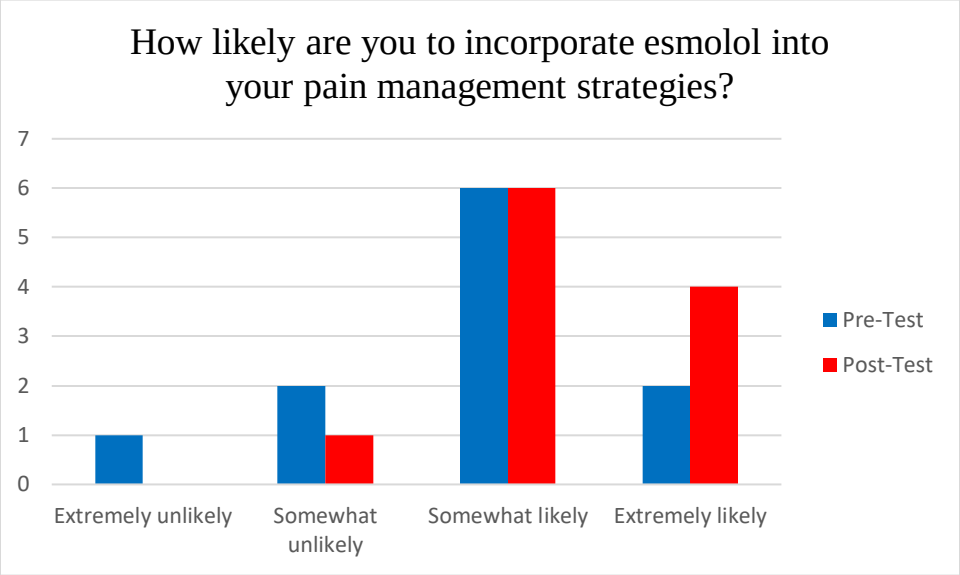


Figure 2. Pre- and Post-Test Comparison: Provider Attitude on Esmolol Incorporation



Summary

Overall, there was an increase in knowledge from pre-test to post-test among all questions. There was a shift in provider attitude both away from the use of opioids and towards the implementation of esmolol into their practice.

Discussion

Timeline

- IRB approval, 1 month
- Creation of educational module, 1 month
- Dissemination of information and response retrieval, 2 months
- Data analysis and results summary, 2 months
- Final defense preparation, 2 months

Strengths

Strengths of this project focus on the study population. The implementation site's strength lies in its potential to extend the project's impact through preceptorship, as the implementation site is a large teaching hospital.

Limitations

Limitations of this study include the small sample size (n=11) and narrow distribution. This single-center project was disseminated solely to 1 anesthesia group at 1 hospital. A multi-center study featuring numerous anesthesia groups would increase sample size, decrease institutional biases, and increase population diversity. Additionally, the short timeframe of this project was a barrier to collecting responses. Having more time to distribute and collect responses would likely yield a higher sample size. Lastly, including other delivery methods would likely increase participation, as online delivery barriers could be surpassed.

Future studies on this topic would benefit from a larger sample size, spanning numerous institutions. Research and educational module dissemination can be both online, as accomplished in this project, and by other methods.

Discussion of the Results with Implications for Advanced Practice Nursing

It was anticipated that providers gain new knowledge regarding multimodal analgesia and nonopioid adjuncts after the completion of this educational module. Esmolol's nociceptive mechanism of action remains unknown, thus many providers are not incorporating it into their anesthetic plan of care. The project team anticipated participant willingness to modify their current practice. Participant knowledge on the adverse effects of opioids would likely not increase significantly after viewing the PowerPoint, though provider attitude towards opioid usage was expected to change.

Becoming an advanced practice nurse is a commitment to lifelong learning. In medicine, new discoveries have the ability to change practice, which is ever-evolving. Until recently, the mechanism of action for inhaled anesthetic agents (IAA) was not known. Scientists now have a more thorough understanding of just how these compounds produce general anesthesia, but these agents were used, and sometimes relied on, before there was an understanding of their mechanism of action.[27] Though there was not a deep understanding of how IAA produce a state of general anesthesia, their side effects were more understood. Just as scientists have yet to uncover esmolol's mechanism of action in preventing postoperative pain, its cardioprotective properties and side effects are known.

As an advanced practice nurse, it is important to always keep up-to-date with research. Doing so ensures safe practice and patient optimization. With an aging population, it is important that changes in drug metabolism are considered in every drug administration. Increased adipose tissue, decreased total body water, decreased muscle mass, decreased plasma protein binding, and increased circulation time changes drug pharmacokinetics. Decreased renal and hepatic blood flow, in addition to decreased glomerular filtration and hepatic function, cause reduced drug clearance.[28] Esmolol is rapidly metabolized and eliminated at a rate that exceeds cardiac output.[29] Esmolol metabolism was believed to be by esterases in red blood cell cytosol.[30] New research, however, is showing that esmolol is hydrolyzed in white blood cells and platelets.[29] Because of the pharmacokinetics of esmolol, it is safe for the aging population, especially as its use yields fewer opioid-related adverse effects.[5,6]

Conclusion

The primary goal of this DNP project was to educate anesthesia providers on the use of esmolol as a nonopioid adjunct to prevent postoperative acute pain. This project's

implementation site was a large teaching hospital that provides high-quality care to a diverse community, emphasizing teaching, research, charity work, and financial responsibility. Because postoperative pain is typically managed by using opioids, this project will benefit the target community at the implementation site. Using nonopioid adjuncts decreases the amount of opioids needed, which decreases the incidence of opioid-related adverse events.

This project included an educational module, bookended with a pre- and post-module assessment. These assessments analyzed provider knowledge on the use of nonopioid adjuncts and how they fit into clinical scenarios at the implementation hospital. Providers were asked the same set of questions after viewing the educational module. By analyzing the amount of correct respondents pre- and post-educational module, it was possible to assess the efficacy of the educational module. The theory of unpleasant symptoms describes the goals of the project, which include preventing discomfort and the long-term effects of acute pain, including chronic pain.

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Appendix A: Summary of the Literature Table

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Song et al., 2021[9]	Single center, prospective, randomized controlled clinical trial 125 colectomy patients were placed into 3 groups Group S = saline, 0.75 ml/kg/hr saline 5 minutes before anesthesia induction, maintenance of 0.25 ml/kg/hr Group E1 = 0.5 mg/kg esmolol 5 min before induction, maintenance 0.5 mg/kg/hr Group E2 = 1.0 mg/kg esmolol 5 min before induction, maintenance 2.0 mg/kg/hr	152 patients ages 20-70, ASA I-III, undergoing colectomy from 7/20/2019-8/31/2020 à 138 randomly split into 3 groups after 14 were excluded à 4 patients excluded à 9 did not follow up à 125 final count Location: The Second Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, China	IV1= saline infusion (group S) IV2= lower dose esmolol infusion (group E1) IV2= higher dose esmolol infusion (group E2) DV1= intubation response DV2= extubation response DV3= changes in MAP DV4= changes in HR DV5= pain score DV6=intraoperative opioid use DV7= amount of opioids within 48 hours after surgery DV8= pain scale within 48 hours after surgery	DV1: nominal DV2: nominal DV3: ratio DV4: ratio DV5: ordinal DV6: ratio DV7: interval DV8: ordinal Kolmogorov-Smirnov was used to test normal distribution; ANOVA; frequency and Chi-square for nominal data; ordinal data used median for statistics; Kruska;-Wallis test to compare overall differences; Wilcoxon test if $P < 0.05$	MAP & HR: statistical significance in time points MAPT4, HRT2, HRT5, HRT6, HRT8 among all 3 groups, no statistically significant difference between both E groups. MAPT8 was lowest in E2. Group S: highest number of intubation responses. Extubation responses: E2 << S and E1. Nitroglycerin was used more in group S. Intraoperative opioids: E1 and E2 << S No difference between amount of opioids and pain scale after 48 hours	E1 and E2 before intubation inhibits the intubation response, E2 reduces extubation response. Esmolol decreases intraoperative opioid use without an increased risk of adverse reactions.	Limitations: nerve block performed may not have been equally effective in each patient; did not measure patient GI recovery; timing for intubation and extubation reactions may not have been reliable, and fluctuations were not recorded. Authors suggest monitoring MAP and HR every 5 minutes. Esmolol does not increase incidence of persistent hypotension and bradycardia due to its half-life. Because of this, there is no harm for reciprocating this study, as long as patients remain stable and are medicated for pain, as appropriate. Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/ Level
Lee et al., 2014[3]	Prospective, observer-blinded, randomized, controlled study Esmolol group: 0.5 mg/kg during induction with 10 mcg/kg/min continuous infusion during the procedure Ketamine group: 0.3 mg/kg induction, 3 mcg/kg/min continuous infusion Control group: normal saline during induction with infusion intraoperatively	60 patients, age 20-70, ASA I&II, laparoscopic cholecystectomy, who met inclusion criteria were randomly assigned into 3 groups: remifentanil + esmolol (esmolol group), remifentanil and ketamine (ketamine group), remifentanil + normal saline (control group)	IV1: esmolol induction and infusion IV2: ketamine induction and infusion IV3: saline induction and infusion DV1: MAP DV2: HR DV3: spO2 DV4: pain score D5: fentanyl requirement post op D6: wakeup time	DV1: ratio DV2: ratio DV3: ratio DV4: ordinal DV5: ratio DV6: ratio Chi-square; Fisher's exact test for categorical variables; parametric analysis ANOVA and non-parametric Kruskal-Wallis for continuous variables	Wakeup time: esmolol >>ketamine & control No difference in MAP, HR, spO2 Esmolol and ketamine groups have reduced pain scores and fentanyl requirements compared to the control group for the first 15 minutes with no difference between groups Total amount of fentanyl administered during the first postoperative hour is lower in the ketamine and esmolol groups, with no difference between groups Pain score from 1-6 hours postop and analgesic use 1 hour post op was not different between groups No group experiences nausea, vomiting, lethargy, etc	Intraoperative esmolol infusion during remifentanil-based anesthesia reduces pain scores and fentanyl requirements immediately postoperatively. There was not a statistically significant difference between outcomes in the esmolol and ketamine groups.	Limitations include a lack of differentiation between what kind of pain the patient could be experiencing, Esmolol does not increase incidence of persistent hypotension and bradycardia due to its half-life. Because of this, there is no harm for reciprocating this study, as long as patients remain stable and are medicated for pain, as appropriate. Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Watts et al., 2017[6]	This systematic review/ meta-analysis used OVID MEDLINE, OVID EMBASE, EBSCO, CINAHL, and the Cochrane Register of Controlled Trials to find RCTs comparing esmolol with a placebo in adults receiving general anesthesia.	Excluded studies: Esmolol vs opioids Studies only looking at hemodynamic responses Studies looking at esmolol effects on arrhythmia, ECT, ICP, BIS attenuation 338 studies identified, 19 RCTs were included, which includes: 936 participants (n=470 esmolol, n=466 placebo)	IV1: esmolol DV1: pain scores DV2: intraoperative opioid consumption DV3: postoperative opioid consumption DV4: emergence time DV5: PONV DV6: anesthetic requirement Primary outcomes: Early (0-6 hours) pain scores at rest Opioid consumption Rescue analgesic administration Secondary outcomes: Emergence time PONV Intraoperative anesthetic requirement Adverse events (bradycardia, hypotension)	Cochrane collaboration's tool was used to assess the risk of bias within each study I^2 and chi-square test goodness of fit For placebo-controlled trials: Fisher's exact test compared the incidences of esmolol-related hypotension and bradycardia	Esmolol does not have an effect on emergence time Esmolol reduced PACU pain scores Postoperative morphine equivalent dose was reduced by 5.1 mg Esmolol reduced rescue opioid use by 69%	Using esmolol as an adjunct can reduce postoperative pain and opioid consumption, along with PONV.	Limitations: timing and dose range for esmolol varied widely among studies. Poorly reported adverse effects. High risk of bias within trials Strengths: Widely extensive search Entire present understanding presented Rationales for future research Evidence level I

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Beloeil et al., 2021[12]	Investigator-initiated, prospective, multicenter, parallel-group, single-blind randomized controlled rial Patients were randomized to 1 of 2 groups: Remifentanil group = standard anesthesia with intraoperative remifentanil + morphine Opioid-free group = standard anesthesia with intraoperative dexmedetomidine	>18 years old, major or intermediate noncardiac scheduled surgery, rigid exclusion criteria 10 centers in France	IV1: remifentanil + morphine IV2: dexmedetomidine Primary composite outcome = postoperative opioid-related adverse events (DV1a hypoxemia, DV1b ileus, DV1c cognitive dysfunction) within 48 hours post extubation Secondary outcomes = DV2a postoperative pain, DV2b opioid consumption, DV2c PONV	DV1: ratio DV2a: ordinal DV2b: ratio DV2c: ordinal Chi-squared, independent samples *t* test, Mann-Whitney test, Q plots	Primary composite outcome: 78% dexmedetomidine group 67% remifentanil group Hypoxemia: 72% dexmedetomidine group 61% remifentanil group No differences in ileus or cognitive dysfunction Dexmedetomidine group: More delayed extubation, prolonged PACU stay	Patients receiving opioid-free anesthesia were more commonly experiencing the primary outcome, which consisted of postoperative hypoxemia, ileus, and cognitive dysfunction. Due to severe bradycardia induced by dexmedetomidine (n=5), the study was terminated early.	Limitations: Dosage depended on heart rate Optimal dosing of dexmedetomidine in GETA is unknown Postoperative hypoxemia isn't a clear definition, and the authors possibly saw more hypoxemia due to their defined threshold Scales were not standardized There is a risk of replicating this study, as there were cases of severe bradycardia. It would be interesting to conduct another study and explore how different doses of dexmedetomidine effect the results. Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
de Morais et al., 2020[7]	Prospective, randomized, comparative, double-blind, paired sample Groups 1: esmolol, 0.5 mg/kg bolus in 30 mL saline before induction & 15 mcg/kg/min continuous infusion until procedure end Group 2: control, 30 mL saline bolus & saline infusion	40 patients, age 18-50, ASA II and III, laparoscopic bypass gastroplasty IGESP Hospital, São Paulo, Brazil	IV1: esmolol DV1: consumption of intraoperative remifentanil DV2: time to first drug DV3: pain intensity DV4: 24 hour morphine dose DV5: side effects Primary outcome: pain intensity reduction Secondary outcomes: remifentanil requirement, morphine dose, adverse effects	DV1: ratio DV2: ratio DV3: ordinal DV4: ratio DV5: nominal Wilcoxon, chi-square, Fisher's test	Pain was lower over 24 hours in the esmolol group, excluding hours T0 and after 12 hours Needed postoperative morphine: 17/20 esmolol, 20/20 saline Morphine dose was lower in esmolol group No difference in time to first pain medication or side effects between groups Intraoperative remifentanil requirements: 3/20 esmolol, 17/20 saline with a higher dose requirement in the saline group Wakeup time was shorter in esmolol group	Esmolol can be used in an opioid-sparing anesthetic technique. Esmolol contributes to a better recovery from anesthesia.	Limitations: PONV may have been attenuated by prophylactic antiemetic, masking adverse effects Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Dereli et al., 2014[5]	Prospective study Groups: I: esmolol infusion added to maintenance (propofol and remifentanil) II: only propofol and remifentanil during maintenance III: esmolol infusion added to maintenance anesthetics (desflurane and remifentanil) IV: only desflurane and remifentanil used during maintenance	60 patients, 18-60 years old, laparoscopic cholecystectomy Brazil	IV: esmolol DV1: 24 hour postoperative pain DV2: PONV	DV1: ordinal DV2: ordinal Frequency distribution analysis ny Kolmogorov-Smirnov's test, one-way ANOVA or Kruskal-Wallis tests, Tukey test for post hoc analysis, chi-square of Fisher's tests	Pain scores and PONV incidence was significantly lower in group I PONV was lower in III than IV HR was lower in esmolol groups compared to controls BP was similar in all groups	Using esmolol during the maintenance of anesthesia decreases analgesic requirements, postoperative pain, and PONV.	Limitations: More research needed 3 other researchers found that there is not a significant difference between propofol, sevoflurane, and desflurane for post operative pain prevention Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Bajracharya et al., 2019[8]	Prospective, randomized, double-blind, non-inferiority clinical trial Groups: 1: IV lidocaine bolus 1.5 mg/kg at induction followed by an infusion (1.5 mg/kg/hr) 2: IV bolus esmolol 0.5 mg/kg at induction + 5-15 mcg/kg/min infusion until surgery end	90 female patients, elective laparoscopic cholecystectomy BP Koirala Institute of Health Sciences	IV1: esmolol DV1: Primary outcome: opioid consumption in first 24 hours postoperative DV2: pain scores DV3: sedation scores DV4: time to first perception of pain DV5: time to first void DV6: PONV	DV1: ratio DV2: ordinal DV3: ordinal DV4: ratio DV5: ratio DV6: nominal Normality was checked using histograms, Skewness-Kurtosis test, and Shapiro-Wilk test; normally distributed data were compared using the unpaired Student *t*-test; Mann-Whitney U-tests for continuous non-normally distributed and ordinal data; pain comparison using mixed effects model; categorical variables used Chi-square test; time to first pain perception plotted with Kaplan-Meier survival curves, compared with log-rank test	Postoperative mean morphine equivalent in esmolol-receiving patients was 1 mg, lidocaine group was 1.5 mg. Median pain scores were similar between groups More lidocaine-receiving patients were sedated in PACU	Esmolol infusion is not inferior to lidocaine for opioid requirement and pain severity 24 hours post operatively. Additionally, patients who received lidocaine were more sedated in the PACU than were those receiving esmolol.	Limitations: Only females were enrolled, and sex could be a confounding factor No placebo group Intraoperative hemodynamics weren't compared Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Chia et al., 2004[17]	Prospective, randomized, double-blind trial Esmolol group: IV loading dose 0.5 mg/kg, 0.05 mg/kg/min infusion before induction Control group: received normal saline	97 ASA 1-2, abdominal total hysterectomy Kaohsiung Veterans General Hospital, School of Medicine, Taiwan	IV1: esmolol DV1: Pain intensity on movement DV2: Pain intensity at rest DV3: Sedation score DV4: Side effects	DV1: ordinal DV2: ordinal DV3: ordinal DV4: nominal ANOVA with post-hoc Bonferroni's adjustment; X2 test or Fisher's exact test, Mann-Whitney U-test, priori power analysis	Esmolol group received less isoflurane and fentanyl during anesthesia Esmolol group had a reduced HR and BP response to intubation, incision, and extubation Esmolol group consumed less PCA morphine in 3 days Pain intensity and medication side effects did not differ between grops	Perioperative esmolol administration reduces intraoperative inhaled anesthetic and fentanyl administrations, decreases hemodynamic response, and reduces postoperative morphine consumption in the first 3 days.	Limitations: not enough is known about the impact of esmolol on the pharmacokinetics of opioids Lack of cardiac events during the study could be due to the healthy patient population Evidence level II

Citation	Design/Method Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Yasui et al., 2011[16]	Animal study Wistar rats (7-21 days. Weighing 17-50 g) were anesthetized with intraperitoneal ketamine or isoflurane and then decapitated. Horizontal slices of the lower brainstem, containing the substantia gelatinosa of the caudal part of the spinal trigeminal nucleus (sp5c) were made with a vibrating slicer. Tokyo, Japan	Effects of esmolol on spontaneous action potential-independent postsynaptic currents in the SG neurons of Sp5C	Nonparametric Mann-Whitney's U test for normalized values Student paired-t test Curve-fitting function of Igor Pro	500 microM esmolol significantly and selectively increased the mIPSC frequency, but not that of mEPSCs, without changing their amplitude. The increase in mIPSC frequency with esmolol was not affected by prior activation of beta receptors with 100 microM isoproterenol, but was significantly attenuated by removal of extracellular Ca2+	Esmolol modulates inhibitory transmitter release in the Sp5c through a mechanism involving Ca2+ entry in a B1 adrenoceptor-independent manner The facilitation of inhibitory transmitter release in the central nociceptive network underlies in part by the antinociceptive effect of esmolol	Not a human study, would be interested to see the translation this could have to human studies to determine if esmolol similarly works in the spinal cord.

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Rekatsina et al., 2021[11]	Double-blind randomized controlled trial Three groups: Dexmedetomidine (DEX) group Lidocaine (LIDO) group Placebo (CONTROL) group Before induction, each group received a loading dose (IV) of 0.9 mL/kg/hr over 10 minutes followed by a 0.15 mL/kg/hr infusion until the last suture	91 women, 30-70 years of age, ASA I-II, who are scheduled for either an abdominal hysterectomy or myomectomy Aretaieio University Hospital, Athens, Greece	IV1: DEX group IV2: LIDO group IV3: CONTROL group Primary outcomes: DV1: Cumulative morphine consumption DV2: Postoperative pain at rest DV3: Cough Other outcomes measured: sevoflurane consumption Nausea/vomiting Postoperative sedation Time to first flatus/ bowel movement Mobilization Sleep quality Satisfaction Discharge time Drug side effects	DV1: ratio DV2: ordinal DV3: nominal	Cumulative morphine consumption in: LIDO<CONTROL Incidences of nausea: DEX<CONTROL Use of vasoconstrictors: DEX<LIDO<CONTROL	Both lidocaine and dexmedetomidine are useful analgesia adjuncts after abdominal surgery. Both agents, specifically dexmedetomidine, required vasopressors for drug-induced hypotension. Lidocaine reduced postoperative opioid consumption more significantly, and dexmedetomidine prevented early postoperative nausea.	Study limitations included researchers not trialing different medication dosages and each drug solely being administered pre- and intraoperatively. Perhaps utilizing different dosages of dexmedetomidine and lidocaine would have yielded different results. Evidence level II

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement and Data Analysis	Findings & Results	Conclusions	Appraisal: Worth to Practice/Level
Ye et al., 2021[14]	Prospective, randomized, double-blind, single center clinical trial 120 patients divided into 4 groups: D1=dexmedetomidine 0.4 mcg/kg D2=dexmedetomidine 0.6 mcg/kg D3=dexmedetomidine 0.8 mcg/kg NS= normal saline	120 patients scheduled for elective laparoscopic cholecystectomy, 18-60 years old, BMI 18.5-28, ASA I-II Affiliated Hospital of North Sichuan Medical College	IV1: normal saline IV2: dexmedetomidine DV1: HR DV2: BP DV3: cough DV4: time of spontaneous respiratory recovery and extubation DV5: visual analogue scale score DV6: tramadol dose	DV1: ratio DV2: ratio DV3: ratio DV4: interval DV5: ordinal DV6: ratio One-way ANOVA with a post hoc analysis, Bonferroni correction, Pearson's X^2 test or *Fisher's* exact test	HR & BP of D2 and D3 groups had smaller fluctuations at times T2-3 and T7 vs. NS and D1 Cough incidence was lower in D2 and D3 than NS Pain score and tramadol doses in D2 and D3 were lower than NS group Spontaneous respiration recovery time and extubation times was longest in D3	0.6 mcg/kg dexmedetomidine, prior to induction, maintains hemodynamics, decreases emergence cough, and relieves postoperative pain in laparoscopic cholecystectomy patients.	Limitations: Cough incidence was used to calculate sample size Confounding variables existed, including other anesthetics used and other doses that could interact with the dexmedetomidine Tramadol dosing in D2 and D3 << NS and D1 Replicating this study while maintaining other anesthetic variables would provide useful data. Evidence level II

Appendix B: IRB FIU

FIU | FLORIDA INTERNATIONAL UNIVERSITY

Office of Research Integrity
Research Compliance, MARC 430

MEMORANDUM

To:	Dr. Fernando Alfonso
CC:	Melanie Grossman
From:	Kourtney Wilson, MS, IRB Coordinator KMW
Date:	February 14, 2024
Protocol Title:	"Using Esmolol as an Adjunct to Prevent Postoperative Pain: An Educational Module"

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #: IRB-24-0061 **IRB Exemption Date:** 02/14/24
TOPAZ Reference #: 114004

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
3) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

KMW

Appendix C: Informed Consent

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CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT
Using Esmolol as an Adjunct to Prevent Postoperative Pain: An Educational Module

SUMMARY INFORMATION
Things you should know about this study:

- **Purpose:** Educational module to increase providers awareness of the use of esmolol in multimodal pain management strategies.
- **Procedures**: If the participant chooses to participate, they will be asked to complete a pretest, watch a voice PowerPoint, and then a post test
- **Duration:** This will take about a total of 20 minutes.
- **Risks**: There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.
- **Benefits:** The main benefit to you from this research is increase the participants knowledge on the use of esmolol in multimodal pain management strategies.
- **Alternatives:** There are no known alternatives available to the participant other than not taking part in this quality improvement project.
- **Participation:** Taking part in this quality improvement project is voluntary.

Please carefully read the entire document before agreeing to participate.

NUMBER OF STUDY PARTICIPANTS:

If the participant decides to be in this study, they will be 1 of approximately 10 people in this research study.

PURPOSE OF THE PROJECT

The participant is being asked to be in a quality improvement project. The goal of this project is to increase providers' knowledge on the use of esmolol in multimodal pain management strategies, with the goal of decreasing narcotic use and postoperative pain. If you decide to participate, you will be 1 of approximately 10 participants.

DURATION OF THE PROJECT

The participation will require about 20 minutes

PROCEDURES

If the participant agrees to be in the project, PI will ask you to do the following things:
1. Complete an online 10 question pre-test survey via Qualtrics, an Online survey product for which the URL link is provided
2. Review the educational PowerPoint Module lasting 15 minutes via Qualtrics, an Online survey product for which the URL link is provided.
3. Complete the online 10 question post-test survey via Qualtrics, an Online survey product for which the URL link is provided.

RISKS AND/OR DISCOMFORTS

The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.

BENEFITS

The following benefits may be associated with participation in this project:
Increased participants knowledge on the the use of esmolol as an adjunct to prevent postoperative pain, and as a result, decreasing narcotic use.The overall objective of the program is to increase the providers' knowledge based on the current literature.

ALTERNATIVES

There are no known alternatives available to the participant other than not taking part in this project. However, if the participant would like to receive the educational material, it will be provided to them at no cost.

CONFIDENTIALITY

The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, PI might publish, it will not include any information that will make it possible to identify the participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this quality improvement project is voluntary.

COMPENSATION & COSTS

There is no cost or payment to the participant for receiving the health education and/or for participating in this project.

RIGHT TO DECLINE OR WITHDRAW

The participation in this project is voluntary. The participant is free to participate in the project or withdraw the consent at any time during the project. The participant's withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove the participant without their consent at such time that they feel it is in their best interest.

RESEARCHER CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Melanie Grossman (631-316-0538 or mgros066@fiu.edu) or Dr. Fernando Alfonso (305-348-3510 or falfonso@fiu.edu).

IRB CONTACT INFORMATION

If the participant would like to talk with someone about their rights pertaining to being a subject in this project or about ethical issues with this project, the participant may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT

I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions I have about this study, and they have been answered for me. By clicking on the "consent to participate" button below I am providing my informed consent.

Appendix D: Letter of Support

January 15, 2024

Fernando Alfonso, DNP, CRNA, APRN
Clinical Assistant Professor
Department of Nurse Anesthesiology
Florida International University

Dr. Alfonso,

Thank you for inviting Mount Sinai Medical Center to participate in the Doctor of Nursing Practice (DNP) project conducted by Melanie Grossman entitles "Using Esmolol as an Adjunct to Prevent Postoperative Pain: An Educational Module" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthesiology at Florida International University. I have granted the student permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best outcomes for patients by selecting interventions supported by the evidence. This proposed quality improvement project seeks to utilize the latest literature to increase providers awareness regarding using esmolol in multimodal pain management strategies, with the goal of decreasing narcotic use and postoperative pain.

We understand that participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password encrypted digital cloud, and only be accessible to the investigators of this study: Melanie Grossman & Dr. Fernando Alfonso

Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. Melanie Grossman will behave professionally, follow standards of care, and not impede hospital performance. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

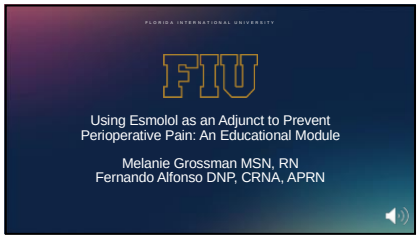
Appendix E: Recruitment Letter

Using Esmolol as an Adjunct to Prevent Postoperative Pain: An Educational Module

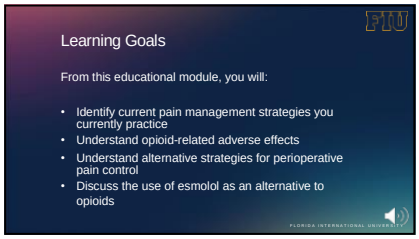
Dear Perioperative Providers:

My name is Melanie Grossman, and I am a student from the Anesthesiology Nursing Program Department of Nurse Anesthesiology at Florida International University. I am writing to invite

Appendix F: Educational Module PowerPoint


FLORIDA INTERNATIONAL UNIVERSITY
FIU
Using Esmolol as an Adjunct to Prevent Perioperative Pain: An Educational Module
Melanie Grossman MSN, RN
Fernando Alfonso DNP, CRNA, APRN

1


FIU
Learning Goals
From this educational module, you will:
• Identify current pain management strategies you currently practice
• Understand opioid-related adverse effects
• Understand alternative strategies for perioperative pain control
• Discuss the use of esmolol as an alternative to opioids
FLORIDA INTERNATIONAL UNIVERSITY

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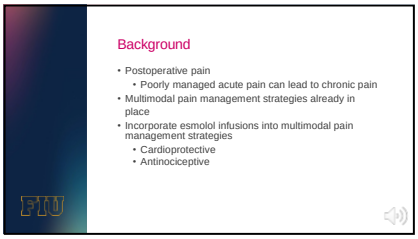
Background
• Postoperative pain
• Poorly managed acute pain can lead to chronic pain
• Multimodal pain management strategies already in place
• Incorporate esmolol infusions into multimodal pain management strategies
• Cardioprotective
• Antinociceptive
FIU

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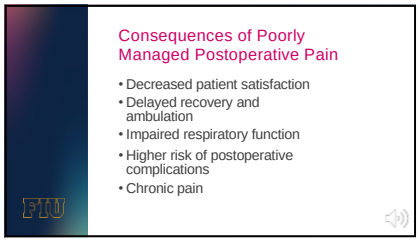
Consequences of Poorly Managed Postoperative Pain
• Decreased patient satisfaction
• Delayed recovery and ambulation
• Impaired respiratory function
• Higher risk of postoperative complications
• Chronic pain
FIU

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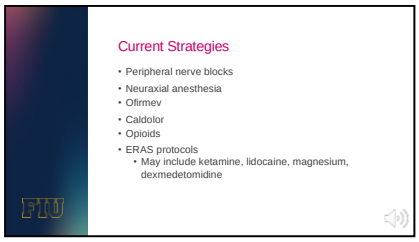
Current Strategies
• Peripheral nerve blocks
• Neuraxial anesthesia
• Ofirmev
• Caldolor
• Opioids
• ERAS protocols
• May include ketamine, lidocaine, magnesium, dexmedetomidine
FIU

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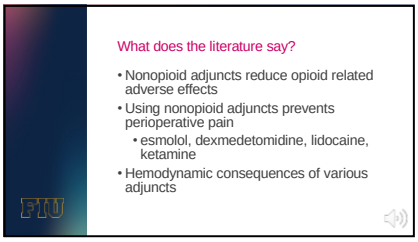
What does the literature say?
• Nonopioid adjuncts reduce opioid related adverse effects
• Using nonopioid adjuncts prevents perioperative pain
• esmolol, dexmedetomidine, lidocaine, ketamine
• Hemodynamic consequences of various adjuncts
FIU

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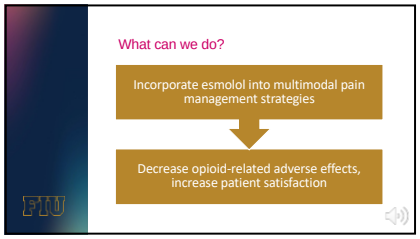
What can we do?
Incorporate esmolol into multimodal pain management strategies
Decrease opioid-related adverse effects, increase patient satisfaction
FIU

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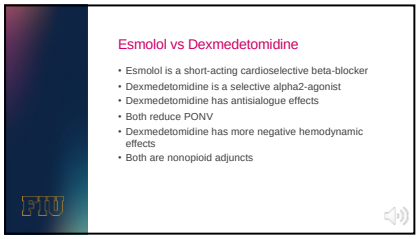
Esmolol vs Dexmedetomidine
• Esmolol is a short-acting cardioselective beta-blocker
• Dexmedetomidine is a selective alpha2-agonist
• Dexmedetomidine has antisialogue effects
• Both reduce PONV
• Dexmedetomidine has more negative hemodynamic effects
• Both are nonopioid adjuncts
FIU

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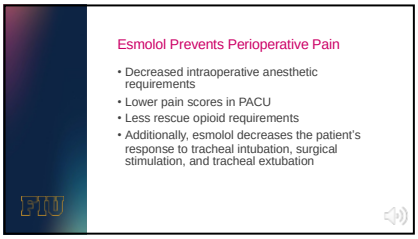
Esmolol Prevents Perioperative Pain
• Decreased intraoperative anesthetic requirements
• Lower pain scores in PACU
• Less rescue opioid requirements
• Additionally, esmolol decreases the patient's response to tracheal intubation, surgical stimulation, and tracheal extubation
FIU

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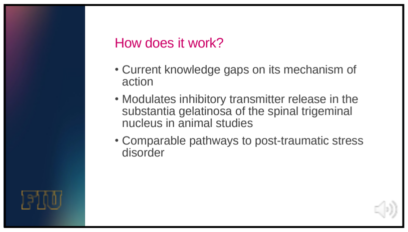
How does it work?
• Current knowledge gaps on its mechanism of action
• Modulates inhibitory transmitter release in the substantia gelatinosa of the spinal trigeminal nucleus in animal studies
• Comparable pathways to post-traumatic stress disorder

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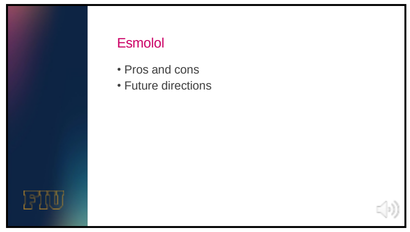
Esmolol
• Pros and cons
• Future directions

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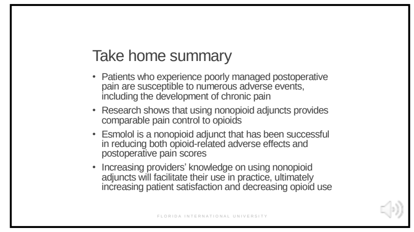
Take home summary
• Patients who experience poorly managed postoperative pain are susceptible to numerous adverse events, including the development of chronic pain
• Research shows that using nonopioid adjuncts provides comparable pain control to opioids
• Esmolol is a nonopioid adjunct that has been successful in reducing both opioid-related adverse effects and postoperative pain scores
• Increasing providers' knowledge on using nonopioid adjuncts will facilitate their use in practice, ultimately increasing patient satisfaction and decreasing opioid use

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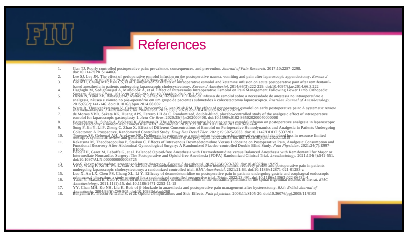
References

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Appendix G: Survey Questions

Pretest and Posttest Questionnaire:

Using Esmolol as an Adjunct to Prevent Postoperative Pain: An Educational Module

INTRODUCTION

The primary aim of this QI project is to increase providers awareness of the use of esmolol as an adjunct to prevent postoperative pain.

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format and are meant to measure knowledge on the use of esmolol in multimodal pain management strategies.

PERSONAL INFORMATION

1. **Gender:** Male Female Other_____
2. **Age:** 20-29 30-39 40-49 50-59 60-69 70-79
3. **Ethnicity:** Hispanic Caucasian African American Asian Other_____
4. **Position/Title:** CRNA Attending anesthesiologist Resident
5. **Level of Education:** Certificate Bachelors Masters DNP PhD MD/DO
6. How many years have you been an anesthesia provider?

   Over 10 5-10 years 2-5 years 1-2 years 0-1 years

QUESTIONNAIRE

1. **Postoperative pain is poorly controlled in what percentage of patients in the United States?**
    a. 80%
    b. 60%
    c. 40%
    d. 25%
2. **Which of the following is NOT an effect of acute pain?**
    a. Delayed recovery
    b. Prolonged opioid use
    c. Infection
    d. Development of chronic pain
3. **Acute postoperative pain shares similar symptomatology with which other condition?**
    a. Post-traumatic stress disorder
    b. Generalized anxiety disorder
    c. Primary hypertension
    d. Chronic pain
4. **Using esmolol intraoperatively decreases patient requirements of which drugs? (select 3)**
    a. Fentanyl
    b. Remifentanil
    c. Decadron
    d. Sevoflurane

e. Glycopyrrolate

5. **Using esmolol decreases post-operative nausea and vomiting?** True or false

6. **One proposed mechanism of action by which esmolol acts as an antinociceptive drug is:**

    a. Slowing down heart rate, thus slowing blood flow to the liver, allowing for a slower metabolism of pain medications

    b. Modulating inhibitory transmitter release in the substantia genatinosa of the spinal trigeminal nucleus

    c. Decreasing bradykinin and histamine release, thus decreasing sensitivity to pain, edema, and vasodilation

    d. Interacting with first order neurons and modulating substance P release

7. **Using esmolol as a non-opioid adjunct has shown significant hemodynamic effects.** True or false

8. **Esmolol produces inferior pain management to fentanyl.** True or false

9. **How likely are you to incorporate less opioids into your pain management strategies?**

    a. Most likely

    b. Somewhat likely

    c. Somewhat unlikely

    d. Most unlikely

10. **How likely are you to incorporate esmolol into your pain management strategies?**

    a. Most likely

    b. Somewhat likely

    c. Somewhat unlikely

    d. Most unlikely

Appendix H: Dissemination PowerPoint

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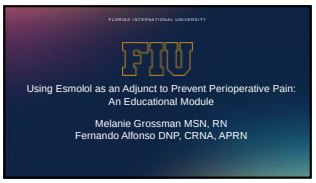

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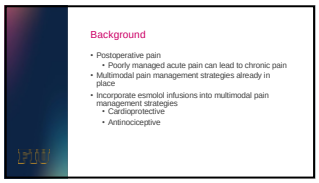

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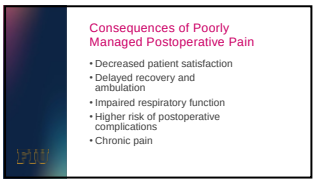

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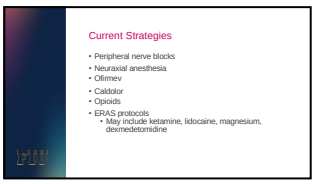

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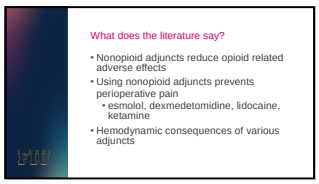

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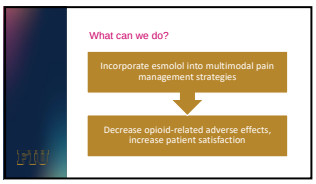

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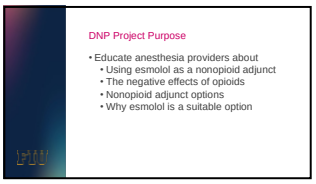

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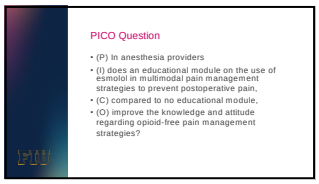

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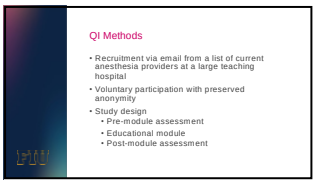

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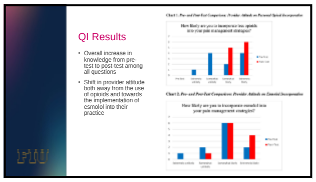

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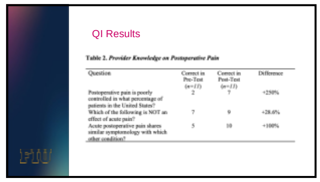

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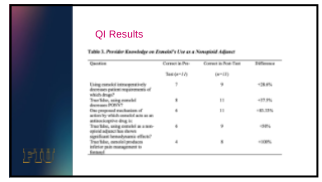

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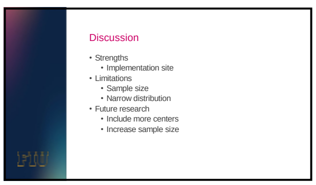

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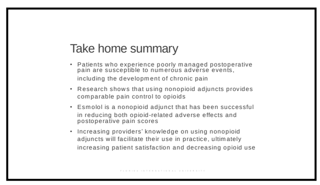

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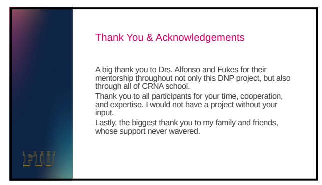

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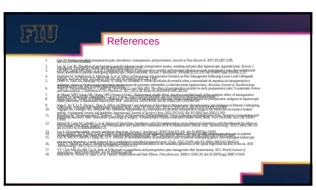

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