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The Use of Continuous Perioperative Dexmedetomidine Infusion to Reduce Opioid Consumption in Adult Patients Undergoing Spinal Lumbar Surgery: A Quality Improvement Project

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ABSTRACT

Background: Exposure to opioids, preoperatively or during surgery, is a significant risk factor for developing opioid addiction and may increase the risk of acute tolerance and chronic use. More specifically, spinal lumbar surgery is associated with increased opioid requirements to counter associated pain secondary to lumbar manipulation. Currently, there is a lack of studies that exemplify the anesthetist's role in minimizing narcotic use while effectively managing pain for this patient-specific population. Dexmedetomidine, an alpha-2 agonist, administered as a continuous infusion, has been shown to reduce opioid consumption in spinal lumbar surgery patients.

Context: The implementation phase of this quality improvement project was completed through the voluntary participation of Miami Beach Anesthesiology Associates (MBAA) at Mount Sinai Medical Center. MBAA provides all anesthesia services for Mount Sinai Medical Center, a not-for-profit, private teaching hospital located in Miami Beach, Florida.

Objectives: The purpose of this study is to improve anesthesia provider knowledge on the role of continuous dexmedetomidine infusion to reduce opioid consumption in patients undergoing spinal lumbar surgery. A literature review including seven research studies addresses the PICO question "In adult patients undergoing lumbar spine surgery does the administration of continuous intravenous dexmedetomidine perioperatively compared to pain management with a traditional opioid approach lead to decreased perioperative opioid administration without an increase in reported pain postoperatively?" The literature review was used as the basis for this study and served as the educational framework to increase anesthesia provider knowledge.

Methodology: The primary methodology used for the proposed project was administered through an online educational module. A pre-implementation survey assessed anesthesia provider knowledge of the current opioid crisis in the United States, dexmedetomidine's role in reducing opioid requirements, and factors that have prevented the use of dexmedetomidine.

Results: There was an overall improvement in anesthesia provider knowledge between pre-test and post-test survey responses following the online educational module. It can be assumed that most providers feel more inclined to use dexmedetomidine for this type of surgery.

Conclusions: Currently, continuous dexmedetomidine infusion is not used as an adjuvant with opioids for spinal lumbar surgery patients. Fentanyl is the intraoperative opioid most utilized to control pain combined with other opioid and non-opioid drugs determined by individual providers. The educational intervention effectively improved provider awareness regarding opioid misuse risk factors, dexmedetomidine's clinical uses, and favoring dexmedetomidine to reduce opioid consumption for this type of surgery. There are still factors that prevent the use of dexmedetomidine that may stem from the medical direction of other anesthesia providers that did not partake in this study.

Keywords: *dexmedetomidine, precedex, lumbar spine surgery, opioid crisis, opioid-sparing techniques for spine surgery*

INTRODUCTION

Description of the Problem

Spinal lumbar surgery often necessitates increased opioid requirements to counter associated pain secondary to decompressing lumbar vertebrae through various procedures and approaches. Adults commonly undergo lumbar surgery for conditions such as fractures, herniations, tumors, spinal stenosis, degenerative disc disease, and spondylolisthesis.[1] Increased perioperative opioid consumption can lead to poor surgical outcomes, constipation, postoperative ileus, increased length of hospital stay, decreased patient satisfaction, and addiction.

In 2011, 488,000 spine surgeries were performed in the United States due to degenerative disc disease, reflecting a 70% increased from 2001.[2] As of 2018, there were more than 1.62 million spinal surgeries performed annually in the U.S.[3] Exponential growth coupled with a 20-55% increase in preoperative opioid use for patients requiring multilevel spine surgery highlights the problem with this condition and the increasing use of opioids for this patient population.[2]

Exposure to opioids, preoperatively or during surgery for the opioid naïve patient, increases the risk of acute tolerance and chronic use.[4] Chronic use is implicated with multiple systemic effects such as sleep-disordered breathing, skeletal fractures, hypothalamic-pituitary axis depression, decreased immunity, heart failure, myocardial infarction, and the psychological risk of addiction or misuse.[2] Acute tolerance may further complicate this problem by increasing the need for opioid prescriptions during patient discharge, thereby increasing the risks associated with unused opioids.[4] To understand and identify opioid risk factors, several studies have detailed opioid consumption in patients surgically treated by lumbar spine surgery. Risk factors include younger age, female sex, depression, anxiety, fibromyalgia, benzodiazepine use, and any history of drug, alcohol, or tobacco abuse.[2,4] The perioperative period associated with spine surgery is thought to be a general risk factor for the development of opioid addiction, according to several studies.[2] Preoperative opioid use was the strongest predictor of opioid consumption at the 1-year postoperative time mark for patients who underwent anterior lumbar interbody fusion

(ALIF) surgery, while older age was the most significant risk factor for patients receiving a posterior/transforaminal interbody fusion (P/TLIF).[4] There were only minor clinical differences in opioid consumption between these two procedures; however, procedure-specific techniques contribute to postoperative pain and directly influence opioid consumption in the distant future.[4] Regardless of whether opioids were consumed before surgery, the perioperative period is a significant risk factor for developing chronic opioid use in this patient population.[2]

Background

Prior to the 1990s, opioids were used infrequently for the treatment of pain.[5] Since their mainstream introduction, physicians were impressed with the associated decrease in pain and subsequently increased their use under the assumption that opioids were a safe and effective method to treat pain. Pharmaceutical companies encouraged this movement and used misguided marketing opportunities to formulate newer opioid medications.[5] This movement resulted in the habit-forming practice of prescribing opioids, which greatly expanded in the 1990s. The surge of prescription opioids correlated directly with an increase in morbidity and mortality related to their use.[5] This practice continued and led to the current opioid crisis despite the absence of randomized trials that linked any substantial benefit of long-term opioid use.[5]

The goal of spine surgery for both the patient and the surgeon is to reduce pain by correcting the underlying condition. In patients taking opioids preoperatively, the goal is to reduce or eliminate postoperative opioid consumption. Unfortunately, many patients have not achieved this benchmark, resulting in postoperative opioid requirements by more than 50% of patients at the one-year mark. Prolonged use of opioids following spinal surgery may be indicative of a failed attempt to provide an improvement in analgesia requirements.[6]

According to the National Institute of Health (NIH),[7] opioid overdose kills 128 Americans daily, highlighting prescription opioids and fentanyl as the main contributors. The social and economic burden is estimated to cost the U.S. over $78 billion annually and includes costs associated with lost productivity, treatment for addiction, criminal justice involvement, and

healthcare.[7] It is estimated that 21%-29% of patients prescribed opioids for chronic pain misuse them and 8%-12% have an opioid disorder.[7] Of the population that misuse opioids, 4%-6% of them will transition to heroin use. Opioid overdose currently surpasses motor vehicle accidents in the U.S. as the leading cause of death due to an injury.[8] The surgery and perioperative use of opioids are not the only contributing factors to this crisis; however, the consequence of not addressing opioid use in patients undergoing lumbar surgery will further increase the economic effects and worsen outcomes.

Knowledge Gap

Over the past two decades, there have been numerous efforts and strategies to prevent or limit opioid use.[8] A focal point of current research is concerned with the benefits of opioid addiction studies, current policies that have contributed to reducing the epidemic, and clinical prescribing. One of the main knowledge gaps for anesthesia providers is the lack of studies that exemplify the anesthetist's role in minimizing narcotic use for surgical patients requiring this type of surgery.[8] The perioperative period represents the initial opioid encounter for many patients or a time that can be used to educate patients already treating back pain with opioids. Anesthetists are in a pivotal position as healthcare providers who can effectively manage pain while potentially decreasing the need for opioids.[8]

Systematic Review Rationale

Considering the current opioid epidemic and associated opioid dependence risk related to providing anesthesia, there is an urgent need to reduce opioid consumption while delivering an effective anesthetic.[2] Anesthetists play a central role in addressing this crisis while employing several options that decrease overall opioid administration.[8] There are several approaches that anesthetists can employ during the perioperative period, including identification of patients who are considered at risk for opioid abuse, multimodal analgesia, and enforcing standards of care that limit narcotic use.[8]

Currently, there are no practice guidelines established by the American Society of Anesthesiologists (ASA) that address this specific issue. The ASA has one practice guideline related to the clinical issue "Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional and Pain Medicine."[9] This guideline only addresses the need for multimodal analgesia for patients with chronic pain through the use of minimally invasive spine surgeries; however, there is no pertinent information on anesthesia approaches during the perioperative phase of surgery.[9]

In 2020, Soffin et al.,[10] conducted a randomized controlled trial, published by the ASA, consisting of fifty-six patients presenting for spinal lumbar fusions. Half of the participants were randomized to an enhanced recovery pathway, while the other half received a traditional opioid anesthetic.[10] The study was initiated due to the lack of prospective trials of enhanced recovery after spine surgery. The tested hypothesis was to evaluate any improvement of patients receiving one- to two-level lumbar fusions, with pain being one of the primary outcomes.[10] The study results were promising, and there were numerous improvements of the patients in the enhanced recovery pathway.[10] The enhanced recovery participants received lidocaine, ketamine, and dexmedetomidine infusions as the primary anesthetics during the intraoperative phase of care.[10] Despite several limitations and biases, the results demonstrate the potential for an enhanced recovery pathway for this patient population; however, the study failed to evaluate which drugs or drug combinations proved to be beneficial.[10] This conclusion is the basis for understanding the role of continuous dexmedetomidine infusion in reducing opioid consumption of adults requiring spinal lumbar surgery.

The use of continuous dexmedetomidine infusion, a newer generation α2 adrenergic receptor (α2-AR) agonist, can be incorporated into current anesthetic plans as an additive pharmacological agent to reduce opioid administration while improving pain scales scores.[11] Dexmedetomidine is beneficial in this type of surgery due to its sedative and analgesic properties

without subsequent respiratory depression, its ability to reduce agitation and delirium, and by providing perioperative sympatholysis.[11] This study is supported by the need to address the global health crisis related to opioid abuse and how lumbar spine surgery is a significant risk factor.

Objectives of the Literature Review

The purpose of conducting this literature review is to analyze current literature that identifies positive outcomes associated with the role of dexmedetomidine in reducing perioperative opioid consumption in patients undergoing spinal lumbar surgery. While several non-opioid anesthetic techniques are available, the benefit of utilizing dexmedetomidine as a continuous infusion for lumbar procedures needs to be further analyzed. Gathering supporting evidence through randomized controlled trials and case studies is crucial to understanding how dexmedetomidine can be added to traditional opioid-based anesthesia. Research analysis will provide an in-depth understanding of how dexmedetomidine can decrease opioid requirements for adults requiring lumbar surgery without limiting the results to specific lumbar spine surgery. This literature review answered the PICO question: "(P) In adult patients undergoing lumbar spine surgery (I) does the administration of continuous intravenous dexmedetomidine perioperatively (C) compared to pain management with a traditional opioid approach (O) lead to decreased perioperative opioid administration without an increase in reported pain postoperatively?"

METHODOLOGY

Information Sources and Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to guide the development of this literature review and electronic database search.[12] A search of the literature was conducted using the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Excerpta Medica Database (EMBASE), and ProQuest (MedLine) electronic databases. A population, intervention, comparison, and outcome (PICO) question was formulated during the initiation phase. The researchable question

was designed to aid in the formal organization of the research needed to challenge, examine, and analyze the clinical problem.[13] Furthermore, the PICO question helped create a basis to develop keywords, boolean phrases, and concepts from each database detailed in Table 1. The CINAHL database yielded 9 results, the Cochrane Library resulted in 34 results, the EMBASE database totaled 78 results, and ProQuest generated 623 results. A cumulative total of 744 articles resulted from all four searches that were eligible for appraisal. After duplicates were removed, there were 446 articles to be appraised. As of October 18, 2020, the search was current.

Table 1. Database Search Table

Topics/Concepts	Drug	Spine	Procedure	Filters/Results
CINAHL	Dexmedetomidine OR Precedex OR alpha 2-agonist OR selective alpha-adrenergic agonist	Spine OR lumbar OR back OR vertebra*	Fusion OR interbody OR spondylodesis OR spondylosyndesis OR lami* OR discectomy OR decompression	Peer-reviewed, all adults, English language, date range: 2005-2020. **9 results** found
Cochrane	Dexmedetomidine OR Precedex OR alpha 2-agonist OR selective alpha-adrenergic agonist	Spine OR lumbar OR back OR vertebra*	Fusion OR interbody OR spondylodesis OR spondylosyndesis OR lami* OR discectomy OR decompression	**34 results** found
MedLine (ProQuest)	Dexmedetomidine OR Precedex OR alpha 2-agonist OR selective alpha-adrenergic agonist	Spine OR lumbar OR back OR vertebra*	Fusion OR interbody OR spondylodesis OR spondylosyndesis OR lami* OR discectomy OR decompression	Peer-reviewed, English **623 results** found
EMBASE	Dexmedetomidine OR Precedex OR alpha 2-agonist OR selective alpha-adrenergic agonist	Spine OR lumbar OR back OR vertebra*	Fusion OR interbody OR spondylodesis OR spondylosyndesis OR lami* OR discectomy OR decompression	Date range: 2005-2020 **78 results** found

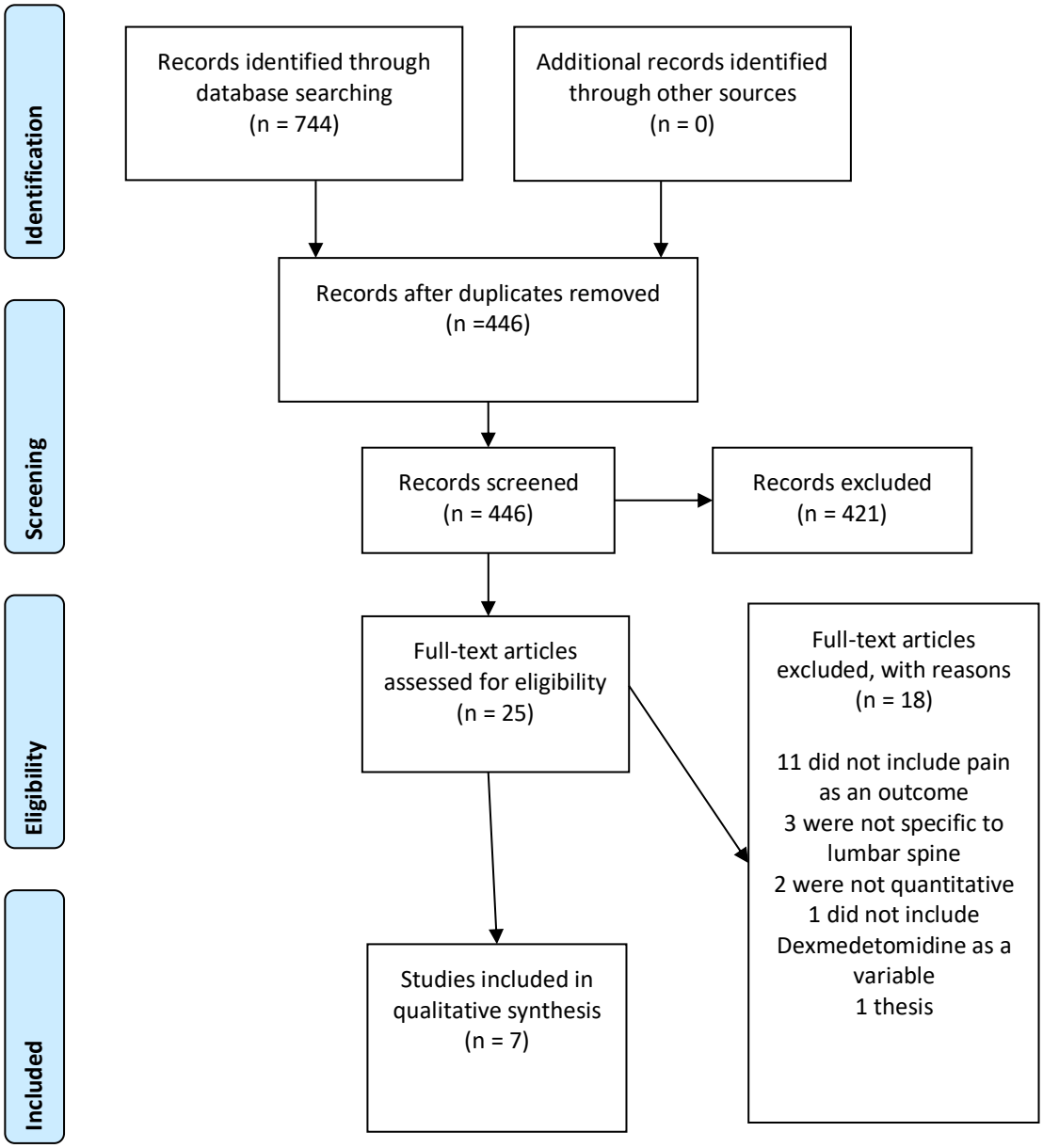
Screening Method

The PICO question guided the search. The exact keywords were applied to all four databases, and results were exported to the EndNote library, where duplicates were removed before organizing the articles. There were five folders created: "CINAHL," "Cochrane Library," "Medline," "EMBASE," and "Potential." Subsequently, strict inclusion and exclusion criteria were applied to all articles, and seven articles were deemed acceptable for full-text screening, as detailed in Table 2. A PRISMA flow diagram in Figure 1 has been included that represents a visual outline of the literature review screening phases.[12]

Table 2. Inclusion and Exclusion Criteria

Population	Exclusion
Population: • Adults (> 18 years old) • Undergoing lumbar spine surgery Type of Procedure: • Fusion • Laminectomy • Discectomy • Decompression • General Anesthesia • Monitored Anesthesia Care Intervention: • Dexmedetomidine infusion • Dexmedetomidine administered with opioids • Dexmedetomidine administered with non-narcotics Primary Outcomes: • Opioid- Studies reporting a decrease in perioperative opioid consumption • Pain- Studies including a decrease in pain score rating Type of Study: • English language • Randomized Controlled Trials (RCTs) • Case Studies • Publication 2005- Present	Population: • Children (<18 years old) • Cervical spine surgery • Thoracic-only spine surgery • Non-spine Type of Procedure: • Regional Anesthesia-only Intervention: • Dexmedetomidine bolus-only Primary Outcomes: • Improvement of postoperative fatigue • Reduction in inflammatory markers • Hypotension • Bradycardia Type of Study: • Non-English • Questionnaire • Theses • Publication prior to 2005

Figure 1. PRISMA Flow Diagram



Collection, Analysis, and Data Items

The Johns Hopkins' Research Evidence Appraisal Tool was used to evaluate all seven articles. There are four levels of evidence that are each further divided by three quality levels.[14] Level I evidence contains experimental studies, RCTs, or systematic reviews with or without meta-analysis. Level II evidence includes quasi-experimental studies or systematic reviews with

a mix of quasi-experimental studies with or without meta-analysis. Level III evidence includes non-experimental studies, systematic reviews that combine RCTs, quasi-experimental, and non-experimental studies.[14] Level IV evidence is reserved for opinionated reviews by respected authorities or nationally recognized committees, including practice guidelines or consensus panels.[14] The subdivisions quality levels of I-III are then applied based on several criteria. High-quality articles denoted with the letter *A* contain consistent and generalized results, adequate sample size, concrete conclusions, and recommendations based on scientific evidence.[14] Good quality articles denoted with the letter *B* have less consistent results, sufficient sample size with some control, reasonably definitive conclusions, and recommendations that offer reviews based on scientific evidence.[14] Lastly, quality *C* articles are considered low quality or have major flaws and are equated with inconsistent results, minimal evidence, inadequate sample size, and do not provide conclusions.[14]

Both reviewers split the task of collecting and analyzing the data from seven selected studies included in this literature review. Disagreements were resolved through discussions regarding the data retrieved and interpreted to answer the PICO question. Evaluation tables were created to summarize critical appraisals from each study and organize individual study characteristics. All articles were rated using the Johns Hopkins' Evidence appraisal tool.

RESULTS

Study Selection

A total of 744 articles initially resulted from the four databases, of which 298 duplicates were removed, leaving 466 articles for review. Upon examination and screening of the titles and abstracts, 421 records were eliminated, resulting in a total of 25 full-text articles assessed for eligibility. Full-text analysis was then performed by two investigators guided by strict inclusion and exclusion criteria resulting in an additional eighteen records that were eliminated. Eleven of the records did not include pain as a primary or secondary outcome. Three records were not

specific to this study's anatomical area of interest, and two were not quantitative. The remaining two articles did not use dexmedetomidine as a variable, while the latter was a thesis.

Further analysis of the 25 records' reference lists were examined and did not result in additional articles that fit the determined criteria. The study selection resulted in seven articles included in this literature review that answered the PICO question mentioned above. Appendix A Evaluation Tables 1 through 7 summarize all the articles within the literature review. Furthermore, all six RCTs were level 1 evidence, and the case study was level 2 evidence according to the Appraisal Tool.[14]

Study Characteristics

Six out of seven selected studies are randomized control trials (RCTs), and one is a case study. A total of 291 patients were included in this literature review who received dexmedetomidine, remifentanil, normal saline as a placebo, dexmedetomidine with lidocaine, opioids-only, or fentanyl perioperatively. Patients had a variety of lumbar spine surgical procedures, including interbody fusion, laminectomy, foraminotomy, and laminotomy with discectomy. Pain, perioperative opioid consumption, and the length of time for postoperative analgesic requirements were either the primary outcome or one of several primary outcomes analyzed in all studies. Opioid consumption was documented perioperatively, rescue opioids were documented perioperatively, postoperative numeric pain scores were used to evaluate pain levels, and length of time for postoperative opioid requirements was documented postoperatively. Six of the seven studies were done under general anesthesia, and one study was performed under conscious sedation.

Definitions and Outcomes

Intraoperative Dexmedetomidine Compared to Saline Placebo. Three RCTs utilized dexmedetomidine in comparison to normal saline as a placebo intraoperatively. Evaluation of several outcomes was considered and varied among the three studies: intraoperative opioid requirements, postoperative opioid requirements based on numeric pain scales, and the time to

first postoperative opioid request[15-17.] Dexmedetomidine dosing strategies differed among the three studies but were all performed under general anesthesia.

In the first study, Kundra et al.,[15] started dexmedetomidine infusion at 0.3 mcg/kg/hr at a designated start time identified as "0" time. Patients in the placebo group received normal saline at the same rate and started at "0" time.[15] Anesthesia was maintained utilizing a mix of oxygen, nitrous oxide, and sevoflurane.[15] Atracurium was selected to achieve muscle paralysis, and the depth of anesthesia was monitored using the BIS with values maintained between 40 and 60.[15] Intraoperative 1 mcg/kg boluses of fentanyl were administered if patients experienced tachycardia or hypertension greater than 20% of baseline vital sign values lasting longer than 1 minute.[15] Additional 0.5 mcg/kg boluses of fentanyl were repeated for episodes of tachycardia and hypertension that did not revert to baseline after 15 minutes of the first bolus.[15] Kundra et al.,[15] reported that the fentanyl requirements in the dexmedetomidine group were less than placebo; however, the difference was not statistically significant (P= 0.131).

Ozkose et al.,[16] also compared dexmedetomidine to normal saline as a placebo but used a loading dose of 1 mcg/kg over 10 minutes, followed by an infusion rate of 0.2 mcg/kg/hr. The saline group received an equal amount of normal saline.[16] Anesthesia was standard for both groups and consisted of desflurane, nitrous oxide, and oxygen titrated to a BIS range of 40 to 60.[16] Rocuronium was used for muscle paralysis.[16] Intraoperative fentanyl boluses of 1 mcg/kg were given during the intraoperative phase if blood pressure or heart rate exceeded baseline vital sign values. The verbal rating scale (VRS) was utilized to assess pain levels at five-minute intervals, and rescue meperidine doses of 1 mcg/kg were given intramuscularly for pain scores greater than 3.[16] Pain scores at 30 and 60 minutes were significantly lower in the Dex group compared to the control group.[16] Two of the patients in the dexmedetomidine group required meperidine during the first hour compared to 11 in the control group.[16]

The third study combined fentanyl-dexmedetomidine (Fen-Dex) infusions and compared them to fentanyl and normal saline infusions. On induction, both groups received 1mcg/kg

fentanyl boluses, followed by a continuous fentanyl infusion rate of 0.2 mcg/kg/hr.[17] The Fen-Dex group received a 0.5 mcg/kg loading dose of dexmedetomidine followed by a maintenance dose of 0.2 mcg/kg/hr continued through the first 24 hours in the postoperative period.[17] Normal saline as a placebo was administered during the intraoperative and postoperative periods as needed. Anesthesia was maintained with sevoflurane, nitrous oxide, and oxygen, while atracurium was used for muscle paralysis.[17] Quantitative measurements were periodically evaluated intraoperatively, and the visual analog scale (VAS) was utilized to assess postoperative pain levels for 24 hours. Postoperative morphine was given for VAS scores > 4 through a morphine infusion pump capable of delivering morphine at a rate of 1 mg/ml/hr.[17] Additionally, the time to first postoperative request for morphine in the PACU was documented. The Fen-Dex group showed a significant decrease in morphine requirements, VAS scores, and time to first morphine request in the PACU compared to the Fentanyl saline placebo group.[17]

Intraoperative Dexmedetomidine with Lidocaine Compared to Traditional Opioid Approach. In this study, dexmedetomidine and lidocaine were evaluated in a case study of a patient undergoing spinal fusion surgery. Results were compared to more traditional methods of anesthesia using an opioid approach but were not specified.[18] Dexmedetomidine was used for induction with a 1 mcg/kg loading dose over 10 minutes with lidocaine, propofol, and succinylcholine. Dexmedetomidine was maintained at 1 mcg/kg/hr, lidocaine at 1.5 mg/kg/hr, and combined with a mix of nitrous oxide and oxygen.[18] No opioids were administered intraoperatively. Kim et al.,[18] evaluated postoperative opioid consumption and compared the results to similar reports of patients undergoing the same procedure without dexmedetomidine and lidocaine infusions using a traditional opioid-based intraoperative anesthetic.[18] In this case study, the patient was not in pain during the operation or on arrival at the PACU. A PCA pump with hydromorphone was used for pain relief. A total of 0.4 mg was administered during the 90-minute PACU phase of care.[18] Oral morphine was given after the patient left PACU and evaluated for 24 hours. The patient was noted to use significantly less morphine milligram

equivalents and did not require IV rescue boluses of opioids. Furthermore, the patient reported a maximum pain score of 3/10 using a numeric pain score.[18]

Intraoperative Dexmedetomidine Compared to Remifentanil. Hwang et al.,[19] compared two groups of patients undergoing lumbar fusion surgery with dexmedetomidine and remifentanil. The Dexmedetomidine group received a continuous infusion of dexmedetomidine at 0.01- 0.02 mcg/kg/min, and the Remifentanil group received a continuous infusion of remifentanil at 0.01-0.2.[19] Anesthesia was maintained with propofol, and muscle paralysis was achieved with rocuronium. Depth of anesthesia was analyzed with a BIS range of 40-60. Both groups received hydromorphone through a PCA pump once they opened their eyes in the PACU. The PCA rate was set at 1 mg/hr with bolus doses of 1 mL every 10 minutes, as needed. Fentanyl and tramadol were administered as rescue drugs in the PACU and in the general hospital ward upon leaving the PACU phase of care.[19] PCA and rescue drug requirements were recorded, and pain levels were assessed using the VAS score. The dexmedetomidine group showed significantly lower PCA requirements at all time points after surgery, except one.[19] The remifentanil group VAS's were significantly higher and required more rescue drug administration at every time point after surgery.[19]

Intraoperative Dexmedetomidine Compared to Fentanyl. Turgut et al.,[20] compared the difference between dexmedetomidine and fentanyl. The dexmedetomidine group received dexmedetomidine at 0.2 mcg/kg/hr while the fentanyl group received fentanyl at 0.5 mcg/kg/hr. Both groups increased their respective infusion rates based on hemodynamic parameters. Anesthesia was maintained with propofol to maintain a targeted range of 50-60 on the BIS monitor. Cisatracurium was used for paralysis in both groups. The fentanyl group required more supplemental opioid analgesia, and at earlier time points than the dexmedetomidine group.[20]

Intraoperative Dexmedetomidine and Fentanyl Compared to Midazolam and Fentanyl. Peng et al.,[21] analyzed the effects of dexmedetomidine and fentanyl versus midazolam and fentanyl undergoing lumbar laminotomy and discectomy surgery with conscious sedation.

Each group received a fentanyl bolus dose of 1 mcg/kg in combination with either 0.5 mcg/kg of dexmedetomidine or 0.005 mg/kg of midazolam over 10 minutes.[21] Subsequent continuous infusions of either dexmedetomidine or midazolam were initiated after that and stopped before the end of surgery. The Ramsey Sedation Scale was used intraoperatively to monitor the depth of anesthesia.[21] Incremental changes to both infusions were permitted based on sedation criteria. Both groups received fentanyl rescue doses of 0.5 mcg/kg. Upon completion of the surgery, both groups received fentanyl delivered through PCA infusion. Peng et al.,[21] found that the Dexmedetomidine group required less intraoperative and postoperative fentanyl consumption. Additionally, this group had fewer patients that required rescue analgesia.[21]

Risk of Bias

Study bias was assessed using the Cochrane Risk of Bias Tool to determine overall bias in the six RCTs included in this study.[22] There are several domains included in the assessment tool which allow for an in-depth evaluation of bias risk intended to profile articles into high risk, low risk, or unclear risk.[22] Five of the six articles were randomized, double-blinded studies. Hwang et al.,[19] was the only RCT to use the randomized, single-blind study technique, concluding that the study's investigators knew which treatment the study participants received, but the participants were unaware. It can be inferred from the assessment tool that all articles carried a low risk of bias for random sequence generation.[22] The second area of selection bias concerns allocation concealment, which determines whether the studies applied measures to hide the sequence of selection randomization.[22] Kundra et al. stated that randomization was conducted through a computer-generated model and enclosed in a sealed envelope.[15] Turgut et al. arranged the two groups with computer-generated codes preserved in sequentially numbered envelopes opened three hours before the start of the procedure.[20] All four other RCTs did not state any measures to conceal this process; therefore, there is an unclear risk of bias in this category.

Performance bias is concerned with any measures used to blind the trial researchers and participants from the information of the specific intervention.[22] Peng et al. used a statistician unaware of the study's purpose and an independent anesthesiologist to prepare medications according to the generated sequence.[21] Ozkose et al. states that one of the study's investigators was blinded to the recorded data while administering dexmedetomidine. A third investigator was blinded to the groups while observing different outcome variables upon completion of the surgery, and one blinded observer was used in PACU.[16] Kundra et al. and Hwang et al. used different software packages for concealment.[15,19] The two other studies did not state their measures, and therefore the risk of bias is unclear.

Attrition bias is another domain in the Cochrane Assessment Tool concerned with any exclusions due to unforeseen circumstances. Hwang et al. is the only article that reported that three of the forty enrolled participants were excluded; therefore, there is a high risk of bias in this domain.[19] Two of the participants in the Remifentanil group were excluded due to follow-up loss, while the third participant in the Dexmedetomidine group was excluded due to massive intraoperative bleeding.[19] All other RCTs did not report participant exclusion. There was no reports of bias due to selective outcome reporting mentioned in any RCTs, so it is unclear if there is any risk.[22] Lastly, the only non-RCT article was a peer-reviewed case study with no bias stated.

DISCUSSION

Summary of the Evidence

Six RCTs and one case study were included in this literature review that evaluated a total of 291 patients undergoing different operative lumbar surgical procedures comparing dexmedetomidine to different narcotics. Exclusion criteria eliminated several articles due to the following reasons: pain was not a primary or secondary outcome (e.g., hemodynamic effects of dexmedetomidine), surgeries on other anatomical locations of the spine not specific to the lumbar region, non-quantitative studies, and studies that did not use dexmedetomidine as a variable. According to the Johns Hopkins' Research Evidence Appraisal Tool, all six RCTs were level one

evidence, with four rated as high quality and two categorized as good quality.[14] One of the RCTs was rated good quality due to a relatively smaller sample.[21] The second RCT could not statistically demonstrate the opioid-sparing effect of dexmedetomidine, although there was a reported reduction of fentanyl use in the control group.[15] All four other RCTs exhibited sufficient sample sizes and defined conclusions with consistent results.[21] Lastly, the only case study evaluated by the Johns Hopkins' Research Evidence Appraisal Tool was rated as good-quality level two evidence since the study was experimental but only explored a comparative analysis of one patient.[18,21] A summarization of the results of this literature review are described below:

- Two RCTs did not administer a loading dose of dexmedetomidine prior to continuous infusion and found a decrease in the intraoperative or postoperative opioid requirements.[15,19]
- Two RCTs admistered a 0.5mcg/kg loading dose of dexmedetomidine before continuous infusion and found that both dexmedetomidine groups required fewer postoperative opioids.[17,21]
- Two studies administered a 1mcg/kg loading dose of dexmedetomidine before continuous infusion and reported a decrease in postoperative opioid consumption.[16,18]
- Three RCTs reported significant decreases in postoperative VAS pain scores in the respective groups that received dexmedetomidine.[16,17,19]
- Four studies started dexmedetomidine infusions during the intraoperative phase of surgery. Although not statistically significant, Kundra et al. reported that fewer fentanyl requirements were needed intraoperatively in the dexmedetomidine group.[15] Peng et al. reported decreased intraoperative, postoperative, and total fentanyl requirements in their dexmedetomidine group.[21] Hadi et al. and Kim et al. found a decrease in either postoperative morphine or hydromorphone, while Hadi et al. also stated that the first

request for postoperative morphine was significantly decreased in the dexmedetomidine group.[17,18]

- Three RCTs initiated continuous dexmedetomidine in the preoperative period and continued it throughout the intraoperative. All three reported a decrease in either meperidine, hydromorphone, or fentanyl consumption in the postoperative period.[16,19,20]
- Peng et al. was the only study to perform a lumbar surgical procedure under local anesthesia with conscious sedation and found a significant decrease in intraoperative, postoperative, and total fentanyl requirements.[21]

Limitations of the Literature Review

There were several limitations to this literature review that must be acknowledged. While all studies compared dexmedetomidine alone or with other anesthetics and analgesics, there were several dissimilarities among all studies regarding how and when dexmedetomidine was initiated and discontinued. Two studies did not include a loading dose before continuous infusion, two gave a 0.5 mcg/kg loading dose, one RCT gave a 0.6 mcg/kg loading dose, and the remaining two studies gave a 1 mcg/kg loading dose.[15-21] Additionally, three RCTs started continuous dexmedetomidine infusion during the preoperative phase of surgery, and four studies started the infusion during the intraoperative period.[15-21]

Another limitation of this literature review was the comparison of several opioids, how and when administered, and when they were monitored for comparative outcomes. Fentanyl, meperidine, remifentanil, morphine, and hydromorphone were administered as rescue boluses or by PCA pumps during varying phases of surgery. Narcotic doses were not the same across all seven studies, while narcotic potency varies significantly among the opioids utilized.[15-21]

From the perspective of how anesthesia was administered, not all the studies utilized the same general anesthetic technique. Three of the studies used different concentrations of several gases, including sevoflurane, desflurane, nitrous oxide, air, and oxygen during the maintenance

phase of anesthesia.[15,16,18] Three studies used total intravenous anesthesia (TIVA), and one study performed the surgical procedure under local anesthesia with sedation.[17,19-21]

Not all studies shared the same primary and secondary outcomes, inclusion and exclusion criteria varied, and different methods were utilized to assess pain intraoperatively and postoperatively. Primary outcomes across all seven studies included: intraoperative and postoperative fentanyl consumption, anesthetic sparing effects, intraoperative hemodynamics, perioperative hemodynamics, blood loss, anesthetic requirements, propofol consumption, recovery profile, postoperative recovery, analgesic requirements after PACU discharge, VAS scores, time, and incidence or rescue analgesics requirements, PONV, and duration of PACU stay. Secondary outcomes included: intraoperative rescue analgesia, sedation levels, pain scores, hemodynamic changes, adverse events, patient satisfaction, and postoperative hospital stay.[15-21]

Inclusion criteria included peer-reviewed articles in English; however, six of the articles were from China, India, Turkey, South Korea, or Jordan, where English is not the native language. Language bias must be considered a limitation due to speculation that research produced in non-English speaking countries has a higher propensity to be published in English-language journals if the outcomes are positive. In contrast, negative outcome research may be produced in foreign language journals.[23] Furthermore, it should be acknowledged that all RCTs were healthy ASA I and II patients without severe coexisting disease[15-17,19-21] Kim et al. was a single case study on an ASA III patient. Therefore the ability of dexmedetomidine to reduce opioid consumption for lumbar surgical procedures cannot be generalized to all patients.[18] Despite the heterogeneity limitations across all studies, this literature review supports the use of continuous dexmedetomidine to reduce perioperative opioid consumption in patients undergoing lumbar surgical procedures.

Recommendations for Future Research

Further research would benefit from standardizing the dose of dexmedetomidine across studies and including whether administering a loading dose is statically significant. Research

studies need to have less heterogeneity to formulate outcomes based on equal comparative studies. All but one RCT stated that their sample sizes were adequate, but the average sample size in this literature review ranged between 40-60 patients, which is considered relatively small. Increasing the sample size and including ASA III and IV patients may help translate whether dexmedetomidine is effective in patients with severe comorbidities. Another significant recommendation that would add to the validity and purpose of this study is to include patients that have a history of narcotic use for pain control. Dexmedetomidine may antagonize perioperative opioid consumption, but it is imperative to understand if this trend is similar in the opioid-dependent patient. This is a significant point, considering that patients who use opioids preoperatively often require more opioids perioperatively and will continue to use opioids past the PACU phase of care.[4]

Lastly, the cost-effectiveness of dexmedetomidine was not discussed and may increase its potential among healthcare institutions. The dexmedetomidine unit price is $1.14- $1.19 compared to the following unit prices: morphine sulfate $0.37, fentanyl $1.09- $1.35, hydromorphone $6.46, meperidine $7.19, and remifentanil $64.94.[22-29] As demonstrated, dexmedetomidine is significantly less expensive than remifentanil, meperidine, and hydromorphone, while morphine is the only narcotic that is more cost-effective. Future cost analysis must also consider how much more opioids are needed compared to dexmedetomidine and the side effects that narcotics carry with their respective use, such as respiratory depression, PONV, and constipation. Adverse side effects are responsible for increasing hospital length of stay.

Conclusions

Based on the literature review, there is sufficient evidence to suggest that the use of dexmedetomidine intraoperatively reduces perioperative opioid consumption and decreases relative pain scales in the postoperative period of patients undergoing lumbar spine surgery. All studies used varying doses of dexmedetomidine with and without loading doses; therefore, an

optimal dexmedetomidine dose has not been identified. Among all studies, the average dexmedetomidine infusion rate was 0.485 mcg/kg/hr.[15-21] The lowest continuous rate of 0.2 mcg/kg/hr was used in two studies.[16,17] The highest continuous rate of 1.2 mcg/kg/hr dexmedetomidine was reported by Hwang et al.[19] Although an optimal dose of dexmedetomidine has not been identified, all studies have indicated that there has been an associated decrease in opioid consumption. Kundra et al.,[15] was the only study to show that the perioperative fentanyl requirement decreases were not statistically significant. Furthermore, these studies have not explored the use of continuous infusion with and without a loading dose to determine whether this factor decreases opioid consumption.

Overall, continuous infusion of dexmedetomidine perioperatively was determined to effectively reduce perioperative opioid consumption in all studies, while several studies showed an additional decrease in pain levels reported. Increased use of opioids also leads to increased recovery time, respiratory depression, increased first-time patient requests for postoperative opioids, and increased perioperative rescue analgesia requirements. Therefore, in this literature review, continuous perioperative dexmedetomidine infusion was found to decrease perioperative opioid consumption in adult patients undergoing spinal lumbar surgery.

QUALITY IMPROVEMENT IMPLEMENTATION PLAN

Setting

The setting for this project took place in Miami Beach, Florida. In 2019, the estimated Miami Beach City and Miami-Dade County populations were 88,885 and 2,497,993, respectively.[30] The leading causes of disease-related death within this community are heart disease, cancer, stroke, chronic obstructive pulmonary disease, and Alzheimer's disease.[31] Mount Sinai Medical Center (MSMC) is a 672-bed not-for-profit teaching hospital established in 1949 and the only hospital located in Miami Beach.[32] Anesthesia services are provided by Miami Beach Anesthesiology Associates (MBAA) throughout the MSMC facility, which houses more than 25 operating suites.[33]

Recruitment

The target population was recruited after obtaining approval from the investigators at Florida International University (FIU) and MBAA. The International Review Board (IRB) deemed the project *exempt* through the Exempt Review process. The population of interest was certified registered nurse anesthetists (CRNAs) and anesthesiologists. MBAA identified the participants and provided an email contact list, which was utilized to connect with the participants virtually.

Project Participants

MBAA staff CRNAs and anesthesiologists were eligible to participate in the educational intervention. Student Registered Nurse Anesthetists (SRNAs) and anesthesia medical residents were excluded from participation in the project. MBAA staff that met inclusion criteria were emailed and provided the voluntary pre-test survey, the educational voice-over PowerPoint, and the post-test survey to complete (See Appendix F and G). A total of 32 participants were contacted, and seven participants completed the pre-test and post-test.

Intervention

An evidence-based education module addressing dexmedetomidine's role in reducing perioperative opioid consumption in adult patients undergoing lumbar spinal procedures is necessary to vanquish perceived barriers. Removing barriers that hinder the use of dexmedetomidine in this patient population will empower anesthesia providers to alter current behavior towards its use potentially. The intervention was staged, with the pre-test survey provided first to analyze the current knowledge of dexmedetomidine and this patient population. Upon pre-test completion, participants were provided with an evidence-based voiceover PowerPoint presentation. The education module provided staff with statistical information regarding the current opioid epidemic in the U.S.; identified postoperative risk factors for opioid use; explained the drug mechanism of action and clinical effects; hypothesized potential barriers to its use; and discussed the results of seven studies used in the literature review that guided this

project. Lastly, subjects completed a post-test survey to determine learning outcomes, the efficacy of the intervention, and overall interest in utilizing dexmedetomidine as an opioid-sparing anesthetic adjuvant.

Procedure

Participants on the email list provided by MSMC were sent an informational email inviting them to participate in the project. Within the content of the email, there was an anonymous link provided, which gave subjects access to the pre-test questionnaire through the Qualtrics survey platform. After completing the survey, participants were able to access the 15-minute voiceover PowerPoint presentation via email. Upon completing the educational intervention, the Qualtrics survey platform was accessed by an anonymous link that directed users to the post-test survey. Participant privacy was never jeopardized as no personal identifiable information was required to partake in this project.

Protection of Human Subjects

IRB approval was obtained before any of the activities involved in this project were initiated. The IRB has deemed this project *exempt* under the Exempt Review process as it fits one of the exempt category descriptions defined by the Federal Regulations for Protection of Human Research Subjects.[34] There is no more than "minimal risk" to human subjects, and the identification of human subjects cannot be readily determined directly or through identifiers associated with the subjects.[34] Additionally, this research project's pre-test and post-test survey responses do not place the subjects at risk for any civil or criminal liability.[34] Participation will not result in damaging consequences that would affect the subjects financially, their employment or education status, or reputation.[34]

Analysis

The primary tools utilized in the study included a preassessment and post-assessment application used to analyze the effects of the educational module. The Qualtrics platform was used to generate both tests and the educational voiceover PowerPoint presentation. Ten questions

in the pre-test survey were used to determine baseline knowledge of dexmedetomidine and spinal lumbar surgery. In contrast, the post-assessment survey included the same questions to validate the effectiveness of the educational PowerPoint and the application of knowledge. All data is confidential, and no subject identifiers were recorded in the study.

Measure

The primary DNP student obtained Miami Beach Anesthesia Associates' email addresses. The emails were used to communicate the study's purpose, intent and to send the pretest, posttest, and voicer PowerPoint presentation. Each question was measured via Qualtrics statistical analysis to identify base knowledge before and after participation in the study. Through analysis, the impact of the educational module will be assessed based on participation outcomes and patterns identified. All data will be stored in a password-protected computer by the co-investigator.

IMPLEMENTATION RESULTS

Pre/Post-Test Demographics

The pre-test demographics are represented below in Table 3.

Table 3. Pre/Post-Test Participant Demographics

Demographics	**N (%)**
Total Participants	7 (100%)
Gender	
Male	3 (42.9%)
Female	4 (57.1%)
Age	
25 - 35 yr.	5 (71.4%)
36 - 45 yr.	2 (28.6%)
46 – 55 yr.	0 (0%)
55 – 66 yr.	0 (0%)
Ethnicity	
Hispanic	5 (71.4%)
Caucasian	0 (0%)
African American	1 (14.3%)

Asian	1 (14.3%)
Other	0 (0%)
Education	
Masters	0 (0%)
Doctorate	7 (100%)
Years of Practice	
0 – 2 yr.	2 (28.6%)
2 – 5 yr.	3 (42.9%)
5 – 10 yr.	1 (14.3%)
10 – 20 yr.	1 (14.3%)

There were a total of seven participants that completed the study in its entirety. The pre-test demographics represent an almost equal representation of female (n=4, 57.1%) to male participants (n=3, 42.9%). Various ethnicities were also represented among the participants, with the majority being Hispanic (n=5, 71.4%), followed by African American (n=1, 14.3%), and Asian (n=1, 14.3%). Most participants fell into the 25 to 35 age group (n=5, 71.4%), while the 36 to 45 age group accounted for the remaining percentage (n=2, 28.6%). No one in the survey was in the 46 to 55 or the 55 to 66 age range. All participants were CRNAs with Doctoral degrees (n=7, 100%). Lastly, all individuals were asked how many years they have been practicing as CRNAs: 0 to 2 years (n=2, 28.6%), 2 to 5 years (n=3, 42.9%), 5 to 10 years (n=1, 14.3%), and 10-20 years (n=1, 14.3%).

Pre-Test Identification of Knowledge of Opioids and Utilizing Dexmedetomidine for Spinal Lumbar Surgery

The pre-test consisted of 10 questions that assessed current knowledge of opioids, their use in spinal lumbar surgery, and the role of dexmedetomidine for this patient population. Most participants could not identify how many Americans overdose daily on opioids (n=6, 85.7%). None of the participants correctly identified factors that increase the risk of chronic opioid use after surgery (n=0, 0%). All but two participants agreed that there is a correlation between preoperative opioid use and an increase in postoperative opioid use for up to 1 year following

surgery (n=5, 71.4%). Most participants also agreed that perioperative exposure to opioids for the opioid naïve patient increases their risk of acute tolerance and chronic use (n=6, 85.7%).

The focus of the latter pre-test questions was focused on dexmedetomidine and its role in spinal lumbar surgery. None of the participants correctly identified the clinical uses of dexmedetomidine (n=0, 0%); however, all participants correctly identified dexmedetomidine's mechanism of action (n=7, 100%). All participants agreed or somewhat agreed that continuous dexmedetomidine infusion reduces intraoperative and postoperative opioid requirements for the given patient population (n=7, 100%). All CRNAs agreed that certain factors had prevented the use of continuous dexmedetomidine for spinal lumbar surgery. Most participants (n=5, 71.4%) identified that the anesthesia culture and attitudes at their facility towards dexmedetomidine, postoperative neurologic assessment, and hemodynamic side effects prevented using dexmedetomidine for this surgical patient population. The remaining CRNAs (n=2, 28.6%) identified that only the culture/attitudes towards dexmedetomidine and postoperative neurologic assessment prevented its use. Lastly, all but one participant agreed that they would use dexmedetomidine to decrease opioid use and recommend its opioid-sparing effects to other providers (n=6, 85.7%).

Post-Test Identification of Knowledge of Opioids and Utilizing Dexmedetomidine for Spinal Lumbar Surgery

Table 4 highlights the pre-test and post-test differences in responses.

Table 4. Difference in Pre- and Post-Test Knowledge

Questions	Pre-test	Post-test	Difference
According to the National Institutes of Health (NIH), opioid overdose kills approximately how many Americans daily?	14.3%	85.7%	71.4%
Identify which of the following factors that are responsible for increasing the risk of chronic opioid use after surgery	0%	57.1%	57.1%
Please indicate your level of agreement with the following statement: Patients presenting for lumbar spine surgery that are prescribed opioids preoperatively to treat pain are more likely to use opioids for up to 1 year following surgery	71.4%	100%	28.6%
Please indicate your level of agreement with the following statement: Perioperative exposure to opioids for the opioid naïve patient increases the risk of acute tolerance and chronic use	85.7%	100%	14.3%
What are the clinical uses of dexmedetomidine?	0%	57.1%	57.1%

What is the mechanism of action of dexmedetomidine?	100%	100%	0%
Continuous intraoperative dexmedetomidine infusion reduces intraoperative and postoperative opioid requirements	100%	100%	0%
What factors have prevented the use of dexmedetomidine for lumbar spine procedures at your clinical site?	100%	100%	0%
How likely are you to use dexmedetomidine to decrease opioid use?	85.7%	85.7%	0%
How likely are you to recommend dexmedetomidine?	85.7%	85.7%	0%

After the voiceover PowerPoint presentation, most of the categories increased from baseline knowledge. There was a significant 71.4% increase in knowledge regarding daily opioid overdose (n=6, 85.7%). There was an increase of 57.1% in knowledge pertaining to factors that increase postoperative chronic opioid use from baseline. All participants agree with the statement, "Patients presenting for lumbar spine surgery that are prescribed opioids preoperatively to treat pain are more likely to use opioids for up to 1 year following surgery," reflecting a 28.6% increase in knowledge from the educational intervention. Additionally, all participants agree with the statement, "Perioperative exposure to opioids for the opioid naïve patient increases the risk of acute tolerance and chronic use," demonstrating a 14.3% increase from baseline knowledge.

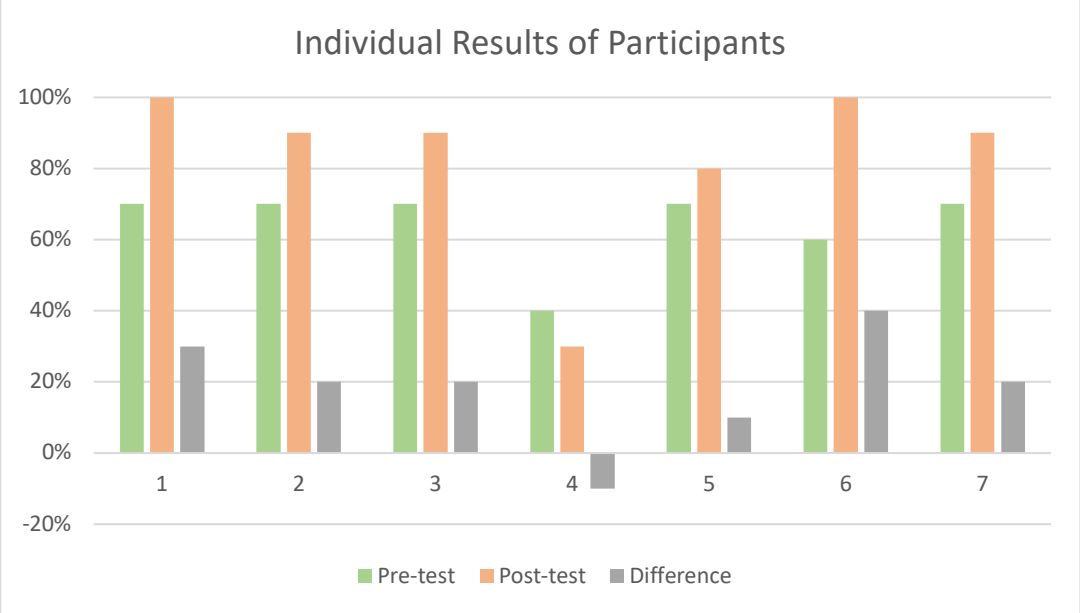
The educational intervention increased the knowledge of dexmedetomidine's clinical uses (n=4, 57.1%). All participants agree that dexmedetomidine reduces perioperative and postoperative opioid requirements (n=7, 100%), while all identified at least two of the three factors that hinder the use of dexmedetomidine at their facility. Lastly, after watching the educational presentation, only one participant would not use dexmedetomidine or recommend its use for patients undergoing spinal lumbar surgery (n=1, 14.3%).

Summary of Data

Overall, the results demonstrate an increase in knowledge between the pre-test and post-tests, except for one of the participants who still would not use dexmedetomidine or recommend its use for this specific patient population. There were drastic increases in knowledge regarding the current opioid crisis and clinical uses of dexmedetomidine. Six CRNAs would use

dexmedetomidine in practice and recommend its use after viewing the educational presentation. Graph 1 below shows individual results.

Graph 1. Individual Results of Participants



IMPLEMENTATION DISCUSSION

Limitations

This study had several limitations, including a small sample size and the length of time required for participants to complete the study. Out of the 32 emails sent to anesthesia providers from Miami Beach Anesthesiology Associates at Mount Sinai Medical Center, seven participants completed the pre-test and post-test survey. A larger and more diverse sample size would have reflected a more accurate representation of the role of dexmedetomidine for the given patient population. Additionally, the email recipients were all CRNAs and excluded anesthesiologists. The inclusion of anesthesiologists may have altered the responses regarding factors that have prevented the use of dexmedetomidine at the hospital. Lastly, participants were given a limited time of 2 weeks to complete the project, and an extended time frame may have increased the response rate.

Future Implications for Advanced Practice Nursing

The expansion of dexmedetomidine's role in reducing perioperative opioid consumption for patients undergoing spinal lumbar surgery will improve patient outcomes, as demonstrated by the literature review. Continuous dexmedetomidine has been shown to decrease the use of several commonly used opioids in anesthesia, thereby reducing the less favorable opioid side effects and decreasing patient exposure. Anesthesia providers' knowledge of the opioid crisis and its relation to this specific surgery has increased through the educational intervention. Improvement of knowledge obtained from this study should be used constructively to expand the use of dexmedetomidine beyond non-spine surgical procedures. The study implies that the providers' hesitancy to use dexmedetomidine is multifactorial, which may stem from anesthesiologists' attitudes who medically direct CRNAs at the facility. Future studies may benefit from understanding anesthesiologists' views and attitudes towards the use of dexmedetomidine while considering how long each provider has been practicing. There may be an indirect relationship between how many years an anesthesiologist has been practicing and how likely they are to use dexmedetomidine while considering that dexmedetomidine is a relatively newer drug.

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APPENDIX A

Evaluation table 1

Citation	Hwang W, Lee J, Park J, Joo J. Dexmedetomidine versus remifentanil in postoperative pain control after spinal surgery: a randomized controlled trial. *BMC Anesthesiology*. 2015; 15(21). doi:10.1186/s12871-015-0004-1.[19] -Level 1, high-quality evidence
Design/Method	Single block RCT of 40 total patients (ASA I and ASA II): -20 in remifentanil group, who received 0.01mcg/kg/min of remifentanil administered continuously using target-controlled infusion (TCI) as a TIVA adjuvant; -20 in the dexmedetomidine group, who received 0.01mcg/kg/min of dexmedetomidine administered continuously using a syringe pump as a TIVA adjuvant.
Sample/Setting	40 total patients (ASA I and ASA II of either sex) without CAD, ischemic disease, bradycardia (<50bpm), arrhythmias, and allergies to study drugs: n=20 remifentanil group patients; n=20 dexmedetomidine group patients; adult population of age range between 18 and 70 years old; undergoing posterior lumbar interbody fusion (PLIF) under general anesthesia.
Major Variables Studied and Their Definitions	Independent variable: -IV1 is remifentanil administration vs dexmedetomidine solution. Dependent variable: -DV1 is visual analog score (VAS) -DV2 amount of patient-controlled analgesia (PCA) administered -DV3 is rescue analgesics required -DV4 is postoperative nausea and vomiting (PONV)
Measurement and Data Analysis	-Anesthesia was maintained using propofol at 3–12 mg/kg/hr and remifentanil at 0.01-0.2 mcg/kg/min in Remifentanil group or dexmedetomidine at 0.01–0.02 mcg/kg/min (e.g. 0.5-1.0 μg/min for 50 kg patient) in Dexmedetomidine group -Bispectral Index (BIS) was maintained between 40 and 60 -Mechanical ventilation was maintained using air (50%) and oxygen (50%), with an end-tidal CO2 of 30– 40 mmHg in both groups. -Remifentanil was discontinued on completion of skin closure in Remifentanil group -Dexmedetomidine was ceased when skin closure was started in Dexmedetomidine group, taking into consideration their respective half-times. -Propofol was terminated upon the completion of skin closure. -PCA was applied when patients opened their eyes in the PACU. PCA consisted of 12 mg of hydromorphone in 100 ml of normal saline and was administered using an AutoMed 3200 pump at a background rate of 1 ml/h and a bolus dose of 1 ml with a lockout interval of 10 minutes. -In the PACU and general ward, 1 mcg/kg of fentanyl and 50 mg of tramadol were intravenously administered as rescue analgesia. -The visual analog scale (VAS) score, amount of PCA administered, rescue analgesics required, and PONV were recorded at the time of discharge from the PACU and 48 hours after surgery.

Findings	-The total amount of propofol used was not significantly different. -The time of eye-opening and first verbal command response in the PACU were significantly delayed in Dexmedetomidine group compared to Remifentanil group. -Significantly more patients in Remifentanil group required rescue analgesics during the early recovery period in the PACU. -PACU stay duration was not significantly different between the two groups. -VAS scores in Remifentanil group were significantly higher than in Dexmedetomidine group at every time point after surgery. -Dexmedetomidine group had statistically significantly lower PCA requirements at every time point after surgery except directly before discharge from the PACU. -Remifentanil group required more rescue analgesics at every time point after surgery and displayed more PONV until 24 hours post-surgery.
Results	-Dexmedetomidine had superior pain control efficacy than remifentanil for the first 48 hours following PLIF surgery, lowering the VAS score and reducing the PCA requirement. -Dexmedetomidine also reduced the analgesic requirement and PONV incidence compared to remifentanil.
Conclusions	Dexmedetomidine as an adjuvant in propofol-based TIVA displayed superior efficacy to remifentanil in alleviating pain and managing postoperative pain for 48 hours following PLIF surgery. Dexmedetomidine reduced the requirement for rescue analgesics and PONV. Therefore, dexmedetomidine may be used as an adjuvant in propofol-based TIVA instead of remifentanil for more efficient pain and PONV management.
Appraisal: Worth to Practice/Level	Strength: adequate pain relief that reduces opioid consumption- adds value to conclusions. Limitations: not listed Risk of harm: not listed. Feasibility of use: adequate, since dexmedetomidine is commercially available and commonly employed in various institutions.
THEME	Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine leads to decreased perioperative opioid administration without an increase in reported pain postoperatively.

Evaluation table 2

Citation	Kundra S, Taneja S, Choudhary AK, Katyal S, Garg I, Roy R. Effect of a low-dose dexmedetomidine infusion on intraoperative hemodynamics, anesthetic requirements and recovery profile in patients undergoing lumbar spine surgery. *J Anaesthesiol Clin Pharmacol*. 2019; 35:248-53. doi:10.4103/joacp.JOACP_338_18.[15] -Level 1, good quality evidence
Design/Method	Double-blind RCT of 60 patients (ASA I and ASA II): -30 in experimental Group A, who received 0.3mcg/kg/hr dexmedetomidine infusion -30 in control Group B, who received an equivalent volume of saline solution at the same rate and at the same time.

Sample/Setting	60 total patients (ASA I and II of, of either sex, adult population of age range between 18 and 65 years old; undergoing elective laminectomy at one- or two-lumbar levels in the prone position under general anesthesia in a tertiary level hospital). -The exclusion criteria were pregnant patients, patients suffering from hypertension (blood pressure >140/90 mm Hg), uncontrolled diabetes mellitus, morbid obesity (BMI >35), severe respiratory disease, such as asthma, chronic obstructive pulmonary disease, severe hepatic, renal, endocrine disease, cardiac dysfunction, such as ischemic heart disease, arrhythmias, and valvular heart disease. Patients having a history of drug abuse or undergoing spine fixation or corrective spine surgery, or those who have undergone previous spine surgery were also excluded. -N=30 experimental group patients -N=30 control group patients.
Major Variables Studied and Their Definitions	Independent variable: -IV1 is dexmedetomidine administration vs. saline solution. Dependent variable: -DP1 is Emergence time (measured as the time between anesthetic discontinuation and the time at which patients opened their eyes). -DP2 is Tracheal extubation time (measured as the time elapsed from anesthetic discontinuation to extubation. -DP3 is Recovery time (measured as the time elapsed from discontinuation of anesthetic agent to the time when patients were able to recall their names and dates of birth). -DP4 is a measure of hemodynamics that includes blood pressure (BP), heart rate (HR), and mean arterial pressure (MAP). -DP5 is mean perioperative fentanyl requirements -DP6 is anesthetic requirements based on BIS scores
Measurement and Data Analysis	-Anesthesia was maintained using oxygen (O2) and nitrous oxide (N2O) (40:60), and sevoflurane (1%–3%). -Lungs were ventilated with a tidal volume of 6–8 mL/kg and respiratory rate of 10–12 per minute to maintain an end-tidal carbon dioxide (EtCO2) of 30–40 mm Hg. -Depth of anesthesia was monitored using the BIS targeting BIS values between 40 and 60 by adjusting the dial settings of sevoflurane. -At ‘0’ time, IV infusion dexmedetomidine was started at a rate of 0.3 mcg/kg/hr in patients in Group A. -Patients in Group B were administered an infusion of 0.9% saline at the same rate and time. -An episode of tachycardia (defined as heart rate >20% of baseline value) and hypertension (defined as blood pressure >20% of baseline value), lasting for more than a minute, was controlled with a bolus of fentanyl (1 mcg/kg) given intravenously. Another bolus of fentanyl 0.5 mcg/kg was repeated after 15 min if the heart rate and blood pressure did not revert to normal. -At the end of surgery, all patients were administered paracetamol 1 g IV and ondansetron 8 mg IV at the beginning of skin closure. -The infusion of study medication was stopped on starting of skin closure -Sevoflurane was stopped once dressing of the incision site was complete.
Findings	Mean perioperative fentanyl requirements were lesser in group A as compared with group B

Results	-Duration of surgery was similar in both groups -Difference in the total amount of fentanyl administered in either group was statistically insignificant -Mean HR was statistically similar in both the groups. -MAP was significantly lower in Group A for the initial 30 min, after which the difference in MAP among the two groups was statistically not significant. -Mean end-tidal sevoflurane concentration was significantly less in Group A -Mean total intraoperative blood loss in group A was significantly less. -Mean emergence time, mean tracheal extubation time, and mean recovery times, were significantly earlier in Group A
Conclusions	Low-dose dexmedetomidine infusion at a rate of 0.3 mcg kg/hr reduces intraoperative blood loss and results in earlier emergence from anesthesia without any significant adverse effects. It also decreases mean perioperative fentanyl requirements.
Appraisal: Worth to Practice/Level	Strength: Dexmedetomidine decreased mean perioperative fentanyl requirements in Group A. No conflicts of interest. Limitations: the study did not measure intra-abdominal pressure, which can have a bearing on intraoperative blood loss. Measurement of plasma levels of dexmedetomidine and cardiac output could have added more value to our findings. We could not demonstrate opioid-sparing properties, whereas some other studies have reported opioid-sparing effects when using dexmedetomidine. More studies are needed to find the reason for this and whether dexmedetomidine's analgesia-sparing properties are dose-dependent.
THEME	Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine lead to decreased perioperative opioid administration

Evaluation table 3

Citation	Kim, DJ, Bengali R, Anderson TA. Opioid-free anesthesia using continuous dexmedetomidine and lidocaine infusions in spine surgery. *Korean J Anesthesiol*. 2017;70(6):652-653. doi:10.4097/kjae.2017.70.6.652.[18] -Level 2, good quality evidence
Design/Method	-Case study of 1 patient who received dexmedetomidine, lidocaine, and propofol as continuous infusions without the use of any intraoperative opioids and minimal opioids postoperatively for 24 hours. -No inclusion or exclusion criteria
Sample/Setting	-1 patient presented for L4-S1 posterior lumbar fusion with: -Past medical history of hypertension, obesity, congenital bicuspid aortic valve status post-aortic valve replacement, a pacemaker for postoperative bradycardia, and lumbar spinal stenosis presented for L4-S1 posterior lumbar fusion. -Surgical history included a previous L4-S1 laminectomy, appendectomy, arthroscopic knee surgery, and a bioprosthetic aortic valve replacement. -Preoperative medications included aspirin 81 mg daily, metoprolol extended-release 50 mg daily, and lisinopril 5 mg daily.
Major Variables Studied and Their Definitions	Independent variable: -IV1 is dexmedetomidine and lidocaine administration. Dependent variable: -DV1 is postoperative pain -DV2 is postoperative nausea and vomiting (PONV) -DV3 is post-anesthesia care unit (PACU) discharge and patient recovery.
Measurement and Data Analysis	-General anesthesia was induced using dexmedetomidine (1 mcg/kg over 10 min, started 10 min preinduction), lidocaine (1.5 mg/kg), propofol (2 mg/kg), and succinylcholine (1 mg/kg).

	-Anesthesia was maintained with intravenous infusions of dexmedetomidine (1 mcg/kg/hr), lidocaine (1.5 mg/kg/hr), and inhaled nitrous oxide: oxygen. -No receive opioids administered intraoperatively -A total of 0.4 mg of hydromorphone was administered during 90-min PACU stay via PCA. -Transitioned to oral morphine within 3 hours of being discharged from the PACU
Findings	-Anesthetic limited the intraoperative opioid requirement and may have resulted in improved analgesia for a minimum of 24 h postoperatively -Total 24-h postoperative oral (PO) morphine milligram equivalent (MME) usage was 70 mg (IV MME 23.3 mg.
Results	-Patient used significantly less MME postoperatively (70 mg PO or 23.3 mg IV in 24 h) compared with similar reports of patients undergoing posterior spinal fusion using a traditional, opioid-based intraoperative anesthetic without dexmedetomidine or lidocaine. -Patient did not require IV rescue boluses of opioids and denied PONV while remaining hemodynamically stable postoperatively.
Conclusions	-Limiting opioids and their potential side effects in the perioperative period while maintaining adequate analgesia may facilitate PACU discharge and patient recovery. -An added benefit of the opioid-free intraoperative course was the potentially safer and relatively fast emergence from anesthesia that facilitated a prompt neurological examination.
Appraisal: Worth to Practice/Level	Strength: adequate pain relief that reduces opioid consumption- adds value to conclusions. Limitations: none listed Risk of harm: none listed. Possible awareness Feasibility of use: adequate, since dexmedetomidine is commercially available and commonly employed in various institutions.
THEME	PICO Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine and lidocaine resulted in an opioid sparring intraoperative phase and decreased postoperative opioid consumption by comparison.

Evaluation table 4

Citation	Hadi BA, Sbeitan SM, Shakya AK. Fentanyl vs fentanyl-dexmedetomidine in lumbar foraminotomy surgery. *Therapeutics and Clinical Risk Management*. 2019; 15: 885-890. doi: 10.2147/TCRM.S195108.[17] -Level 1, high-quality evidence
Design/Method	Double-blind RCT of 40 total patients (ASA I and ASA II): -20 in Fentanyl group, who received a fentanyl loading dose of 1.0 mcg/kg and maintenance infusion dose of 0.2 mcg/kg/hr and normal saline (0.9%) placebo; -20 in Fentanyl- dexmedetomidine group (Fen-Dex), who received a fentanyl loading dose of 1.0 mcg/kg and maintenance infusion dose of 0.2 mcg/kg/hr and dexmedetomidine infusion (0.5 μg/kg/h) along with the fentanyl infusion.
Sample/Setting	40 total patients (ASA I and ASA II, of either sex, and adult population from ages 48 to 55). -Patients with major systemic diseases or those taking chronic narcotics were excluded. -N=20 fentanyl group patients -N=20 fentanyl-dexmedetomidine group patients -Undergoing lumbar foraminotomy surgery under general anesthesia.

Major Variables Studied and Their Definitions	Independent variable: -IV1 is fentanyl and saline administration vs fentanyl and dexmedetomidine solution. Dependent variable: -DV1 is time to first post-operative request for analgesic agent -DV2 is total morphine postoperative morphine consumption -DV3 is severity of postoperative pain using the visual analog scale (VAS) score -DV4 is nausea and vomiting side effects
Measurement and Data Analysis	-Patients of both groups received midazolam (0.25 mg/kg PO) as a pre-medication. -General anesthesia was induced with propofol (2 mg/kg) bolus intravenous (iv) injection, followed by atracurium (0.6 mg/kg) and sevoflurane/nitrous oxide mixture. -Both groups received Fentanyl (1 mcg/kg) bolus iv injection followed by a fentanyl infusion (0.2 mcg/kg/hr). -Patients in the Fen-Dex group received dexmedetomidine (loading dose of 0.5 mcg/kg and maintenance dose of 0.2 mcg/kg/h)r infusion for the first 24 hours after surgery. -Patients in the Fentanyl group received normal saline as needed during surgery and postoperatively. -Whenever the postoperative pain score was more than 4 on VAS, morphine was given intravenously in the PACU until the pain score was reduced. -Morphine was given using a morphine infusion pump which can deliver morphine solution at the rate of 1 mg/mL/h.
Findings	-The time to first postoperative request for an analgesic agent in PACU, total morphine consumption, VAS score, MAP, and HR were observed over the first 24 hours after surgery -Findings were significantly different between the two groups.
Results	-Morphine requirements for the Fen-Dex group were significantly reduced compared to the Fentanyl group (Fen group) (p=0.001). -The first request for an analgesic agent during the treatment at PACU was also significantly (P=0.001) reduced. -The VAS value was also significantly (P=0.001) reduced in the Fen-Dex group compared to the Fentanyl group. -Hemodynamic measurements were satisfactory and normal, showing no significant differences between the two groups (MAP [p=0.339] and HR [p=0.767]) -Patients in the Fen-Dex group experienced fewer episodes of nausea and vomiting.
Conclusions	Adding dexmedetomidine to fentanyl in lumbar foraminotomy surgery at different levels could be a supplementary therapy to maintain a hemodynamic level and ensure postoperative analgesic control while reducing the consumption of postoperative morphine, thereby minimizing nausea and vomiting side effects
Appraisal: Worth to Practice/Level	Strength: adequate pain relief that reduces opioid consumption- adds value to conclusions. None of the patients were excluded from the study due to any complications Limitations: not listed Risk of harm: not listed. Feasibility of use: adequate, since dexmedetomidine is commercially available and commonly employed in various institutions.

THEME	Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine and fentanyl lead to decreased perioperative opioid administration without an increase in reported pain postoperatively compared to fentanyl only

Evaluation table 5

Citation	Turgut N, Turkmen A, Gokkaya S, Altan A, Hatiboglu MA. Dexmedetomidine-based versus fentanyl-based total intravenous anesthesia for lumbar laminectomy. *Minerva Anestesiol*. 2008:74(9):469-74. PMID: 18762754.[20] -Level 1, high-quality evidence
Design/Method	RCT of 50 total patients (ASA I and ASA II): -25 in Dexmedetomidine group (Group D), who received dexmedetomidine 0.6 mcg/kg as bolus before induction and 0.2 mcg/kg/hr by infusion; -25 in Fentanyl group (Group F), who received fentanyl 1 mcg/kg as a bolus before induction and 0.5 mcg/kg/hr by infusion.
Sample/Setting	50 total patients (ASA I and ASA II, of either sex, and adult population of ages 18 to 63 years). -Patients were excluded if they satisfied one or more of the following criteria: a bodyweight of more than 130% of ideal weight, uncontrolled hypertension (uncontrolled hypertension with blood pressure higher than 140/90 mmHg), severe respiratory diseases such as asthma or ischemic heart disease. -N=25 dexmedetomidine group (Group D) patients -N=25 fentanyl group (Group F) patients -Undergoing lumbar laminectomy surgery under general anesthesia at the Okmeydani Research and Training Hospital in Istanbul, Turkey.
Major Variables Studied and Their Definitions	Independent variable: -IV1 is dexmedetomidine administration vs fentanyl solution Dependent variable: -DV1 is recovery time and consumption of anesthetic and analgesic agents -DV2 is hemodynamics -DV3 is adverse events
Measurement and Data Analysis	-Group D received dexmedetomidine 0.6 mcg/kg -Group F received fentanyl 1 mcg/kg over 15 minutes before induction of anesthesia. -Twenty milligrams of propofol were given every 15 seconds by the manually-controlled infusion (MCI) technique until BIS was below 60. -After induction with propofol, cisatracurium was administered. -Depth of anesthesia was monitored by using a BIS with a target range between 50 and 60. -Anesthesia was maintained with air (50%), oxygen (50%), and propofol infusion. -Propofol maintenance dosages were 50-150 mcg/kg/min. -Group D- dexmedetomidine infusion dose started at 0.2 mcg/kg/hr and increased by 0.1 mcg/kg/hr. Dexmedetomidine was terminated at the beginning of the skin closure. -Group F- fentanyl infusion was maintained with a dosage of 0.5 mcg/kg/hr. According to the heart rate and mean arterial pressure, the dose was increased by 0.1 mcg/kg/hr /hr. Fentanyl was terminated at the end of the laminectomy. -The infusion of dexmedetomidine or fentanyl was started before induction and adjusted to keep the mean arterial blood pressure at -20% to +10% from the preoperative value. -Tramadol (1mg/kg) was given before the skin closure.

Findings	Fentanyl patients required supplemental analgesia earlier than dexmedetomidine group, and there is a significant decrease in consumption of hypnotic and sedative agents with dexmedetomidine both in induction and maintenance.
Results	-MAP values in Group D were significantly higher than in Group F only after intubation (P<0.05). MAP values before and after extubation in Group F were significantly higher than in Group D (P<0.05). -There was no statistical difference in heart rate between the groups -Propofol doses for induction and the maintenance of anesthesia were lower with dexmedetomidine (P<0.01). -Extubation time and PACU discharge time was similar in the two groups. -The fentanyl patients required supplemental analgesia earlier than the dexmedetomidine group (median time 35 min vs. 60 min). -Postoperative nausea and vomiting were significantly higher in Group F (P<0.01).
Conclusions	-Propofol-dexmedetomidine is suitable for patients who undergo elective spinal laminectomy, and it provides stable perioperative hemodynamic responses. -Propofol-fentanyl medication requires higher dosages of postoperative analgesics and causes frequent postoperative nausea and vomiting compared with propofol-dexmedetomidine.
Appraisal: Worth to Practice/Level	Strength: adequate pain relief that reduces opioid consumption compared to fentanyl group- adds value to conclusions. Limitations: not listed Risk of harm: not listed. Feasibility of use: adequate, since dexmedetomidine is commercially available and commonly employed in various institutions.
THEME	Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine leads to decreased postoperative opioid administration compared to fentanyl group.

Evaluation table 6

Citation	Ozkose Z, Demir FS, Pampal K, Yardim S. Hemodynamic and anesthetic advantages of dexmedetomidine, an alpha 2-agonist, for surgery on the prone position. *Tohoku J Exp Med*. 2006;210(2):153-160. doi:10.1620/tjem.210.153.[16] -Level 1, high-quality evidence
Design/Method	Double-blind RCT of 40 patients (ASA I and ASA II): -20 in the dexmedetomidine group, who received a loading dose of 1 mcg/kg Dexmedetomidine over 10 minutes, followed by an intravenous (I.V.) infusion of dexmedetomidine 0.2 mcg/kg/hr until the closure of the surgical incision. -20 in saline group, who received the same amount of saline was given to the patients in the control
Sample/Setting	40 total patients (ASA I and ASA II of either sex) -Emergency cases and patients with valvular heart disease, intracardiac shunts, severe pulmonary, hepatic or renal disease, pregnancy, chronic alcoholism, drug abuse, or morbid obesity (Body Mass Index [BMI] > 35) were excluded. -None of the patients were using beta-blockers or alpha 2-agonists, and there existed no history of exposure to dexmedetomidine -N=20 dexmedetomidine group patients

	-N=20 saline group patients -Adult population with age range not specified and undergoing elective lumbar surgery for disc disease.
Major Variables Studied and Their Definitions	Independent variable: -IV1 is dexmedetomidine administration vs. saline solution. Dependent variable: -DV1 is hemodynamic profile (HR, BP MAP); -DV2 is recovery profile (spontaneous eye-opening, extubation time, response to verbal commands, Aldrete score, PONV, numeric pain score, analgesic requirements.
Measurement and Data Analysis	-Anesthesia was standard for all patients. Induction was performed with thiopental sodium (5-7 mg/kg) and fentanyl (2mg/kg). Muscle relaxation was achieved with 0.6 mg/kg rocuronium. The lungs were ventilated by maintaining a tidal volume of 7-10 ml/kg, respiratory rate of 8-12 per minute, and an end-tidal CO_2 concentration of 35-40 mmHg. Desflurane was delivered in 4 L/min fresh gas flow combined with 50% N_2O in oxygen for the maintenance of anesthesia. Intraoperative BIS range of 40 to 60 was maintained throughout the surgery. -Dexmedetomidine group received a loading dose of 1 mcg/kg of dexmedetomidine over 10 min, followed by an intravenous (I.V.) infusion of dexmedetomidine at 0.2 mcg/kg/hr until the closure of the surgical incision. -Saline group received the same amount of saline. -If hypertension or tachycardia developed during anesthesia while BIS was between 40 and 60, it was assumed to be due to insufficient analgesia, and a bolus dose of 1 mcg/kg fentanyl was given. -Postoperative pain was evaluated at 5 min intervals using a 10-point verbal rating scale (VRS) (0: no pain; 10: severe pain). Rescue analgesia with 1 mg/kg meperidine was administered intramuscularly after the operation in the presence of a pain score of ≧ 3 or if the patient requested analgesia during pain assessment.
Findings	Combination of preoperative loading and intraoperative I.V. infusion of dexmedetomidine blunted the pressure response to intubation and surgery, decreased the desflurane requirements, shortened recovery times, improved hemodynamic stability, and decreased postoperative pain level and meperidine requirement in patients who underwent lumbar discectomy under desflurane anesthesia.
Results	-The amount of thiopentone used for induction of anesthesia was higher in the control group (385.22 ± 45.1 mg) compared with Dex group (210.19 ± 27.4 mg) ($p < 0.05$). -End-tidal desflurane concentration required to maintain the target BIS level (40-60) was lower in Dex group than control group ($p < 0.05$) -The time spent until eye-opening, extubation, and following commands were consistently shorter in Dex group than control group ($p < 0.05$). -Postoperative pain scores at 30 and 60 min. were significantly lower in Dex group than control group ($p < 0.05$). Eleven of 20 patients in the control group and two of 20 patients in Dex group required meperidine during the first hour in the postoperative period ($p < 0.05$).

Conclusions	Dexmedetomidine may provide an alternative to the currently used adjunctive anesthetic agent in lumbar surgery, especially in treating intraoperative hypertension and when severe postoperative pain is expected.
Appraisal: Worth to Practice/Level	Strength: adequate pain relief that reduces opioid consumption- adds value to conclusions. Limitations: not listed Risk of harm: not listed. Feasibility of use: adequate, since dexmedetomidine is commercially available and commonly employed in various institutions.
THEME	PICO Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine leads to decreased postoperative opioid administration.

Evaluation table 7

Citation	Peng K, Liu HY, Liu SI, Ji FH. Dexmedetomidine-fentanyl compared with midazolam-fentanyl for conscious sedation in patients undergoing lumbar disc surgery. Short Communication. 2016;38(1):P192-201. doi:https://doi.org/10.1016/j.clinthera. 2015.11.016.[21] -Level 1, good quality evidence
Design/Method	Double-blind RCT of 60 patients (ASA I and ASA II): -30 in Dexmedetomidine-Fentanyl group, who received 0.5mcg/kg/ dexmedetomidine and 1mcg/kg of fentanyl -30 in Midazolam-Fentanyl group, who received 0.05 mg/kg/hr midazolam and 1mcg/kg of fentanyl.
Sample/Setting	60 total patients (ASA I and II of, of either sex, adult population of age range between 18 and 65 years old) undergoing elective lumbar laminotomy or discectomy under local anesthesia and conscious sedation. -The exclusion criteria were known allergies to medications used, an ASA classification of III or more, body mass index >35 or <15 kg/m^2, asthma, sleep apnea syndrome, evidence of heart block, ischemic heart disease, major renal or liver diseases (known renal or hepatic disease with serum albumin concentration <30 g/L or creatinine 4120 mmol/L), long term use of opioids or benzodiazepine, alcohol abuse, pregnancy, and patient refusal. -Patients were informed preoperatively about using a verbal rating scale for pain (VRS; 0–10, where 0 represented no pain and 10 indicated the worst pain imaginable) and using a patient-controlled analgesia (PCA) device for postoperative pain management. -N=30 Dexmedetomidine-Fentanyl Group -N=30 Midazolam-Fentanyl Group
Major Variables Studied and Their Definitions	Independent variable: -IV1 is dexmedetomidine with fentanyl administration vs midazolam with fentanyl administration. Dependent variable: -DP1 is hemodynamic and respiratory changes. -DP2 is sedation scores -DP3 is pain scores -DP4 is fentanyl consumption -DP5 is patient satisfaction -DP6 is postoperative hospital stay -DP6 is adverse events

Measurement and Data Analysis	-No premedication was given. -Oxygen was administered at 2 L/min via nasal cannula throughout the procedure. -Each patient received an intravenous bolus dose of 1 mg/kg fentanyl combined with either 0.5 mg/kg dexmedetomidine (DF group) or 0.05 mg/kg midazolam (MF group) for 10 minutes, followed by a continuous infusion with either 0.5 mcg/kg/hr dexmedetomidine (DF group) or 0.05 mg/kg/hr midazolam (MF group) until the end of the surgery. -Increases or decreases of 0.1 mcg/kg/hr dexmedetomidine or 0.01mg/kg/hr midazolam could be repeated to maintain a Ramsay Sedation Scale score of 3 to 4 (full sedation). -After full sedation was accomplished, local anesthesia was provided with 2% lidocaine by the surgeons. -Additional 0.5 mg/kg boluses of fentanyl were available for rescue analgesia intraoperatively. -The PCA device was set to deliver fentanyl boluses of 10 mg with a lockout interval of 5 minutes for 24 hours (in the PACU and in the ward). -Patients were encouraged to push the demand button when they experienced pain and repeat until they felt pain relief. -Flurbiprofen axetil (50mg) was administered as an additional analgesic if the pain scores remained >4 for 15 minutes.
Findings	The main finding of the present study is that patients given a DF combination for conscious sedation during lumbar disc surgery required less intraoperative and postoperative fentanyl and had a similar level of sedation and pain relief compared with patients who received MF.
Results	-HR was lower in the DF group at all time points -Difference in mean SpO2 was not significant -No significant difference was found in the Ramsay Sedation Scale scores between groups at each time point -No significant difference was found between the groups' VRS scores at each time point during the procedure, in the PACU, and in the ward. -Patients in the DF group required less intraoperative, postoperative, and total fentanyl -None of the patients reported insufficient analgesia or received flurbiprofen axetil after surgery.
Conclusions	DF combination was associated with less consumption of opioid analgesics; therefore, it may be a better alternative as a sedative regimen for patients who undergo awake lumbar laminotomy and discectomy
Appraisal: Worth to Practice/Level	Strength: Dexmedetomidine decreased mean perioperative fentanyl consumption in the dexmedetomidine-fentanyl group. No dropouts. All surgical procedures were successfully performed with conscious sedation without conversion to GETA. Limitations: -First, the study's primary endpoint was fentanyl consumption, and the results indicated that dexmedetomidine provided a beneficial analgesic effect. Therefore, this study may not be sufficiently powered to detect differences in adverse events between the two treatment groups. -Second, it may not be sufficiently powered to show differences in patient satisfaction and postoperative hospital stay, and patient satisfaction may only truly be assessed in a cross-over study. Third, MF was selected as the comparison medication. Although this combination is most commonly used for sedation during surgical and other procedures, alternatives such as propofol and remifentanil were not tested. -Finally, the sample size in the present study was relatively small, so the results may not be extrapolated beyond the population studied.

THEME	Outcome: Decreased perioperative opioid administration without an increase in reported pain postoperatively. -Dexmedetomidine- fentanyl leads to decreased perioperative opioid administration while still maintain a similar pain level.

APPENDIX B

FIU | FLORIDA INTERNATIONAL UNIVERSITY

Nicole Wertheim College of Nursing and Health Sciences
Department of Nurse Anesthetist Practice

Uses of Immersive Virtual Reality Distraction as an adjunct to anesthesia to decrease levels of pain in patients experiencing acute procedural pain: An Evidence Based Educational Module

Dear Miami Beach Anesthesiology Associates, Inc. Anesthesia Provider:

My name is Michael Otte and I am a student from the Anesthesiology Nursing Program Department of Nurse Anesthetist Practice at Florida International University. I am writing to invite you to participate in my quality improvement project. The goal of this project is to improve health care provider knowledge on the use of continuous perioperative dexmedetomidine infusion to reduce opioid consumption in adult patients undergoing spinal lumbar surgery. You are eligible to take part in this project because you are a member of Miami Beach Anesthesiology Associates, Inc. at Mount Sinai Medical Center.

If you decide to participate in this project, you will be asked to complete and sign a consent form for participation. Next, you will complete a pre-test questionnaire, which is expected to take approximately 5 minutes. You will then be asked to view an approximately 15 minute long educational presentation online. After watching the video, you will be asked to complete the post-test questionnaire, which is expected to take approximately 5 minutes. No compensation will be provided.

Remember, this is completely voluntary. You can choose to be in the study or not. If you'd like to participate or have any questions about the study, please email or contact me at motte004@fiu.edu or 786-514-8904.

Thank you very much.

Sincerely,

Michael Otte, SRNA, BSN, CCRN

APPENDIX C

Miami Beach Anesthesiology Associates, Inc.

Mount Sinai Medical Center • Division of Anesthesia

March 3, 2021

Fernando C Alfonso, DNP, CRNA, APRN
Assistant Clinical professor
Department of Nurse Anesthetist Practice
Florida International University

Dr. Alfonso,

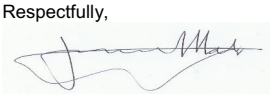
Thank you for inviting Mount Sinai Medical Center to participate in Doctor of Nursing Practice (DNP) project conducted by Michael Otte entitled “An Education Intervention on The Use of Continuous Perioperative Dexmedetomidine Infusion to Reduce Opioid Consumption in Adult Patients Undergoing Spinal Lumbar Surgery” in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthetist Practice at Florida International University. I have given 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 investigate and synthesize the latest evidence.

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: Michael Otte and Dr. Fernando Alfonso.

Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. Michael Otte 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.

Respectfully,



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APPENDIX D

FLORIDA INTERNATIONAL UNIVERSITY

Office of Research Integrity
Research Compliance, MARC 414

MEMORANDUM

To:	Dr. Vicente Gonzalez
CC:	Michael Otte
From:	Elizabeth Juhasz, Ph.D., IRB Coordinator EJ
Date:	May 28, 2021
Protocol Title:	**"An Education Intervention on the Use of Continuous Perioperative Dexmedetomidine Infusion to Reduce Opioid Consumption in Adult Patients Undergoing Spinal Lumbar Surgery"**

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-21-0194 **IRB Exemption Date:** 05/28/21
TOPAZ Reference #: 110224

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.

EJ

APPENDIX E

FLORIDA INTERNATIONAL UNIVERSITY

CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT
"An Educational Intervention on the Use of Continuous Dexmedetomidine Infusion to Reduce Opioid Consumption in Adult Patients Undergoing Spinal Lumbar Surgery."

SUMMARY INFORMATION
Things you should know about this study:

- **Purpose:** Educational module concerning the use of continuous perioperative dexmedetomidine to reduce opioid consumption in adult patients undergoing spinal lumbar surgery.
- **Procedures**: If you choose to participate, you will be asked to complete a pre-test, watch a voice PowerPoint, and then a post-test
- **Duration:** This will take about a total of 20-minutes.
- **Risks**: The main risk or discomfort from this research is minimal
- **Benefits:** The main benefit to you from this research is to increase the participant's knowledge on the role of dexmedetomidine in reducing perioperative opioid consumption.
- **Alternatives:** There are no known alternatives available to you other than not taking part in this study.
- **Participation:** Taking part in this research project is voluntary.

Please carefully read the entire document before agreeing to participate.

PURPOSE OF THE PROJECT
You are being asked to be in a quality improvement project. The goal of this project is to increase the knowledge of health care providers in using continuous dexmedetomidine infusion to reduce opioid consumption in adult patients undergoing spinal lumbar surgery.

NUMBER OF STUDY PARTICIPANTS

If you decide to be in this project, you will be one of ten people in this research study.

DURATION OF THE PROJECT
Your participation will require about 20 minutes of your time.

PROCEDURES
If you agree to be in the project, we will ask you to do the following things:

- Complete a 5-minute pre-test survey
- Watch a 15-minute educational module with information on the role of perioperative dexmedetomidine infusion to reduce opioid consumption in adult patients undergoing spinal lumbar surgery.
- Complete a 5-minute post-test survey.

RISKS AND/OR DISCOMFORTS
There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may have included mild emotional stress or mild physical discomfort from sitting on a chair for an extended period of time, for instance.

BENEFITS
The following benefits may be associated with your participation in this project: An increased understanding of the role of perioperative dexmedetomidine infusion in reducing opioid consumption in adult patients undergoing spinal lumbar surgery. This will help you to better manage perioperative pain with a non-opioid alternative and decrease patient exposure to opioids in the perioperative period. The overall objective of the program is to increase the quality of healthcare delivery and improve healthcare outcomes for our patients.

ALTERNATIVES
There are no known alternatives available to you other than not taking part in this project. However, if you would like to receive the educational material given to the participants in this project, it will be provided to you 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, we might publish, we will not include any information that will make it possible to identify you as a participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this research project is voluntary.

COMPENSATION & COSTS
There is no cost or payment to you for receiving the health education and/or for participating in this project.

RIGHT TO DECLINE OR WITHDRAW

Your participation in this project is voluntary. You are free to participate in the project or withdraw your consent at any time during the project. Your withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove you without your consent at such time that they feel it is in the 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 Michael Otte at 786-514-8904/motte004@fiu.edu or Dr. Fernando Alfonso at 305-348-3510/falfonso@fiu.edu.

IRB CONTACT INFORMATION
If you would like to talk with someone about your rights pertaining to being a subject in this project or about ethical issues with this project, you 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 F

Pretest and Posttest Questionnaire:

Continuous Dexmedetomidine Infusion to Reduce Perioperative Opioid Consumption

INTRODUCTION

The primary aim of this QI project is to improve the knowledge of CRNAs pertaining to the use of continuous dexmedetomidine infusion to decrease opioid consumption in adults undergoing lumbar spine surgery.

Please answer the question below to the best of your ability. The questions are in multiple choice format and are meant to measure knowledge and perceptions on the use of dexmedetomidine and patients requiring lumbar spine surgery.

PERSONAL INFORMATION

1. **Gender:** Male Female Other_____
2. **Age:** _____
3. **Ethnicity:**

   Hispanic Caucasian African American Asian

   Other_____
4. **Position/Title:** _____
5. **Level of Education:** Bachelor Masters Doctorate Other

   _____
6. How many years have you been an anesthesia provider?

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

QUESTIONNAIRE

1. **According to the National Institute of Health (NIH), opioid overdose kills approximately how many Americans daily?**
    a. 25-50
    b. 50-100
    c. 100-150
    d. 150+
2. **Identify which of the following factors that are responsible for increasing the risk of chronic opioid use after surgery.** (Select all that apply)
    a. Female
    b. Depression/anxiety
    c. Fibromyalgia
    d. History of benzodiazepine use
3. **Please indicate your level of agreement with the following statement:** ***Patients presenting for lumbar spine surgery that are prescribed opioids preoperatively to treat pain are more likely to use opioids for up to a year following surgery with subsequent opioid tolerance.***
    a. Strongly agree
    b. Agree
    c. Neutral
    d. Disagree
    e. Strongly disagree
4. **Please indicate your level of agreement with the following statement:** ***Perioperative exposure to opioids for the opioid naïve patient increases the risk of acute tolerance and chronic use.***
    a. Strongly agree

b. Agree

c. Neutral

d. Disagree

e. Strongly disagree

5. **What are the clinical uses of dexmedetomidine?** (Select all that apply)

a. Sedation

b. Anxiolysis

c. Amnesia

d. Analgesia

e. Sympatholytic

6. **What is the mechanism of action of dexmedetomidine?**

a. N-methyl-D-aspartate (NMDA) receptor antagonism

b. Mu receptor agonism

c. Alpha-2 adrenoreceptor agonism

d. Gamma-aminobutyric acid (GABA) receptor antagonism

7. **Continuous intraoperative dexmedetomidine infusion reduces intraoperative and postoperative opioid requirements**

a. Effectively

b. Somewhat effectively

c. Somewhat ineffective

d. Most ineffectively

8. **Which opioids are more cost-effective in comparison to dexmedetomidine?**

a. Remifentanil

b. Meperidine

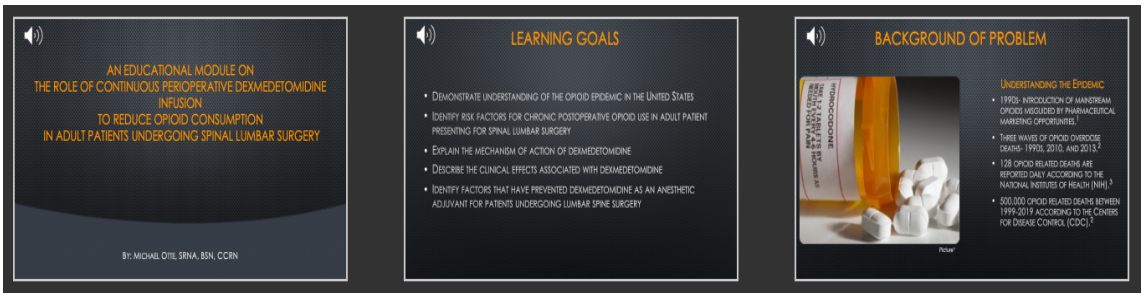
c. Hydromorphone

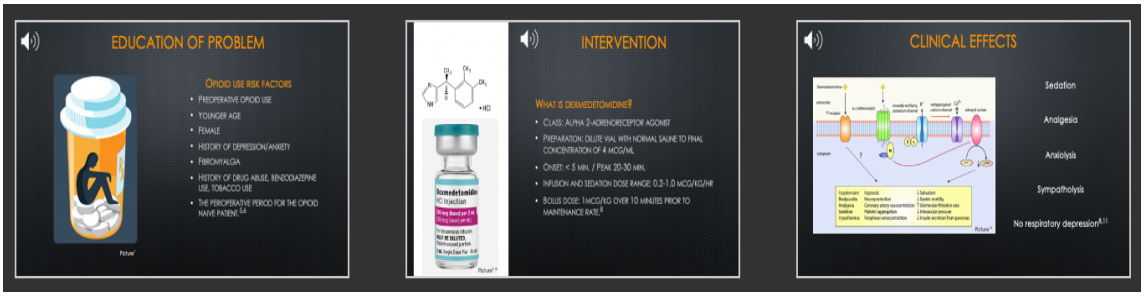
d. All of the above

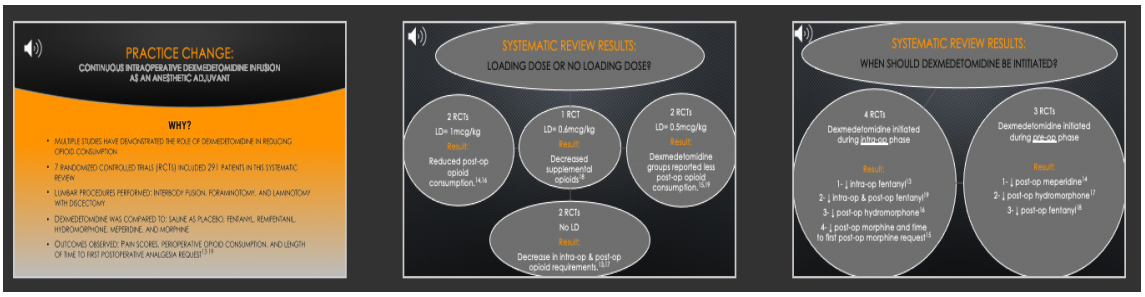
e. None

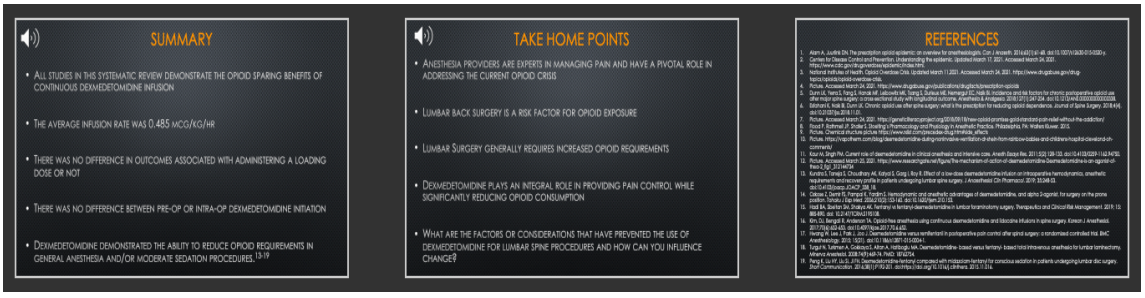
9. **What factors have prevented the use of dexmedetomidine for lumbar spine procedures at your clinical site?**
    a. Anesthesia culture/attitudes toward dexmedetomidine
    b. Postoperative neurological assessment
    c. Hemodynamic side effects
    d. A and B
    e. All of the above
10. **How likely are you to use dexmedetomidine to decrease opioid use?**
    a. Most likely
    b. Somewhat likely
    c. Somewhat unlikely
    d. Most unlikely
11. **How likely are you to recommend dexmedetomidine?**
    a. Most likely
    b. Somewhat likely
    c. Somewhat unlikely
    d. Most unlikely

APPENDIX G


AN EDUCATIONAL MODULE ON
THE ROLE OF CONTINUOUS PERIOPERATIVE DEXMEDETOMIDINE INFUSION
TO REDUCE OPIOID CONSUMPTION
IN ADULT PATIENTS UNDERGOING SPINAL LUMBAR SURGERY
BY: MICHAEL OTTE, SRNA, BSN, CCRN
LEARNING GOALS
DEMONSTRATE UNDERSTANDING OF THE OPIOID EPIDEMIC IN THE UNITED STATES
IDENTIFY RISK FACTORS FOR CHRONIC POSTOPERATIVE OPIOID USE IN ADULT PATIENT PRESENTING FOR SPINAL LUMBAR SURGERY
EXPLAIN THE MECHANISM OF ACTION OF DEXMEDETOMIDINE
DESCRIBE THE CLINICAL EFFECTS ASSOCIATED WITH DEXMEDETOMIDINE
IDENTIFY FACTORS THAT HAVE PREVENTED DEXMEDETOMIDINE AS AN ANESTHETIC ADJUVANT FOR PATIENTS UNDERGOING LUMBAR SPINE SURGERY
BACKGROUND OF PROBLEM
UNDERSTANDING THE EPIDEMIC
1990S- INTRODUCTION OF MAINSTREAM OPIOIDS MISGUIDED BY PHARMACEUTICAL MARKETING OPPORTUNITIES.[1]
THREE WAVES OF OPIOID OVERDOSE DEATHS- 1990S, 2010, AND 2013.[2]
128 OPIOID RELATED DEATHS ARE REPORTED DAILY ACCORDING TO THE NATIONAL INSTITUTES OF HEALTH (NIH).[3]
500,000 OPIOID RELATED DEATHS BETWEEN 1999-2019 ACCORDING TO THE CENTERS FOR DISEASE CONTROL (CDC).[3]


EDUCATION OF PROBLEM
OPIOID USE RISK FACTORS
PREOPERATIVE OPIOID USE
YOUNGER AGE
FEMALE
HISTORY OF DEPRESSION/ANXIETY
FIBROMYALGIA
HISTORY OF DRUG ABUSE, BENZODIAZEPINE USE, TOBACCO USE
THE PERIOPERATIVE PERIOD FOR THE OPIOID NAIVE PATIENT.[5,6]
INTERVENTION
WHAT IS DEXMEDETOMIDINE?
CLASS: ALPHA 2-ADRENORECEPTOR AGONIST
PREPARATION: DILUTE VIAL WITH NORMAL SALINE TO FINAL CONCENTRATION OF 4 MCG/ML
ONSET: < 5 MIN. / PEAK 20-30 MIN.
INFUSION AND SEDATION DOSE RANGE: 0.2-1.0 MCG/KG/HR
BOLUS DOSE: 1MCG/KG OVER 10 MINUTES PRIOR TO MAINTENANCE RATE.[8]
CLINICAL EFFECTS
Sedation
Analgesia
Anxiolysis
Sympatholysis
No respiratory depression[8,11]


PRACTICE CHANGE:
CONTINUOUS INTRAOPERATIVE DEXMEDETOMIDINE INFUSION AS AN ANESTHETIC ADJUVANT
WHY?
MULTIPLE STUDIES HAVE DEMONSTRATED THE ROLE OF DEXMEDETOMIDINE IN REDUCING OPIOID CONSUMPTION
7 RANDOMIZED CONTROLLED TRIALS (RCTS) INCLUDED 291 PATIENTS IN THIS SYSTEMATIC REVIEW
LUMBAR PROCEDURES PERFORMED: INTERBODY FUSION, FORAMINOTOMY, AND LAMINOTOMY WITH DISCECTOMY
DEXMEDETOMIDINE WAS COMPARED TO: SALINE AS PLACEBO, FENTANYL, REMIFENTANIL, HYDROMORPHONE, MEPERIDINE, AND MORPHINE
OUTCOMES OBSERVED: PAIN SCORES, PERIOPERATIVE OPIOID CONSUMPTION, AND LENGTH OF TIME TO FIRST POSTOPERATIVE ANALGESIA REQUEST[13-19]
SYSTEMATIC REVIEW RESULTS:
LOADING DOSE OR NO LOADING DOSE?
2 RCTs
LD= 1mcg/kg
Result:
Reduced post-op opioid consumption.[14,16]
1 RCT
LD= 0.6mcg/kg
Result:
Decreased supplemental opioids.[18]
2 RCTs
LD= 0.5mcg/kg
Result:
Dexmedetomidine groups reported less post-op opioid consumption.[13,17]
2 RCTs
No LD
Result:
Decrease in intra-op & post-op opioid requirements.[13,17]
SYSTEMATIC REVIEW RESULTS:
WHEN SHOULD DEXMEDETOMIDINE BE INITIATED?
4 RCTs
Dexmedetomidine initiated during intra-op phase
Result:
1- ↓ intra-op fentanyl[13]
2- ↓ intra-op & post-op fentanyl[19]
3- ↓ post-op hydromorphone[16]
4- ↓ post-op morphine and time to first post-op morphine request[14]
3 RCTs
Dexmedetomidine initiated during pre-op phase
Result:
1- ↓ post-op meperidine[14]
2- ↓ post-op hydromorphone[17]
3- ↓ post-op fentanyl[18]


SUMMARY
ALL STUDIES IN THIS SYSTEMATIC REVIEW DEMONSTRATE THE OPIOID SPARING BENEFITS OF CONTINUOUS DEXMEDETOMIDINE INFUSION
THE AVERAGE INFUSION RATE WAS 0.485 MCG/KG/HR
THERE WAS NO DIFFERENCE IN OUTCOMES ASSOCIATED WITH ADMINISTERING A LOADING DOSE OR NOT
THERE WAS NO DIFFERENCE BETWEEN PRE-OP OR INTRA-OP DEXMEDETOMIDINE INITIATION
DEXMEDETOMIDINE DEMONSTRATED THE ABILITY TO REDUCE OPIOID REQUIREMENTS IN GENERAL ANESTHESIA AND/OR MODERATE SEDATION PROCEDURES.[13-19]
TAKE HOME POINTS
ANESTHESIA PROVIDERS ARE EXPERTS IN MANAGING PAIN AND HAVE A PIVOTAL ROLE IN ADDRESSING THE CURRENT OPIOID CRISIS
LUMBAR BACK SURGERY IS A RISK FACTOR FOR OPIOID EXPOSURE
LUMBAR SURGERY GENERALLY REQUIRES INCREASED OPIOID REQUIREMENTS
DEXMEDETOMIDINE PLAYS AN INTEGRAL ROLE IN PROVIDING PAIN CONTROL WHILE SIGNIFICANTLY REDUCING OPIOID CONSUMPTION
WHAT ARE THE FACTORS OR CONSIDERATIONS THAT HAVE PREVENTED THE USE OF DEXMEDETOMIDINE FOR LUMBAR SPINE PROCEDURES AND HOW CAN YOU INFLUENCE CHANGE?
REFERENCES