The Utilization of Dexmedetomidine as an Anesthetic Adjunct in Spinal Anesthesia to Reduce Perioperative Consumption of Opioids

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The Utilization of Dexmedetomidine as an Anesthetic Adjunct in Spinal Anesthesia to Reduce Perioperative Consumption of Opioids

A DNP Project Presented to the Faculty of the Nicole Wertheim College of Nursing and Health Sciences

Florida International University

In partial fulfillment of the requirements For the Degree of Doctor of Nursing Practice

By

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Approval Acknowledged: ______________________________, DNA Program Director
Date:________________

Approval Acknowledged: ______________________________, DNP Program Director
Date:________________
# TABLE OF CONTENTS

ABSTRACT ..................................................................................................................................... 5

INTRODUCTION ........................................................................................................................... 7

Description of the Problem.......................................................................................................... 7

Background.................................................................................................................................. 7

Scope of the Problem................................................................................................................... 9

Consequences of the Problem...................................................................................................... 9

Knowledge Gaps ....................................................................................................................... 10

Proposed Solution ...................................................................................................................... 11

Literature Review Rationale ...................................................................................................... 10

METHODOLOGY ........................................................................................................................ 11

Information Sources and Search Strategy.................................................................................. 11

Study Selection and Screening Method with Inclusion/Exclusion Criteria............................... 12

Table 1. Inclusion/Exclusion Criteria ........................................................................................ 13

Collection, Analysis and Data Items ......................................................................................... 13

RESULTS ...................................................................................................................................... 13

Study Selection .......................................................................................................................... 13

Table 2. Characteristics of Selected Studies ................................................................................. 16

Study Characteristics ................................................................................................................. 16

Results of Individual Studies and Intervention Effect on the Outcome of Interest ................... 20

Risk of Bias ............................................................................................................................... 22
Unintended Consequences......................................................................................................... 22

Limitations of the Literature Review.......................................................................................... 23

Recommendations ..................................................................................................................... 24

DISCUSSION ................................................................................................................................ 24

Summary of Evidence ............................................................................................................... 24

Limitations of the Study ............................................................................................................ 26

Recommendations for Future Research ..................................................................................... 27

Recommendations for Practice .................................................................................................. 29

Figure 1. Reduction in Opioid Consumption With Dex as Adjunct Therapy During Surgery... 29

Conclusions ............................................................................................................................... 30

IMPLEMENTATION .................................................................................................................... 24

Setting and Participants ............................................................................................................. 24

Recruitment ............................................................................................................................... 24

Description of Approach and Project Procedure ....................................................................... 24

Protection of Human Subjects ................................................................................................... 24

Data Collection and Analysis .................................................................................................... 24

Data Management and Measure ................................................................................................ 24

IMPLEMENTATION RESULTS ................................................................................................. 35

Table 3. Pre/Post-Test Demographics ....................................................................................... 24

Pre-Test Likelihood of Utilization of Dex in Patients Receiving Spinal Anesthesia ................. 24

Pre-Test Identification of Current Knowledge About Perioperative Management of Surgical
Patients Receiving Dex as an Anesthetic Adjunct to Spinal Anesthesia ..................................... 24
Table 4. Difference in Pre- and Post-Test Knowledge .............................................................. 24

Post-Test Likelihood of Utilization of Dex in Patients Receiving Spinal Anesthesia.............. 24

Summary.................................................................................................................................... 24

IMPLEMENTATION DISCUSSION ........................................................................................... 24

Limitations................................................................................................................................. 24

Future Implications for Anesthesia Practice.............................................................................. 24

REFERENCES .............................................................................................................................. 40

Appendix A .................................................................................................................................... 46

Figure 3. PRISMA Flow Diagram............................................................................................. 13

Figure 2. Smart Goals................................................................................................................ 24

Table 5. SWOT Matrix.............................................................................................................. 24

Appendix B .................................................................................................................................... 53

Appendix C .................................................................................................................................... 53

Appendix D .................................................................................................................................... 53

Appendix E .................................................................................................................................... 53

Appendix F .................................................................................................................................... 53
ABSTRACT

Background: Opioid consumption is at an alarming rate in the United States. Their side effects have attracted debates on whether they are indispensable and continuously prompt further consideration of alternative approaches. Recent studies have suggested that dexmedetomidine has a good analgesic profile and can reduce opioid consumption. Additional studies are warranted to establish whether dexmedetomidine as an adjunct therapy can influence opioid consumption in surgical units.

Objectives: This literature review aimed to evaluate the current randomized controlled trials (RCTs) on the impact of dexmedetomidine as adjunct therapy on opioid consumption and further recommend best available practices on the current issue.

Methodology: Seven randomized control trials (RCTs) were evaluated in this systematic review. The RCTs found a statistically significant decrease in opioid consumption with the application of dexmedetomidine in patients receiving spinal anesthesia. With this information, a pre-test, educational module, and post-test were created for anesthesia providers to evaluate both baseline knowledge and knowledge growth.

Results: The evidence search and screening resulted in 7 RCTs. Three studies demonstrated dexmedetomidine infused at the induction of anesthesia to reduce post-operative and perioperative opioid consumption. Four studies demonstrated dexmedetomidine to reduce cumulative opioid consumption when administered before induction of anesthesia. One study demonstrated intranasal dexmedetomidine to impact cumulative opioid consumption.

Conclusion: Evidence shows that dexmedetomidine as adjunct therapy reduces opioid consumption preoperatively and post-operatively. The least effective dose is 0.5 μg/kg-1 μg/kg, and can be infused before or at the induction of anesthesia.

Keywords: Dexmedetomidine, opioids, spinal anesthesia, opioids consumption, surgical units, surgery, postoperative, perioperative.
INTRODUCTION

Description of the Problem

The current situation in the US is that opioid consumption during surgical operations is significantly high. Nearly all US patients are prescribed and receive opioids during surgery. Opioids are generally approved by the FDA to be used in every phase of surgery. Uses may include during induction and maintenance of anesthesia, control of postoperative pain, and to reduce agitation. The most commonly used are IV preparations of morphine, fentanyl, and hydromorphone. These uses have made healthcare centers a major dispensation point for opioids and have made opioids nearly essential in American surgical rooms. In a retrospective study, the mean daily consumption for opioids among women who underwent caesarian surgery was 48.6%, and morphine was 44.6%. The issue does not stop in surgical wards; 6% of previously opioid naïve surgical patients continue taking opioids 3-6-month post-surgery. For an extended time, surgical wards have been a vehicle for high opioid use in the American community. Clinicians attending to patients throughout the perioperative period find this situation a major concern.

Background

The use of opioids has presented devastating challenges to US public health and individual health. On October 26, 2016, the United States president declared the opioid epidemic a public health emergency in the US. Over the past two decades, the incidence of overdose-related deaths has markedly increased. The death rate rose to 46,802 (65% of total drug overdose-related deaths) in 2018. These statistics do not represent other long term impacts such as sexual abuse, opioid use disorder, nutritional neglect, and children born to opioid-dependent mothers. The deadly nature of the opioid epidemic is clear and warrants an upstream approach.

The opioid epidemic is hindered by diverse players. Pharmaceutical manufacturers have contributed to the crisis by marketing pain drugs and impressing them on patients. Political and social influences have also contributed. Of the many participants, the healthcare sector cannot be ignored. The opioid crisis ideally combines both prescription and non-prescription opioid use.
According to the Centers for Disease Prevention and Control (CDC), two out of three drug
overdoses are caused by prescription opioids, heroin, or synthetic opioids. 7 99% of USA surgical
patients receive opioid prescriptions perioperatively. 1 Many of the patients that develop substance
abuse tend to have a history of surgical procedures, supporting the notion that opioid use begets
opioid use. 8 Generally, the healthcare system, particularly surgical units, significantly contribute
to the opioid crisis and warrant further investigation.

Opioids are consistently prescribed in surgical units with the intent of providing effective
pain management. Opioids provide reliable analgesia for prolonged periods of time, however,
clinicians are extensively trained to be judicious in their administration. 9 Opioids like fentanyl,
hydromorphone, morphine, oxycodone, oxymorphone, and tramadol have been persistently used
in various perioperative phases, including pre-induction, induction of anesthesia, maintenance,
reduction of immediate postoperative pain, and to decrease agitation. 10 During surgery, they are
often administered intravenously as an adjunct medication to blunt sympathetic responses.
Opioids administered for postoperative pain or breakthrough pain (experiencing pain while
currently on an acute or chronic pain regimen) is also known as rescue analgesia. If opioids were
consistently prescribed in surgical units with overt caution, there is often little need for alarm. 11
However, their use has presented the US healthcare system with challenges in public and
individual health.

Opioid use in surgical units has been associated with many adverse effects. The primary
effect, as discussed in earlier paragraphs, is opioid dependence and the larger opioid crisis.
Patients who have been prescribed opioids as the leading pain management modality have often
required higher doses of opioids to maintain analgesia. 1 Adverse effects like opioid-induced
endocrinopathy, hyperalgesia, respiratory depression, urinary retention, postoperative respiratory
depression, bradycardia, and somnolence have also been reported. 10,12 These adverse effects
warrant alternative adjunct therapies during surgery.
Dexmedetomidine has been documented as a potential adjunct for opioid administration. Dexmedetomidine is a highly selective α2-adrenergic receptor (α2-AR) agonist that has sedative and analgesic effects. According to Seongheon, dexmedetomidine may provide stable hemodynamics, minimal respiratory depression, and produce less delirium. The concept of minimal respiratory depression is significant in that it is often observed in many analgesics. Even at higher doses, dexmedetomidine does not cause significant respiratory depression. Patients under dexmedetomidine have a comfortable sleep to wakefulness transition. This drug produces profound sedation at higher doses and has both spinal and peripheral action. These attributes suggest dexmedetomidine as a superior analgesic supplement to reduce opioid use compared to other analgesics.

**Scope of the Problem**

Indeed, many Americans are affected by the opioid crisis or epidemic. In 2018, it was reported that 10.3 million Americans 12 years and older partook in the misuse of opioids. Out of the 10.3 million, 9.9 million Americans misused pain prescription opioids. These numbers cut across all demographic factors, including age, race/ethnicity, gender, geographical groups, and across all socioeconomic cadres. The trend for opioid use has sharply been increasing. Between 2016-2018, there was a 146% increase in patients with opioid-related treatments. These statistics exemplify how the US is susceptible to the opioid crisis and that the surgeon general was in order to call it an epidemic.

The rate of opioid consumption alone should not be considered the sole reason for addressing the opioid crisis. Statistics regarding opioid-related mortalities are significant and concerning. Since 1999, more than 760,000 Americans have died from an opioid overdose. Opioid-related overdose deaths have tripled in the past eighteen years. These mortalities are significantly high and necessitate addressing. If the opioids crisis is not attacked from multiple target points, the mortalities may increase to more than fourfold in the future.
Consequences of the Problem

Opioid use causes devastating effects on individuals and patients. In the perioperative period, opioid use may cause urinary retention, increased length of hospital stay, respiratory depression, and constipation. Post-surgery, effects like immunosuppression, endocrinopathy, and hyperalgesia have been noted. Patients with chronic respiratory conditions are often at high risk. The most glaring impact is opioid addiction and use disorder, which increases the risk of endocarditis, infections, and narcotic bowel syndrome. Despite these issues being understood by healthcare providers, they are often understated. In the end, patients have higher chances of morbidity and mortality.

The above consequences can be quantified in terms of cost. The US spends more than $78.5 billion annually to manage opioid-related complications, abuse, and loss of productivity. Between 2016-2019, $9 billion was granted to fight the opioid crisis. Post-surgery, patients with opioid abuse disorders spend at least 21% higher healthcare readmission costs than their opioid-free counterparts. These high costs augmented by earlier mentioned consequences should compel stakeholders and policymakers to find feasible solutions. No solution may be considered absolute for the opioid epidemic. However, an excellent starting point would be through anesthesiologists, nurse anesthetists, and perioperative pain management.

Knowledge Gaps

As earlier stated, the use of opioids in surgical units is almost indispensable. As Egan (2019) illustrates, using one drug to produce anesthesia has been a long-term challenge. Available medications like propofol require higher concentrations to cause unconsciousness and immobility. To this end, opioids have been considered a better adjunct to control the autonomic nervous system. Their effect on nociception-induced arousal is widely known. Also, opioids have been fundamentally used to control postoperative pain, which may increase morbidity and mortality if poorly controlled.
Studies are currently underway to demonstrate opioid-sparing modalities that can produce comparable analgesic effects. Such options should confer greater benefit than risks to a surgical candidate. These studies demonstrate varied results depending on their settings and doses of their candidate drugs. Notably, many drugs have been proposed, but there is no consensus on a specific compound. This contention creates a knowledge gap that compels one to think and explore how to replace opioids.

**Proposed Solution**

Amid the current contention, this research proposes dexmedetomidine as a pain management adjunct and possible solution to help battle the opioid crisis. Dexmedetomidine is a highly selective α2-adrenergic receptor (α2-AR) agonist that produces analgesic effects and sedation. The FDA approved this medication in 1999 for use in critically ill patients. The medication was approved for procedural sedation in 2008 for non-intubated patients. This latter approval broadened the use of dexmedetomidine for patients requiring spinal anesthesia.

Dexmedetomidine is a possible solution because studies continue to show promising benefits. Dexmedetomidine has better hemodynamic stability and produces superior pain control than selected opioids. Using dexmedetomidine during nerve block has demonstrated a reduction in perioperative pain along with reduced risk of respiratory depression. The above findings suggest that dexmedetomidine would be an ideal solution to help counteract the adverse effects of opioid use and ultimately the opioid crisis.

**Literature Review Rationale**

Opioids are consistently used throughout the perioperative period. More than 80% of the 51 million Americans who undergo surgery annually are prescribed opioids for acute pain management. The most commonly prescribed opioids include oxycodone and hydrocodone. According to Wilson, these two opioids medications are the leading causes of opioid overdose and death in the US. Surgical units appear to be a significant dispatch point for this unfortunate trend. Aside from the opioid crisis, opioid use has been associated with many postoperative
adverse effects. These long-standing issues draw attention to modalities that could reduce opioid consumption in surgical units. Such modalities can consequentially reduce opioid's impact on the general American population. Theories posit dexmedetomidine as a favorable alternative and can be supported through evidence. The purpose of this literature review is to discern whether there is evidence that dexmedetomidine as an analgesic could reduce perioperative consumption of opioids.

METHODOLOGY

Information Sources and Search Strategy

The literature sample was obtained from various databases. The PICOT question that guided the search was, “In the surgical patient undergoing spinal anesthesia (S), how does the use of dexmedetomidine as an anesthetic adjunct (I), compared to its non-use (C), affect the postoperative (or perioperative) consumption of opioids (O)?” Once this question was formulated, various phrases were coined for use in the databases. The key phrases “dexmedetomidine and opioids,” “dexmedetomidine and spinal anesthesia,” “dexmedetomidine and opioids consumption,” and “reducing opioids consumption” were used. Databases such as MedLine, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE), Pubmed and Google Scholar were used. authorities have agreed that these are the most useful bibliographic databases for nurses.20

While searching through the databases, various qualifiers were used to narrow the results. The database’s filters were set to produce articles published from 2016 to 2020 because restricting the year of publication allows the limitation of outdated studies while highlighting current data. The search was further filtered to allow only systematic reviews, randomized controlled trials, or meta-analysis being that such resection makes results more specific and allows one to obtain quality evidence. The search also allowed full text as opposed to abstracts,
though some of these restrictions were not possible with a general google search. The final restriction was "peer review," ensuring articles that were peer-reviewed only.

After removing duplicate articles with the same opioid medication, the database search results were as follows: PubMed yielded 70 articles, CINAHL yielded 230 articles, and MedLine yielded 150 articles. While only articles published from 2019 were selected, one article published in 2016 was selected for its sample size. Most of the results were relevant, hence the need to apply further restrictions. Ultimately, after thorough consideration, the study selected seven articles.

**Study Selection and Screening Method with Inclusion/Exclusion Criteria**

According to Moran et al., the DNP project must include inclusion and exclusion criteria. The current research adopted various aspects of inclusion and exclusion. The exclusion criteria included articles published before 2019, systematic analysis and meta-analyses, non-peer-reviewed, not published in English, unrelated to spinal anesthesia, and studies without dexmedetomidine as the intervention. Inclusion criteria included randomized controlled studies (RCTs), peer-reviewed, published from 2019, involve spinal anesthesia, published in English, involving dexmedetomidine as intervention, and focusing on opioid consumption. Those that compared the magnitude of sedation and postoperative pain and postoperative events were included.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type</td>
<td>Study type</td>
</tr>
<tr>
<td>- Randomized controlled trials</td>
<td>All studies that are not RCTs (for instance, meta-analysis, systematic analysis, clinical trials)</td>
</tr>
<tr>
<td>Procedure</td>
<td>Procedure</td>
</tr>
<tr>
<td>- Spinal anesthesia</td>
<td>- Any procedure not requiring spinal anesthesia</td>
</tr>
<tr>
<td>Intervention</td>
<td>Intervention</td>
</tr>
</tbody>
</table>
Table 1: Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Collection, Analysis and Data Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data were extracted systematically in that information was read from the abstracts and passed through the inclusion and exclusion criteria. The Johns Hopkins research evidence appraisal tool was used to critically appraise the studies and quality of evidence (see Polit and Beck). The Johns Hopkins research evidence appraisal tool groups evidence into three cadres of high quality, good quality, or low quality. High-quality evidence has consistent and generalizable results and a sufficient sample size. Good-quality evidence has reasonably consistent results, fairly definitive conclusions, and reasonably consistent recommendations. Low-quality evidence refers to little evidence with inconsistent results.</td>
</tr>
</tbody>
</table>

RESULTS

Study Selection

Three databases, PubMed, CINAHL, and Medline, yielded the most valuable results to answer the PICOT question. The preliminary search yielded 450 articles distributed disproportionately across the databases. Fifty duplicates were eliminated, leaving 400 sources for
screening. The investigators further reviewed the abstracts and removed 307 references, leaving 99 articles for full-text screening. The majority of the studies that were excluded reported low-quality evidence on dexmedetomidine (Dex). Full-text analysis factoring in the exclusion/inclusion criteria resulted in the exclusion of 92 articles total. Reasons that lead to exclusion were: articles published before 2019, systematic analysis and meta-analyses, non-peer-reviewed, not focusing on opioid consumption, not published in English, dexmedetomidine used in surgeries not involving spinal anesthesia, and studies without dexmedetomidine as the primary comparator.

The investigator also curated articles whose results did not reveal dexmedetomidine benefits, including the reduction of opioid use and postoperative adverse events. In the end, the studies included were randomized controlled trials as well as studies where Dexmedetomidine was used as an adjunct therapy in spinal anesthesia, thereby featuring the magnitude of analgesia, postoperative pain, and reduction of adverse events post-operatively. Therefore, the seven articles included provided level 1 evidence as appraised by the Johns Hopkins research evidence appraisal tool.30

The selected articles appropriately answered the PICOT question: “In the surgical patients undergoing spinal anesthesia (S), how does the use of dexmedetomidine as an anesthetic adjunct (I), compared to its non-use (C), affect the postoperative (or perioperative) consumption of opioids (O)?”. The table below summarizes the selected studies:

<table>
<thead>
<tr>
<th>Author</th>
<th>Year of Publication</th>
<th>Primary Outcome</th>
<th>Study Design</th>
<th>Sample Size</th>
<th>Sampling Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ren, Chunguang et al.15</td>
<td>2019</td>
<td>Total consumption of nimodipine during the first 48 hr after surgery</td>
<td>Prospective RCT</td>
<td>86 participants undergoing EITs</td>
<td>Purposive sampling</td>
</tr>
<tr>
<td>Authors</td>
<td>Year</td>
<td>Study Design</td>
<td>Outcomes</td>
<td>Participants</td>
<td>Sampling Method</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------</td>
<td>-------------------------------</td>
<td>-----------------------------------------------</td>
<td>--------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Shin, Hyun-Jung et al.</td>
<td>2019</td>
<td>Postoperative fentanyl consumption</td>
<td>Block randomized parallel-group trial</td>
<td>48 participants</td>
<td>Purposive sampling</td>
</tr>
<tr>
<td>Sherif, Abeer A., and Hazem E. Elsersy.</td>
<td>2019</td>
<td>Total morphine consumption</td>
<td>Prospective RCT</td>
<td>150 ASA I to III patients</td>
<td>Purposive sampling</td>
</tr>
<tr>
<td>Bielka, Kateryna, et al.</td>
<td>2019</td>
<td>Postoperative morphine consumption</td>
<td>A randomized, single-center, parallel-group, placebo-controlled study</td>
<td>30 patients in each group</td>
<td>Purposive sampling</td>
</tr>
<tr>
<td>Kang, Ryung A., et al.</td>
<td>2019</td>
<td>Time to first rescue analgesic request</td>
<td>RCT</td>
<td>Sixty-six patients undergoing arthroscopic shoulder surgery</td>
<td>Purpose sampling</td>
</tr>
<tr>
<td>Uusalo, Panu, et al.</td>
<td>2019</td>
<td>Impact of intranasal dexmedetomidine on postoperative hemodynamics and length of stay</td>
<td>RCT</td>
<td>120 participants</td>
<td>Purposive sampling</td>
</tr>
<tr>
<td>Li, Jing, et al.</td>
<td>2019</td>
<td>Morphine consumption</td>
<td>RCT</td>
<td>57 participants</td>
<td>Purposive sampling</td>
</tr>
</tbody>
</table>

Table 2: Characteristics of Selected Studies
**Study Characteristics**

Cumulatively, the 7 RCTs reviewed had participants n=587 where n= 344 was enrolled into the control group, and n=243 into the treatment group. The treatment group was subjected to Dexmedetomidine as an adjunct therapy, and the placebo group had the routine anesthesia protocols depicting varied drug choices. Patient characteristics, type of surgery, and route of dexmedetomidine administration differed across the studies. These differences could have an impact on the generalizability of the study findings. The differences in surgical operations included: total knee arthroplasty- Shin et al.,\textsuperscript{23} endovascular interventional therapies- Ren et al.,\textsuperscript{27} orthoscopic shoulder surgery- Kang et al.,\textsuperscript{25} laparoscopic cholecystectomy- Bielka et al.,\textsuperscript{24} lumbar fusion surgery- Li et al.,\textsuperscript{28} hip arthroplasty- Uusalo et al.,\textsuperscript{22} laparoscopic sleeve gastrectomy- Sherif et al.,\textsuperscript{26}. Shin et al.,\textsuperscript{23}, Ren et al.,\textsuperscript{27}, and Kang et al.,\textsuperscript{25}. The differences in routes of administration included: intravascular-, Li et al. subcutaneous, - Sherif et al.,\textsuperscript{26} orally (PO), and intranasally- Uusalo et al.\textsuperscript{22}. These differences are significant factors to consider when analyzing the magnitude of outcomes.

**Patient demographics.** All the seven studies reported the recruitment of both males and females. The age range varied with the youngest subject at 20 years in Shin et al.,\textsuperscript{23} and the oldest at 80 years in Uusalo et al.\textsuperscript{22}. Four of the studies selected participants between 35-60. All participants scheduled for surgery were classified as American Society of Anesthesiologists (ASA) Physical Status class I through III. All of the studies explicitly stated the type of surgery involved as well as any inclusion/exclusion criteria. Three of the seven studies discussed underlying comorbidities including hypertension, diabetes, coronary heart disease, and asthma. Six of the seven studies included patients with BMI 23—27 while only Bielka et al.,\textsuperscript{24} worked with obese patients (defined by World Health Organization (WHO) standards). While the periods of enrollment differed across studies, the majority of patients were enrolled between 2017-2019.

**Hospital demographics.** The 7 RCTs were run in hospitals distributed globally. Shin et al.,\textsuperscript{23} conducted their study at Seoul National University Bundang Hospital, South Korea. These
researchers did not provide further details about the hospital. However, in a different study by Yoo et al., Seoul National University Bundang Hospital is a tertiary university hospital with about 1340 hospital beds and performs at least 12,180 surgeries per year. Ren et al., Kang et al., and Li et al. did not explicitly state their study settings. However, the Ren et al. study obtained approval from the Liaocheng People's Hospital (China) institutional review board. Also, Liaocheng People's Hospital is present in the correspondence. Kang et al. study was approved by the Samsung Medical Center (SMC) Research Ethics Board, Seoul, Korea. The authors either work at the Department of Anesthesiology and Pain or the Department of Orthopedics at SMC; hence, this could be the possible study setting. Uusalo et al. conducted their study at Turku University hospital in the Salo unit in southwest Finland. Turku University hospital is one of the largest hospitals in Finland and has 900 beds. The hospital has several branches with no clarity on the number of beds and the total number of surgeries conducted in said Salo unit. The Li et al. publication correspondence indicates all the researchers from Honghui Hospital, Xi’an Jiaotong University, Xi’an, Shannxi, China. Bielka et al. conducted their study at the Department of Surgery, and at Anesthesiology and Intensive Care of the Postgraduate Institute of Bogomolets National Medical University, Kiev, Ukraine. The center conducts about 70000 surgeries annually. Sheriff et al. conducted their study at Menofa University Hospital, Egypt. The hospital has 400 beds with 13 rooms of operative theatre.

**Methodology and quality.** The methodology and interventions consistently varied across the 7 RCTs. A marked consistency was dexmedetomidine use as an adjunct therapy with controls using placebo or a sedative of a different class. The studies differed in what they used to induce anesthesia. Two studies used fentanyl 100 µg, propofol 2.5 mg/kg IV, and rocuronium 0.6 mg/kg IV, 1 study propofol (1–2 mg/kg), and cisatracurium (0.2 mg/kg), 3 studies propofol 2 to 3 ug/mL and remifentanil at 3 to 4 ng/mL, and 1 study 1.5 to 2.0 mg/kg propofol and 0.8 mg/kg rocuronium and maintained with inhaled sevoflurane. Ren et al. additionally used
sevoflurane (1.5%–2.0%), remifentanil (0.05–0.15 μg/kg/min), and sufentanil for anesthesia maintenance.²⁷

All studies differed in the time of dexmedetomidine infusion, including at the induction of anesthesia in 2 studies,²³, ²⁴ 10 minutes before anesthesia induction in 1 study,²⁵ five minutes before anesthesia induction in 1 study,²⁸ and 30 minutes before anesthesia induction in 1 study.²² The majority of the studies administered Dex continuously/as needed until the end of surgery,²⁶, ²⁴, ²⁷ except Shine et al. who stopped infusion 40 minutes following propofol infusion (about the time they began subcutaneous and skin suture)²³ and Kang et al. who stopped after 30 minutes following initial dex infusion.²⁵ Le et al. and Uusalo et al. did not mention when they stopped dex infusion.²⁸

Three studies reported using analgesic or pain pre-medications (medications to treat pain prophylactically). These variances could affect the impact of dexmedetomidine in the end. The variances included 50 mg of IV dexketoprofen before induction in 1 study,²⁴ preoperative administration of 1000 mg paracetamol orally in 1 study,²² and preoperative administration of pregabalin 75 mg PO, celecoxib 200 mg PO, acetaminophen 650 mg PO, and dexamethasone 10 mg IV about 40 minutes before surgery in 1 study.²³ However, three studies did not mention additional pain or analgesic premedication.²⁶, ²⁷, ²⁸ Kang et al. reported restricting premedication with analgesics/NSAIDs.²⁵

Studies used different doses for initial and continuous Dex therapy and are as follows: Shin et al. administered a loading dose of 1 μg/kg dexmedetomidine over 10 minutes, then continuously at a dose of 0.1–0.5 μg/kg/hr.²³ Uusalo et al. discussed administration of 50 mg of Dex intramuscularly (IM);²² Li et al. reported 1 μg/kg of dexmedetomidine given at two doses subcutaneously,²⁸ Ren et al. reported administration dose of 0.5 μg/kg of Dex for 10 min adjusted to 0.2–0.6 μg/kg/hr;²⁷ Beika et al. discussed a Dex infusion running at 0.5 μg/kg/hr, beginning at induction of anesthesia and lasting until extubation;²⁴ Sherif et al. reported a 1 μg/kg IV Dex
loading dose over 10 minutes, followed by 0.4 µg/kg/hr of infusion;\textsuperscript{26} and Kang et al. mentioned 1.0 mg/kg/hr.

**Data collection.** Data collected significantly varied across the 7 RCTs. Five studies measured total morphine consumption as their primary outcome while Sheriff et al., however, further considered sedation, pain, QOR-40 score, nausea, and vomiting.\textsuperscript{26} Bielka et al. also measured duration of hospital stay (LOS), time to first use of rescue analgesia, number of patients with severe pain, intraoperative fentanyl consumption, time from the end of surgery to extubation, lengths of intensive care unit (ICU) and general ward stay, degree of postoperative pain 3, 6, 12 and 24 hours after surgery, and incidence of persistent post-surgical pain (6 months after surgery).\textsuperscript{24} Unlike Sheriff et al. and Bielka et al., who had an interest in morphine, Ren et al. measured total sufentanil consumption.\textsuperscript{27} Ren et al. further studied LOS, pain intensity, hemodynamics, narcotic and vasoactive prescriptions, the incidence of complications and symptomatic cerebral vasospasm, patient/physician satisfaction scores, and duration of postoperative anesthesia care unit (PACU) stay.\textsuperscript{27} Kang et al. measured time of request of first rescue analgesia, pain intensity at rest, duration of motor blockade, dexmedetomidine-related side effects, dexamethasone-related side effects, and total postoperative opioid consumption.\textsuperscript{25} Li et al. further measured cumulative patient-controlled analgesia (PCA) analgesia, VAS at rest, postoperative nausea and vomiting, delayed wound healing, bradycardia, hypotension, and cardiac arrhythmia.\textsuperscript{28} Uusalo et al. measured pharmacodynamics measurements (heart rate (HR) and mean arterial pressure (MAP)), PACU time and time of discharge, and the total amount of opioids administered.\textsuperscript{22} The MAP and HR were collected before surgery, during incision, 1 hour after anesthesia induction, at the end of the surgery, and 1 hour after surgery.\textsuperscript{22} Shin et al. studied the total amount of fentanyl administered via IV PCA 24 and 48 hours postoperatively. Shin et al. also measured pain scores, amount of rescue analgesics and antiemetics consumed, PACU time, HR, systolic blood pressure (SBP), and patient satisfaction. These variables were seamlessly curated to answer the PICOT question.
Results of Individual Studies and Intervention Effect on the Outcome of Interest

The overall PICOT question aimed to examine how dexmedetomidine as an anesthetic adjunct affects opioid consumption. While opioid consumption remained the primary goal, it is pertinent to consider whether dexmedetomidine contributes to a reduction in adverse events and improvement in beneficial outcomes during surgery. Generally, the project focused on the safe and effective ways to reduce opioid consumption in surgical units. In this literature review, the effects of opioid consumption were considered as either a reduction or increase in opioid use. The review predicted that dexmedetomidine would reduce cumulative opioid consumption. However, the analysis was not specific to a particular opioid, hence any opioids included in the RCTs were valid. Side effects or adverse events were defined as undesirable occurrences due to medications used during surgery. Beneficial outcomes were discussed around the time of first use of rescue analgesia, reduction in pain, and better quality of life.

Effects on cumulative opioid consumption: All the 7 RCTs reported that Dex given in any approach reduces cumulative opioid consumption. Sheriff et al. demonstrated that dexmedetomidine given at 1 µg/kg IV loading dose over 10 minutes, followed by 0.4 µg/kg/h reduces total morphine consumption by at least 35%. These authors learned that the group that was not exposed to dexmedetomidine (group L and C) had higher consumption of morphine, including 18±4 and 29±5 mg compared to group D, which had a morphine consumption at 14±4. Like other studies, Shin et al. shows that Dex significantly reduced postoperative total fentanyl consumption via IV PCA. Uusalo et al. established that including Dex as adjunct therapy reduced cumulative opioid consumption. The cumulative morphine requirement in the Dex group was low, 152 mg, compared to 178 mg in the control group. Uusalo et al.’s findings are interesting in that Dex was administered intranasally. Li et al. proved that subcutaneous dexmedetomidine, can lower cumulative opioid consumption as well. In this study, cumulative opioid consumption was low at 7.6 mg in the Dex group compared to 16 mg in the control group. Sheriff et al., Shin et al., Li et al., Uusalo et al., and Kang et al. demonstrated that Dex can be
infused before induction and still affect opioid consumption postoperatively. In 2018, Bielka et al. proved, that dexmedetomidine as adjunct therapy contributes to postoperative morphine consumption reduction.\(^\text{24}\) Bielka et al. observed that the treatment group consumed 5 mg of morphine over 24 hours compared to 15 mg in 24 hours in the control group. Ren et al. made their case that dexmedetomidine at a loading dose of 0.5 μg/kg for 10 min, adjusted to 0.6 μg/kg/hr during surgery reduces cumulative consumption of sevoflurane, remifentanil, and sufentanil within 48 hours of surgery. Cumulative opioid consumption was low in Kang et al. study where the dexmedetomidine group had median consumption of 18.9 mg compared to the two “controls” D1 at 27.1 mg and real control group at 39.9 mg.\(^\text{27}\) Generally, given in any route as defined by surgery type, Dex is effective in reducing cumulative opioid consumption.

**Possibility of adverse events:** Respiratory complications were lowest in the dex group (1/49) than controls 5/49 and 2/49 in the Sherif et al. study.\(^\text{26}\) There were also reduced incidences of nausea, vomiting, hypertension and tachycardia in Sherif et al., Kang et al., Li et al., and Bielka et al. studies.\(^\text{26,25,24}\) Ren et al. and Uusalo et al. did not report any adverse events of interest to the literature review. There was no statistical difference in these adverse events in the Shin et al. study.\(^\text{23}\)

**Potential benefits:** Most studies reported a decrease in post-operative pain. Bielka et al. reported the incidence of severe postoperative pain as 1(3) in the Dex group and 7(23) in the control group, the number in parenthesis signifying 25-75% interquartile ranges.\(^\text{24}\) Sherriff et al. and Ren et al. reported decreased pain intensity at all-time points, including 8, 24, and 48 hours from the emergence of anesthesia. In Li et al., the VAS score was low (highest score 1.5) compared to the highest score of 4 in the control group. The time to first rescue analgesic request was also prolonged across studies as follows: Bielka et al. up to 180 minutes, Kang et al. 66.3 hours, and Li et al. 10.5 hours.\(^\text{23,25,28}\) Ren et al. found no statistical difference in the time of request of rescue analgesia, while Shin et al. were not interested in such findings.
Risk of Bias

Bias arising from the randomization process: All the 7 RCTs solved this bias and lowered the risk of selection bias. Selection bias is often minimized when the allocation sequence is random and adequately concealed, and when baseline characteristics are integrated into the process.\textsuperscript{35} Four studies reported using computer algorithms, such as research randomizer (Sheriff et al.), computer algorithm (Bielka et al.), computer-generated randomization table/sequence (Ren et al., Kang et al., Li et al.), and web-based randomization system (Shin et al.).\textsuperscript{26,24,27,25,28,23} Uusalo et al. were not clear about their randomization protocol despite the study being an RCT.

Bias due to missing outcome data: The risk of attrition bias in the Shin et al. study is high. According to Shin et al., 54 participants were enrolled in the study and distributed into two groups.\textsuperscript{23} However, only 48 participants completed the study.\textsuperscript{23} There are several uncertainties as to the reasons for such a change. Participants withdrawing from the study, participants' data record lost, or participants no longer experiencing the outcome due to death can lead to missing measurements and cause bias in estimating the intervention effect.\textsuperscript{35} The other six studies have a low risk of attrition bias.

Bias in measurement of the outcome: This bias was significantly low because most studies blinded outcome assessors. Blinding reduces the risk of under-ascertainment/over-ascertainment. The potential for this bias cannot be ignored because it affects the intervention's estimates.\textsuperscript{35} Across the 7 RCTs, the authors reported blinding outcome assessors.\textsuperscript{24,25,28,23} Ren et al., Sheriff et al., and Uusalo et al. were not clear about blinding the investigators.

Unintended Consequences

Positive

Even though the primary aim was total opioid consumption reduction, dexmedetomidine is beneficial in other unprecedented ways. In the Shin et al. and Kang et al. studies, patients in the dexmedetomidine group recorded more satisfaction with the quality of post-operative analgesia.\textsuperscript{23,25} Including Dexmedetomidine can also reduce the need for NSAIDs as established in
the Uusalo et al. study. Other potential benefits include improved quality of sleep, shorter recovery time in PACU, lower LOS, improved surgeon satisfaction score, and higher QOR-40 scores. Anesthesia providers working in surgical units can always leverage these benefits.

Negative

Like other pain management drugs, dexmedetomidine has been associated with adverse events. Shin et al. recorded bradycardia and hypotension in their study. These authors also attempt to link the increased systolic blood pressure (SBP) due to Dex with α2B action in the postsynaptic cells. Regardless of the veracity of the hypothesis, such adverse events are worth monitoring during surgery. Perineal pruritus upon infusion is also possible, according to the Kang et al. study. However, this event may resolve within 48 hours and tend not to have any detrimental effects in the end. According to Ren et al. study, dexmedetomidine at an initial dose of 0.5 μg/kg for 10 min adjusted to 0.2 μg/kg/hr throughout the surgery may cause symptomatic cerebral vasospasm. Even though these events were not consistent across other studies (some studies did not report any statistically different adverse event), they should not be underestimated during surgery.

Limitations of the Literature Review

- There were significant variances across the studies, including presence or absence of premedication with analgesics. While three studies included NSAIDs/analgesia, three studies did not mention prophylactic pain control and one study eliminated these drugs. Upon comparison of all of the studies, it was determined that there was a lack of uniformity in premedication.

- There was a lack of uniformity in the initiation and continuous dose of Dex as well. This limitation makes it challenging to generalize a particular dose.

- There was heterogeneity in initiating Dex as an adjunct therapy. While some studies infused Dex before induction. others administered the medication at the point of anesthesia induction.
There was no uniformity on the route of Dex delivery. Route of delivery is crucial to drug metabolism as some administration routes allow the drug to exert its effects quicker than others.

**Recommendations**

The strategic plan aimed at compelling anesthesia teams is to focus on tactics that reduce opioid consumption. Given this perspective, the literature review recommends the following:

- Five studies established dexmedetomidine before anesthesia induction to reduce cumulative opioid consumption.\(^{26,23,28,22,25}\) Dex can be introduced 5, 10, or 30 minutes before induction.

- Dex can be effective when administered at the time of anesthesia induction.\(^{27,24}\)

- Dex can reduce cumulative opioid use whether given as a loading and adjusted dose, or a single shot throughout the surgery. Three studies have confirmed loading dose of 0.5 μg/kg-1 μg/kg dexmedetomidine administered over 10 minutes, then administered continuously at a dose of 0.1–0.5 μg/kg/hr.\(^{23,26}\) Two studies have confirmed 0.5 μg/kg/hr-1.0 mg kg\(^{-1}\) throughout the surgery.\(^{24,25}\)

- The route of Dex delivery should not be a barrier to prescription. Five studies have shown Dex can be effective through IV administration.\(^{23,24,25,26,27}\) One study has shown benefits of low-dose Dex intranasally\(^{22}\) and one study has shown benefits when delivered subcutaneously.\(^{28}\)

**DISCUSSION**

**Summary of Evidence**

The study yielded seven RCTs with a total of 587 participants where n= 344 was enrolled into the control group and n=243 into the treatment group. 437 articles were excluded based on systematic exclusion/inclusion criteria that excluded duplicates, articles published before 2019, studies, meta-analyses and systematic reviews, and studies that did not center on dexmedetomidine. Randomized controlled trials (RCTs) and articles that focused on the reduction of opioid
consumption were included in the systematic review thereby providing level I evidence. Studies were considered level I evidence if they satisfied all the aforementioned items, including random sequence generation, allocation concealment, intent-to-treat analysis, blind or independent assessment for important outcomes, co-interventions applied equally, F/U rate of 80%+, and adequate sample size. All studies had a rigorous approach to their findings; the methodologies are reproducible and believable. The 7 RCTs were graded as level I (low-risk bias) evidence following a critical appraisal using the John Hopkin's appraisal scale and Grades of Recommendation Assessment, Development and Evaluation (GRADE) schematic developed by the Agency for Healthcare Research and Quality (AHRQ). The level of recommendation used in this study follows the Berkman et al. outline for i) high, ii) moderate, iii) low, and iv) insufficient levels of recommendation. The recommendations can be translated as i) high (A)- very confident on the estimated effect for this outcome”, ii) moderate (B)- moderately confident on the estimated effect for this outcome, iii) low (C)- Limited confidence on the estimated effect for this outcome”, and iv) insufficient (D)- No evidence and ability to estimate the effect for this outcome. The evidence is summarized below:

i.) All studies reported a significant decrease in opioid consumption when dexmedetomidine was administered as an adjunct therapy. The timing of administration did not influence this outcome.

ii.) Three studies established that dexmedetomidine at the induction of anesthesia reduces cumulative opioid consumption.

iii.) Other studies established a reduction in opioid consumption when Dex was administered 10 minutes, five minutes, and 30 minutes before induction of anesthesia.

iv.) Three studies found a loading dose of 0.5 μg/kg-1 μg/kg dexmedetomidine administered over 10 minutes, then administered continuously at a dose of 0.1–0.5 μg/kg/hr to reduce overall opioid consumption.
v.) Two studies found that a dex dose of 0.5 μg/kg/h-1.0 mg kg⁻¹ throughout the surgery reduced cumulative opioid consumption²⁴,²⁵

vi.) One study found that intranasal Dex reduces cumulative opioid consumption.²⁸

Limitations of the Study

One minor limitation of the study is the restriction to articles that date from 2019. To this end, bias could exist if earlier rigorous studies reported no effect of Dex on opioid consumption. However, the fact that studies used are updated address such a limitation.

One major limitation of the literature review was heterogeneity in the methodology. This review cannot debate precisely about the standard dose and time of administration of Dex. The RCT differed about these issues. For instance, when one study used a loading dose of 1 μg/kg dexmedetomidine over 10 minutes, followed by a continuous infusion of 0.1–0.5 μg·kg⁻¹·hour⁻¹, another study used 0.5 μg/kg/h DEX infusion throughout the surgical process.²³,²⁴ The trend was consistent throughout the RCTs. Therefore, this study cannot generate a standardized approach to dosing Dex. The studies also differed in their time of induction. While three studies administered Dex at induction,²³,²⁴,²⁷ four studies administered the medication before induction with a further difference like 5²⁸, 10,²⁵, and 30²² minutes before induction. Even though the core result is similar, such differences limit the generalizability of the standard time for Dex administration. Additionally, anesthesia used was also a significant variable across the studies. Studies differed on the choice and dose of anesthesia. Two studies combined fentanyl, propofol and rocuronium,²⁶,²⁴ one study combined propofol and cisatracurium,²⁷ three studies combined propofol and remifentanil,²²,²³,²⁸ and one study used propofol and rocuronium and maintained with inhaled sevoflurane.²⁵ These differences challenge the discussion about which combinations could yield optimal outcomes.

There was heterogeneity about premedication with analgesia/NSAIDs. Kang et al. clarified about restricting premedication with analgesics/NSAIDs.²⁵ Their approach differed from Bielka et al. who premedicated with 50 mg of IV dexketoprofen,²⁴ Uusalo et al. with 1000 mg
paracetamol orally,\textsuperscript{22} and Shin et al. with pregabalin 75 mg PO, celecoxib 200 mg PO, acetaminophen 650 mg PO, and dexamethasone 10 mg IV.\textsuperscript{23} Premedication with non-opioid analgesics reduce the consumption of opioid analgesics as demonstrated in many studies. Therefore, there is a possibility of premedication with analgesics as a confounder. Such variances distort the discussion about whether Dex should be prescribed with or without non-opioid premedication. This literature review may fail to account for many of the covariates mentioned above and could confound the findings.

All the RCTs cannot be generalized. Even though the studies differ on the surgical procedure, they all report using a single unit/center. No study reported using a multicenter approach. Therefore, it is not definite that the results can be replicated in all settings. The studies also worked with small sample sizes. This may be largely due to the number of surgeries conducted in a certain time frame. Small sample size and focus on a single-center reduce the chances of generalization. However, the geographical diversity of the studies may address generalizability. The studies report similar trends in outcomes from different geographical regions, including Asia and Africa. Therefore, there is consistency.

**Recommendations for Future Research**

Future studies should address the generalizability of the findings. There is a need to consider multicenter RCTs with large sample sizes.\textsuperscript{37} The current studies were deficient in these areas. Even though one study compared different doses of Dex, the comparison was not sufficient in judging the optimal dose of administration. The studies were not homogenous in their dex doses; this is a potential gap that could affect practice. Ideally, Dex shows a dose-dependence relationship, where large doses cause deep sedation and cardiovascular effects.\textsuperscript{38} Future studies are warranted to compare optimal doses of Dex against associated adverse events. For instance, future studies need to compare the optimal effect of using 0.5 $\mu$g/kg/h dex throughout the study starting with a loading dose of 1 $\mu$g/kg dexmedetomidine over 10 minutes, followed by a
continuous infusion of 0.1–0.5 μg·kg⁻¹·hour⁻¹. Studies comparing different dex doses should also measure plasma concentrations. None of the RCTs measured plasma concentrations despite the possibility of such values influencing practice. Ideally, Dex shows a dose-dependent relationship. Different doses produce different plasma concentrations. Therefore, there is a possibility of variance in effective dex concentration.

Besides investigations on the optimal dose of Dex, future studies should clarify the necessity for premedication with analgesics/NSAIDs when using Dex as an adjunct therapy. There are conflicting views on this issue. For instance, Kang et al. excluded NSAIDs/analgesia from their methodology. In this study, patient satisfaction with pain management within 24 hours was high in both the control and treatment groups. Three other studies, Bielka et al., Uusalo et al., and Shine et al., mentioned using NSAIDs/analgesia in their methodology. Among these two approaches, there is no clarification of the best standard of care in anesthesia practice. Studies should evaluate the magnitude of pain on the inclusion or exclusion of premedication NSAIDs/analgesics.

Also, future studies should investigate Dex's implication in pediatric surgery. The current RCTs were strongly biased towards the adult population; the results remain irrelevant in the pediatric population. Like adults, children and adolescents have also been prescribed opioids after, and the youths have an increased risk of opioids misuse after surgery. According to Cardona-Grau et al., clinicians can reduce opioid prescription in the pediatric population without increasing pain scores. Dex could be a possible route; however, current studies cannot answer the feasibility and outcomes in this population. Studies already allude to better outcomes like stabilization of the circulatory system, better stress response, reduction in restlessness, pain, and reduced psychomotor agitation. These outcomes set a precedence that Dex could safely and effectively reduce opioid consumption in the pediatric community.
**Recommendations for Practice**

Opioid use has been a source of undesirable events as a result of surgery. Some of the commonly reported consequences including opioid use and misuse, hyperalgesia, and respiratory distress. Several approaches have been proposed to reduce opioid consumption throughout the perioperative period, and the majority of the proposals are yet to be confirmed. Nonetheless, dexmedetomidine has proven to reduce opioid consumption perioperatively and has possibly changed the opioid narrative. Nurses, clinicians and anesthesia providers involved in surgical procedures should rely on evidence-based proposals in mitigating the consequences of opioids. Recommendations (evidence-based) that should guide the use of dexmedetomidine as an adjunction therapy to reduce opioid consumption include:

i.) Administration of dexmedetomidine (Dex) before induction of anesthesia (Level I evidence, Grade A recommendation). Clinicians can administer Dex five minutes (Level I evidence, Grade C recommendation), 10 minutes (Level I evidence, Grade C recommendation), or 30 minutes (Level I evidence, Grade C recommendation) before surgery.

ii.) Administration of Dex at the induction of anesthesia (Level I evidence, Grade A recommendation).

iii.) Administration of Dex intranasally (Level I evidence, Grade C recommendation).

iv.) Starting Dex at a loading dose of 0.5 μg/kg-1 μg/kg dexmedetomidine administered over 10 minutes, then administered continuously at a dose of 0.1–0.5 μg/kg/hr (Level I evidence, Grade A recommendation).

v.) Starting Dex at 0.5 μg/kg/h-1.0 mg kg⁻¹ and maintaining this dosage throughout the surgery (Level I evidence, Grade B recommendation).

The following flow diagram is a proposed algorithm based on current evidence:
Figure 1: Reduction in opioid consumption with dexmedetomidine as adjunct therapy during surgery

Conclusions

After a rigorous appraisal of seven RCTs, empirical evidence determined that dexmedetomidine infused at varying doses and periods reduces the consumption of opioids during and after surgery. The systematic review established that a loading dose of 0.5 μg/kg-1 μg/kg dexmedetomidine for ten minutes followed by a continuous dose of 0.1–0.5 μg/kg/hr or a starting and continuous dose of 0.5 μg/kg/hr-1.0 mg kg⁻¹ reduce opioid consumption. The review also determined that 50 mg Dex intranasal has a similar effect. However, this study has made no determinations on side effects of using or not using Dex as an adjunct therapy during surgery.

Given the findings, clinicians can use the algorithm provided to change surgical modalities. The algorithm proposed is a synthesis of the underlying evidence and is capable of reducing opioid consumption. Healthcare providers should have a patient-specific approach since
the algorithm offer multiple viable options. Notwithstanding, the inclusion of Dex as an adjunct therapy reduces opioid consumption during surgery.

IMPLEMENTATION

Setting and Participants

The setting will take place via an online survey and a PowerPoint educational module with alumni of Florida International University’s (FIU) Nurse Anesthesia Program. The study will include Certified Registered Nurse Anesthetist (CRNAs). The participation will be based on individuals within an email list that is provided by FIU faculty. These individuals will be asked to provide feedback regarding the educational module's anesthesia providers' experience. The anticipated sample size will be between 10-15 participants.

Recruitment

The target population consisted of CRNAs who have taken care of patients receiving spinal anesthesia. Participants were acquired through an email list provided by FIU faculty. The anesthesia providers recorded on the email list were sent an email containing an invitation along with a link to participate in the educational module.

Description of Approach and Project Procedures

The primary methodology of the proposed project is to have the survey taker participate in an online Zoom educational module that focuses on the perioperative management of patients receiving dexmedetomidine during spinal anesthesia. The project will be implemented by conducting an online pre-test survey that will assess the anesthesia provider’s knowledge about utilizing dexmedetomidine in a patient receiving spinal anesthesia and its effects during the perioperative period. The existing knowledge and baseline understanding of the anesthesia provider will be analyzed using a pre-evaluation tool that will subcategorize information regarding the impact of the intervention and determine its significance.
The second segment will include a Zoom educational PowerPoint. The primary means of learning will be through a voiceover PowerPoint presentation with information regarding the utilization of dexmedetomidine in a patient receiving spinal anesthesia and its effects during the perioperative period. Understanding anesthesia providers' current level of education is essential in bridging existing gaps in knowledge and supporting the need for additional tools to ensure patients receiving dexmedetomidine during spinal anesthesia are receiving evidence-based care during the perioperative period. Viewing the presentation will offer insight and perspective for anesthesia providers regarding the importance of reducing opioid consumption by utilizing dexmedetomidine during the administration of spinal anesthesia. The observed and documented evidence backs an evidence-based project with inclusive information regarding utilization of dexmedetomidine in the patient receiving spinal anesthesia and its significance in reducing opioid requirements.

The third segment of the project will contain an online post-assessment test to determine if the CRNAs participating in the module achieved the learning objectives as well as examine perception to the intervention and the contents that were delivered. This data will provide useful feedback regarding the impact of the educational intervention and will determine how to further progression in expanding the use of dexmedetomidine in spinal anesthesia. The post-test results will provide applicable information regarding the effectiveness of the module and willingness of the anesthesia provider concerning administration of dexmedetomidine during spinal anesthesia and reduction of the need of rescue opioid administration perioperatively.

Protection of Human Subjects

CRNAs participating in the survey remained anonymous and the data was secured via utilization of randomized code identifiers. The electronic data collected from both the pre- and post-test were protected by a laptop locked with a password. Using laptop passwords as well as spyware safeguarded the security of the information. There are no identifiable risks to the study
as the only requirement is the time allotted by each CRNA in the educational module which took approximately less than 20 minutes to finish.

**Data collection and analysis**

The study involves administration of a pretest and a posttest to decipher the educational module’s impression. The pre- and posttest were conducted using Qualtrics as the survey platform to determine if participants have an understanding of handling surgical patients receiving spinal anesthesia and dexmedetomidine throughout the perioperative period. The survey had a total of 10 questions that focus on knowledge surrounding the opioid epidemic and applying opioid-sparing methods in practice. The pre-test survey will measure the practitioner’s basic knowledge on the subject at hand. The post-test survey will interpret the participants knowledge obtained from the educational presentation as well as application of said knowledge to professional practice. Any data collected will be strictly confidential in that no subject identifiers will be recorded throughout the duration of the study.

**Data Management and Measure**

The investigator of the project will be the DNP student responsible for acquiring FIU alumni via an email list for participation in the educational module. Each response will be recorded to evaluate the survey taker’s knowledge base before watching the PowerPoint and after to identify if learning has occurred. No personal identifiers will be recorded for any of the study participants so that anonymity will be maintained. The ramifications of the educational module will be determined upon receiving the results of the pre- and post-test. A thorough analysis of the study should reveal evidence that will be utilized to interpret the efficacy of the educational module and if the CRNA’s knowledge has been enhanced. The co-investigator on this project will also store any data obtained from participants in a password-protected laptop computer.
IMPLEMENTATION RESULTS

Pre/Post-Test Demographics

The pre-test demographics are shown in Table 3., shown below.

<table>
<thead>
<tr>
<th>Demographic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Participants</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (70%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>18-25</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>26-40</td>
<td>7 (70%)</td>
</tr>
<tr>
<td>41-55</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>&gt;55</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>African American</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Years of Experience</td>
<td></td>
</tr>
<tr>
<td>1 to 2 years</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>2 to 5 years</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>5 to 10</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>More than 10 years</td>
<td>1 (10%)</td>
</tr>
</tbody>
</table>

A total of 10 CRNAs participated in the pretest demographic section. The majority of the participants were female (n=7, 70%) as opposed to male (n=3, 30%). A variety of ethnicities were represented in this group: Caucasian (n=3, 30%), Hispanic (n=5, 50%), and other (n=2, 20%). The participants were questioned about the amount of time in years that they have been practicing anesthesia and the findings ranged: 1 to 2 years (n=1, 20%), 2 to 5 years (n=2, 40%), 5 to 10 years (n=2, 20%) and more than 10 years (n=1, 10%). The survey takers comprised of DNP-prepared CRNAs (n=7, 70%) as well as Master level prepared CRNAS (n=3, 30%).
Pre-Test Likelihood of Utilization of Dexmedetomidine in Patients Receiving Spinal Anesthesia

The pre-test contained information regarding the perioperative management of surgical patients receiving dexmedetomidine as an anesthetic adjunct in spinal anesthesia. The majority of participants (n=7, 70%) stated that they were unlikely to utilize dexmedetomidine in spinal anesthesia. The survey concluded that most respondents (n=7, 70%) were unaware of the exact prevalence of the opioid epidemic. This group of participants admitted to not knowing that the use of dexmedetomidine in spinal anesthesia reduced opioid consumption by 35%.

Pre-Test Identification of Current Knowledge about Perioperative Management of Surgical Patients Receiving Dexmedetomidine as an Anesthetic Adjunct to Spinal Anesthesia

The survey focuses on identifying the benefits of utilization of dexmedetomidine as an anesthetic adjunct in spinal anesthesia. The majority of the participants understood the mechanism of action of dexmedetomidine; the question was correctly answered by 9 participants (n=9, 90%). When asked about the benefits of dexmedetomidine use, all 10 participants answered the questions correctly (n=10, 100%). All participants (n=10, 100%) answered correctly when questioned about dexmedetomidine’s side effect profile. The participant's scores improved in the post-test when asked about questions pertaining to opioid related deaths (n=10, 100%). The participants were asked questions involving the prevalence of opioid misuse and the side effects of opioids. Their scores showed a universal improvement upon comparison of the pre-and post-survey. Table 4 shows the difference in responses from the pre- to post-test.
Table 4. Difference in Pre- and Post-Test Knowledge

<table>
<thead>
<tr>
<th>Questions</th>
<th>Pre-test</th>
<th>Post-test</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>6% of previously opioid naïve surgical patients continued taking opioids approximately how long post-surgery?</td>
<td>50%</td>
<td>100%</td>
<td>50%</td>
</tr>
<tr>
<td>What do the adverse effects of chronic opioid consumption include?</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>In 2018, how many Americans reported 12 years and older partook in the misuse of opioids?</td>
<td>60%</td>
<td>90%</td>
<td>30%</td>
</tr>
<tr>
<td>Since 1999, how many Americans have died from an opioid overdose?</td>
<td>40%</td>
<td>80%</td>
<td>20%</td>
</tr>
<tr>
<td>On what receptor does Dexmedetomidine exert its action?</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>What do the benefits of Dexmedetomidine include?</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>What are some of the side effects of Dexmedetomidine?</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Dexmedetomidine given at 1 µg/kg IV loading dose over 10 minutes, followed by 0.4 µg/kg/h reduces total morphine consumption by at least _____.</td>
<td>70%</td>
<td>100%</td>
<td>30%</td>
</tr>
<tr>
<td>How likely are you to use dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia?</td>
<td>40%</td>
<td>50%</td>
<td>10%</td>
</tr>
<tr>
<td>How likely are you to recommend utilizing dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia?</td>
<td>40%</td>
<td>50%</td>
<td>10%</td>
</tr>
</tbody>
</table>

On average, the scores on the post-test increased compared to that of the pre-test after the participants viewed the online PowerPoint presentation. All of participants improved knowledge about the prevalence of the opioid epidemic and the importance of decreasing opioid used when possible (n=10, 100%). The majority of respondents report improved knowledge about perioperative management of patients receiving dexmedetomidine during spinal anesthesia (n=7, 70%). When asked questions dexmedetomidine regarding mechanism of action, benefits of use as well as side effects, there was no decipherable proof of learning as all the participants answered these questions correctly on the pre- and post-test (n=10, 100%) There was an increase in understanding how much the consumption of opioids decreases upon incorporation of dexmedetomidine in the anesthetic plan of care (n=3, 30%). Lastly, half of the participants in the post-test stated they would be likely to use and/or recommend dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia (n=5, 50%).
Post-Test Likelihood of Utilization of Dexmedetomidine in Patients Receiving Spinal Anesthesia

A minority of the participants stated they were somewhat unlikely to utilize dexmedetomidine in patients receiving spinal anesthesia in the pretest (n=4, 40%). The post-test showed that one participant changed their answer from “somewhat unlikely” to “somewhat likely” (n=1, 10%). A minority of the participants stated they were somewhat unlikely to recommend utilization of dexmedetomidine in patients receiving spinal anesthesia in the pretest (n=4, 40%). The post-test displayed that one participant also changed their answer from “somewhat unlikely” to “somewhat likely” (n=1, 10%).

Summary

Overall, the results displayed improvement in knowledge upon evaluating the scores of the pre-test and post-test. The average knowledge gain was a total of 15%. The post-test exhibited that participants are somewhat likely (n=5, 50%) to utilize dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia.
IMPLEMENTATION DISCUSSION

Limitations

One of the limitations of the study was a small sample size; the survey was emailed to alumni of FIU’s Nurse Anesthesia Program. The email list contained 61 CRNAs, however only ten people responded to the survey. A greater sample size is ideal to augment the study's findings and offer a sample size that is representative FIU’s graduated anesthesia practitioners. The survey link, which consisted of a pre-test that included demographics questions, a voice-over PowerPoint lecture, and a post-test, was available to the respondent for two weeks; it is possible that lengthening the time of survey availability may have produced more responses. Lastly, the study was executed completely online, preventing it from being distributed through other modalities.

Future Implications for Anesthesia Practice

The literature demonstrated that Dex given in any approach reduces cumulative opioid consumption. Bringing the insight that total morphine consumption is decreased by at least 35%\textsuperscript{26} when utilizing dexmedetomidine in spinal anesthesia can help encourage its use by anesthesia providers. Even though the primary aim was total opioid consumption reduction, it was discovered that dexmedetomidine is beneficial in that patients receiving dexmedetomidine during spinal anesthesia reported more satisfaction with the quality of post-operative analgesia.\textsuperscript{23,25} Incorporation of Dexmedetomidine has also reduced the need for NSAIDs, improved quality of sleep, and exhibited a shorter recovery time in PACU.\textsuperscript{22,27,24}

Heavy reliance on opioid use has been a cause of undesirable occurrences in the perioperative period, including opioid abuse, hyperalgesia, and respiratory distress. Dexmedetomidine has been proven to reduce opioid consumption perioperatively in patients receiving spinal anesthesia and can possibly change opioid perceptions. This study displays that anesthesia providers involved in surgical procedures should rely on evidence-based applications in modifying the consequences of opioids. The quality improvement project showed that the intervention of bringing awareness to these factors was effective in increasing healthcare providers
knowledge and increased the likelihood of utilizing/recommendation of dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia.
REFERENCES


Primary Aim

Opioids constitute the biggest share of analgesics used in surgical units throughout the US. Most surgical patients are prescribed opioids perioperatively.\textsuperscript{1} In reality, patients have benefited significantly from prescribed opioids. The rapid onset of action, lack of analgesic ceiling- dose (beyond which there is no additional pain relief), and consistent relief of post-surgical pain have increased their preference among surgeons, nurses, and patients.\textsuperscript{1} While the benefits remain at the forefront, the adverse events have raised significant concerns among
surgical teams. The use of opioids in surgical units has been noted to significantly impact the opioids crisis, which has led to many deaths.\textsuperscript{5,4,7,9} Surgical units have also witnessed higher rates of opioid-induced endocrinopathy, hyperalgesia, urinary retention, postoperative respiratory depression, bradycardia, somnolence, nausea, vomiting, and rash.\textsuperscript{10,12} These occurrences have the potential to increase medical costs and lead to poor outcomes. Therefore, there is a need to reduce opioid consumption in surgical units with adjuncts like dexmedetomidine.

The primary aim of the DNP project is to reduce the current opioid dosages being used as analgesic therapies during surgeries by incorporating dexmedetomidine. Some of the opioids this intervention aims to reduce throughout the perioperative period include morphine, hydromorphone, fentanyl, oxycodone, oxymorphone, and tramadol. Well-executed studies have demonstrated that dexmedetomidine has the potential to help reduce opioid requirements and produce better effects overall. These include studies that show that dexmedetomidine infusion at an initial dose of 0.5-1 μg/kg with 0.11- 0.6 μg/kg\textsuperscript{-1} hr\textsuperscript{-1} dose adjustment reduces perioperative opioid consumption, time of first analgesia demand, reduction in VAS score, and fewer adverse events.\textsuperscript{27,23,26,24,25,13,22} These studies also show that dexmedetomidine is not associated with increased occurrence of nausea, vomiting, and respiratory distress. Surgical teams, therefore, ought to adopt this novel adjunct therapy for various surgical procedures.

**Goals and Outcomes**

Sufficient evidence underscores the inclusion of dexmedetomidine in the anesthetic plan and has the potential for better analgesic effects than the sole use of opioids. It is prudent for surgical teams to understand the urgency of reinventing current opioid practice by incorporating a comparable and safe option. The goals and outcomes described below are Specific, Measurable, Attainable, Realistic, and Time-specific (SMART). These SMART goals emphasize tangible outcomes and improve the skills, knowledge, and attitude of members of the surgical team.\textsuperscript{28} Moreover, the outcomes are measurable and congruent with a timeline.
Strength, Weakness, Opportunities, and Threats (SWOT) Analysis

The SWOT analysis involves discussing factors that could impact the DNP project's implementation and success or failures. The process analyzes the surgical unit’s strengths (S), weaknesses (W), opportunities (O), and threats (T) to achieving organizational goals and desires outcomes. Briefly, analysis of the surgical unit’s strengths involves reflection about what the facility does well and its unique resources. Weaknesses are factors that the surgical unit could improve, especially in instances where resources are lacking. Opportunities are what the surgical facility could leverage to improve the unit’s position to effect change. Finally, potential threats
may be underlying issues that can prove harmful to the project. Analyzing the above items allows the DNP project implementation team to establish itself in an environment that cannot be easily displaced by opposing factors.\textsuperscript{31} Table 4 below provides a matrix of the SWOT analysis that could impact the implementation of the DNP project as well as its aim, goals, and objective.

<table>
<thead>
<tr>
<th>STRENGTHS (+)</th>
<th>WEAKNESSES (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The surgical unit has a good reputation for evidence-based practice (EBP). The evidence-based team has a good history of ensuring quality improvement proposals are well accepted and run.</td>
<td>• Healthcare professionals working in surgical units have in the past expressed dissatisfaction with dexmedetomidine.</td>
</tr>
<tr>
<td>• Over the past few months, members of surgical teams within the facility had begun registering the challenges with opioid use during surgery. The project will, therefore, provide a sense of relief.</td>
<td>• The surgical team is often poorly staffed. Training these professionals is unlikely to be seamless.</td>
</tr>
<tr>
<td>• Reducing opioid prescriptions by the addition of dexmedetomidine will not involve an additional cost. Technically, costs will be cut.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OPPORTUNITIES (+)</th>
<th>THREATS (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The healthcare facility plans to hire new healthcare professionals. This could be a chance to propose the recruitment of specialists in surgery.</td>
<td>• While dexmedetomidine may be safe compared to opioids, the adverse effects cannot be ignored.</td>
</tr>
<tr>
<td>• While dissatisfaction has been reported with dexmedetomidine use, healthcare professionals have expressed concerns about opioid side effects.</td>
<td></td>
</tr>
</tbody>
</table>

**Quality Improvement Project Details and Rationale**

The quality improvement model will be based on the revised Iowa model for evidence-based practice to promote healthcare excellence. The Iowa model comprises seven steps that clinicians can use to implement change. The first step is to identify triggering issues and opportunities. This step involves questioning current practice and is highly motivated by patient outcomes.\textsuperscript{32} In the context of the DNP project, this step involves realizing the impact of opioids in surgical units and
the need to identify alternatives. The next step in the Iowa model is to state the question and reframe it in the PICOT format. Stating the question determines boundaries for change and provide a bearing to the evidence-based practice team. Once clinical questions have been formulated, the third stage in the Iowa model is to assign priority to each question. This model proposes that not all questions can be solved through the EBP process. The model further proposes that high-priority should be assigned to topics related to patient safety, high-cost, or high-risk patients. Low priority topics that do not align with the organization's mission and goals often do not attract resources. The project leader has accomplished these first three steps.

The next step in the Iowa model is to form an EBP team. Selecting the EBP team should reflect on interprofessional involvement and the skills required by the project for implementation and evaluation. To this end, the EBP team for the DNP project will include the chief nurse of the surgical units, head of CRNAs, head of surgery, the medical director, nurse administrator, and nurses assigned to the emergency department. This team will perform the rest of the tasks within the model. The nurse administrator will be included as an ex-officio member to lobby for resources and petition for additional healthcare professionals in the coming recruitment initiative.

The next step in the Iowa model is to assemble, appraise, and synthesize the body of evidence. This step has been partly accomplished. The EBP team will appraise and synthesize the body of evidence already assembled. The team will grade the evidence from high-quality to low-quality. Upon review of the available evidence, the team will determine whether the amount of evidence collected will be sufficient. Insufficient evidence will prompt the team to look further with the help of the librarian. When an adequate amount of evidence is gathered, the EBP team will move to the next stage to design and pilot practice change. Piloting involves controlled environments, which allows the EBP team to evaluate whether there is a difference with the placebo. To this end, the team must collect pre-pilot and post-pilot data. This data will allow the team to acknowledge the success of the pilot project and change protocol. Once the pilot stage is complete; the EBP team will decide if the change is appropriate for practice. If the change is
indeed appropriate, the EBP team will redesign the practice change and integrate it into routine practice. Once the above step is accomplished, the team will engage other stakeholders to implement the change. The final stage will be to disseminate the findings. The team will share reports within and outside of the organization.

The rationale for the Iowa model is that the process is simple and allows the team to monitor expected benefits before rolling the program throughout the healthcare facility. The team must have a pilot program to determine if the change protocol will fit the facility’s goals and mission. The model also allows only high-priority issues to run to completion. The above ideas allow the EBP team to limit wastage of resources and ensure certainty for quality and positive outcomes. The model also ensures patient safety, especially before the project is mandated throughout all healthcare facilities and surgical units. Therefore, the Iowa model is a safe design for ensuring a safe transition for the reduction of opioids and to increase dexmedetomidine use.

**Evaluation Plan**

The evaluation process will be based on the Iowa model of project evaluation. The process will include collecting and analyzing post-pilot data and comparing it with baseline data. Also, the evaluation plan will acknowledge verbal feedback from the project implementers. Feedback will be evaluated to determine if dexmedetomidine was a successful adjunct, thereby meeting objectives. Baseline and post-pilot data will include information about opioid consumption, quality of recovery score, pain intensity, length of hospital stay, the incidence of nausea and vomiting, time of request of the first analgesia, time to the first use of rescue analgesia, and postoperative depression. This feedback may provide insights into necessary adjustments. Once all the data is well-organized, the EBP team will decide whether to adapt, adopt, or reject the proposed change.
Sustaining the Practice Change

Once the proposed change has been determined to reduce the consumption of opioids, the EBP team will lobby for policy formulation. Currently, no policy mandates which analgesics to be used in the hospital. This gap in hospital policies is a promising avenue to sustain the change. A policy can ensure that all surgical teams adopt the change to improve patient outcomes. Ideally, a policy is a way of integrating the change into practice.32 Once the team has analyzed and certified the data and has made recommendations for adopting the change, they will develop a policy. To this end, the policy would be known as "reducing opioid use with dexmedetomidine."

Formulating such a policy will guide anesthesia providers in actively taking steps to reduce opioid dosages in the perioperative period. The next strategy would be to involve in-service education.32 In-service education is warranted because the project implementation should include all surgical units and will ensure that all providers understand the rationale behind the policy change. In-service education will also improve compliance with the policy.

The final protocol would be a plan for continuous monitoring and reporting of data. Frequent monitoring will project how the goals and outcomes of the project are being met.32 Monitoring will also acknowledge necessary adjustments such as dose adjustments and timing of the dexmedetomidine administration. Frequent monitoring will be vital for procuring evidence that the change is necessary. The EBP team will report to the organization and other organizations as well as this will be vital for a nationwide approach to the opioid pandemic. Once the project receives national interest, it’s implementation within the healthcare facility will be solidified.
### Appendix B: Matrix Tables

#### Evaluation table 1

| **Design/Method** | Prospective randomized controlled trial: 86 patients undergoing EITs randomized into three groups. All groups had dexmedetomidine at an initial dose of 0.5 µg/kg for 10 minutes. Dose adjustment varied per group throughout the EIT. RD1 dose was adjusted to 0.2 µg/kg\(^{-1}\) hr\(^{-1}\); RD2 adjusted to 0.4 µg/kg\(^{-1}\) hr\(^{-1}\); RD3 0.6 µg/kg\(^{-1}\) hr\(^{-1}\) |
| **Sample/Setting** | 86 patients (ASA I or II), BMI < RD1 n=29, RD2 n=28, and RD3 n=29. Patients adults of age 60-75 undergoing endovascular interventional therapies in PACU |
| **Major Variables Studied and Their Definitions** | Dependent variables: Intraoperative variables such as duration of surgery, duration of anesthesia, remifentanil dosage, dexmedetomidine, nimodipine dosage, propofol dosage, and cisatracurium dosage; postoperative variables such as recovery time at PACU, duration of hospitalization, patient satisfaction score, surgeon satisfaction score, GOS of three months, and cerebral infarction after 30 days. Independent variable: dexmedetomidin administration. |
| **Measurement and Data Analysis** | IntelVue monitor: Used to obtain intraoperative hemodynamic data. Glasgow coma scale: Used for neurologic examination. Bruggrmann comfort scale obtained at 1, 4, 8, 16, and 24 hrs after surgery |
| **Findings** | Dexmedetomidine at an initial dosage of 0.5 µg/kg adjusted to 0.6 µg/kg\(^{-1}\) hr\(^{-1}\) reduced the consumption of total nimodipine and sufentanil and narcotic drugs |
during surgery. Surgeon's satisfaction was low, and the length of hospital stay was increased at 0.5 after surgery. More patients in RD3 needed atropine than RD1 and RD2.

<table>
<thead>
<tr>
<th>Results</th>
<th>RD2 and RD3 showed a more stable hemodynamic profile than RD1. GCS, BCS, and FAS were not statistically significant across groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conclusions</td>
<td>Dexmedetomidine can be used to reduce opioid consumption in the first 48 hours of surgery with better pain scores</td>
</tr>
<tr>
<td>Appraisal:</td>
<td>Strength: Consistent and stepwise administration of dexmedetomidine Limitations include small sample size, inability to assess plasma levels of dexmedetomidine and catecholamines. Feasibility of use: Results are appropriate to inform practice</td>
</tr>
<tr>
<td>THEME</td>
<td>Reducing opioid consumption in surgical units.</td>
</tr>
</tbody>
</table>

**Evaluation table 2**

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Design/Method</td>
<td>Block randomized controlled trial: 48 patients randomized into dexmedetimine (dex) group n=24 or propofol group n=24. Dexmedetomidine group received a loading dose 1 µg/kg dexmedetmidine over 10 minutes. They received additional dex 0.1-0.5 2 µg/kg.hr⁻¹. The propofol group received a dose between 0.5-2.0 µg/mL.</td>
</tr>
<tr>
<td><strong>Sample/Setting</strong></td>
<td>Fifty-four participants (ASA I or II) dex group, n=24, or propofol group, n=24, scheduled for total knee arthroplasty in a hospital setting. Age range was 20-80 years</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **Major Variables Studied and Their Definitions** | Independent variable: Dexmedetomidine vs. propofol infusion  
Dependent variable: postoperative cumulative fentanyl consumption via IV PCA, NRS scores, postoperative pain burden, serial SBPs, and HRs, |
| **Measurement and Data Analysis** | Variables were analyzed using the Shapiro-Wilk test. Other statistical tests such as the Fischer exact test, Friedman test, and Kruskal Wallis test were used. |
| **Findings** | Administration of dexmedetomidine that propofol reduced postoperative opioids consumption and pain scores 48 hours after surgery. |
| **Results** | Postoperative fentanyl consumption was significantly reduced in the dexmedetomidine group. The baseline NRS scores were not significantly different in both groups. At six hours, the postoperative NRS scores were lower in the dexmedetomidine group compared to the propofol group. There was no significant difference in postoperative serial systolic blood pressure (SBP) and heart rate (HR) in both groups. |
| **Conclusions** | Intraoperative dexmedetomidine infusion causes a clinically significant reduction in opioid consumption in patients undergoing total knee arthroplasty. |
| **Appraisal: Worth to Practice/Level** | Strength: Robust pain management protocol. Limitation: sedation levels were not assessed at PACU. Risk of harm: Reduced by excluding patients with contraindications to spinal anesthesia. Feasibility of use: Appropriate, the protocol is easily reproducible. |
| **THEME** | Reducing opioid consumption in surgical units. |
**Evaluation table 3**

<table>
<thead>
<tr>
<th><strong>Citation</strong></th>
<th>Sherif AA, Elsersy HE. The impact of dexmedetomidine or xylocaine continuous infusion on opioid consumption and recovery after laparoscopic sleeve gastrectomy. <em>Minerva anestesiologica</em>. 2017;83(12):1274-1282. doi:10.23736/S0375-9393.17.11855-9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design/Method</strong></td>
<td>Prospective RCT: 150 patients randomized into the control lidocaine or dex groups. Control group: saline bolus and continuous infusion. Lidocaine group: 2 mg/kg bolus over ten minutes followed by 1.5 mg/kg/hr continuous infusion. Dexmedetomidine group: 1 µg/kg bolus over ten minutes, followed by 0.4 µg/kg continuous infusion.</td>
</tr>
<tr>
<td><strong>Sample/Setting</strong></td>
<td>150 patients (ASA I to II, BMI &gt; 40 kg/m(^2) or &gt; 35 kg/m(^2) with comorbidities) scheduled for laparoscopic bariatric surgery in a hospital setting.</td>
</tr>
<tr>
<td><strong>Major Variables Studied and Their Definitions</strong></td>
<td>Dependent variables: Primary variable; total morphine consumption. Other variables were pain score and quality of recovery. Independent variable: dexmedetomidine vs. lidocaine infusion.</td>
</tr>
<tr>
<td><strong>Measurement and Data Analysis</strong></td>
<td>Wilson’s four-point sedation scale was used to examine the degree of sedation in PACU. Emotional scale, physical comfort, psychological support, physical dependence, physical support, and pain domains were used to examine the quality of recovery.</td>
</tr>
<tr>
<td><strong>Findings</strong></td>
<td>Continuous infusion of dex or lidocaine reduced total morphine require and improve the quality of recovery.</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Total morphine consumption was 14 (dexmedetomidine group), 18 (lidocaine group), and 29 (control). This means including both dexmedetomidine or lidocaine reduces morphine consumption while dexmedetomidine provides better results.</td>
</tr>
</tbody>
</table>
Conclusions
Continuous infusion of dexmedetomidine better reduces opioid consumption than lidocaine.

Appraisal:
Worth to Practice/Level
Strength: All patients monitored by capnography, electrocardiography, pulse oximetry, and noninvasive arterial blood pressure. Limitation: The medications were not provided preoperatively. Risk of harm: Minimal through careful monitoring. Feasibility of use: Adequate results to support applicability.

THEME
Reducing opioid consumption in surgical units.

Evaluation table 4

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Design/Method</td>
<td>Single-centered, parallel-group placebo-controlled RCT: 60 patients n=30 group C and n=30 group D. Group D patients received dexmedetomidine 0.5 µg/kg. Patients in group C received normal saline.</td>
</tr>
<tr>
<td>Sample/Setting</td>
<td>60 patients (ASA I-II) elected to laparoscopic cholecystectomy. Patients were aged 18-79. Patients were in a hospital setting.</td>
</tr>
<tr>
<td>Major Variables Studied and Their Definitions</td>
<td>Dependent variable: postoperative morphine consumption in the first 24 hours. Cumulative hospital stay. Other variables include the incidence of post-surgical pain, length of intensive care unit stay, intraoperative fentanyl consumption, time of use of first rescue analgesia, and the number of patients with severe pain.</td>
</tr>
</tbody>
</table>
Richmond's agitation sedation scale and the verbal rating scale were used for sedation and pain, respectively.

### Findings
Dexmedetomidine 0.5 µg/kg reduces postoperative requirements for opioid analgesics and increase the sedation level.

### Results
There was no significant difference in postoperative pain levels in both groups. Dexmedetomidine infusion reduced the incidence of severe pain and increased the time to use of first rescue analgesia. Dex infusion also reduced postoperative morphine consumption (at mean 5 mg/24 h vs. 15 mg/24 h in group D). length of ICU stay was not statistically different that is 14 h group D and 13 h group C.

### Conclusions
Dex infusion is an effective modality for better analgesic outcomes during elective laparoscopic cholecystectomy.

### Appraisal:
**Worth to Practice/Level**
Strength: Proper monitoring through Philips vital signs monitor, BIS, and ANI-improved outcomes. Limitation: small sample size. Risk of harm: minimal, patients ASA I and II selected. Feasibility of use: Applicable in practice, as shown by data and results.

### THEME
Reducing opioid consumption in surgical units.

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### Evaluation table 5

<table>
<thead>
<tr>
<th>Citation</th>
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<tr>
<td><strong>Design/Method</strong></td>
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<tr>
<td><strong>Sample/Setting</strong></td>
</tr>
<tr>
<td><strong>Major Variables Studied and Their Definitions</strong></td>
</tr>
<tr>
<td><strong>Measurement and Data Analysis</strong></td>
</tr>
<tr>
<td><strong>Findings</strong></td>
</tr>
<tr>
<td><strong>Results</strong></td>
</tr>
<tr>
<td><strong>Conclusions</strong></td>
</tr>
<tr>
<td><strong>Appraisal: Worth to Practice/Level</strong></td>
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<tr>
<td><strong>THEME</strong></td>
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<tr>
<td><strong>Evaluation table 6</strong></td>
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<td><strong>Design/Method</strong></td>
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<td><strong>Sample/Setting</strong></td>
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<tr>
<td><strong>Major Variables Studied and Their Definitions</strong></td>
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<tr>
<td><strong>Measurement and Data Analysis</strong></td>
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<td><strong>Findings</strong></td>
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<td><strong>Results</strong></td>
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<td><strong>Conclusions</strong></td>
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Evaluation table 7

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</thead>
<tbody>
<tr>
<td>Design/Method</td>
<td>RCT: 57 patients randomized into group R, 20 mL 0.5% ropivacaine and group RD 20 mL 0.5% ropivacaine coadministered with dexmedetomidine 1µg/kg. all patients received postoperative morphine.</td>
</tr>
<tr>
<td>Sample/Setting</td>
<td>57 patients (aged between 18 to 75 years, ASA I-II, BMI≥30) scheduled for elective posterior lumbar interbody fusion surgery. R n=28, and R n=29</td>
</tr>
<tr>
<td>Major Variables Studied and Their Definitions</td>
<td>Independent variable: Dexmedetomidine vs. ropivacaine infusion. Dependent variable: Total consumption of IV morphine in the first 24 hours after surgery. Time of first analgesic demand.</td>
</tr>
<tr>
<td>Measurement and Data Analysis</td>
<td>VAS was used to rate pain.</td>
</tr>
<tr>
<td>Findings</td>
<td>Adding dexmedetomidine to preemptive ropivacaine lowers postoperative morphine consumption and prolongs time to the first rescue analgesia.</td>
</tr>
</tbody>
</table>
The mean PCA morphine consumption in the RD group was 16.5, while the R group was 7.6. More morphine was consumed in the RD group. The RD group had a prolonged time for the request of the first analgesic, which is 10.5 hours. R group had a short time to the request of the first analgesic, which is 5.3 hours. There was a marked reduction in the VAS score in RD than the R group.

Dexmedetomidine/ropivacaine combination improves analgesia and reduces opioid consumption.

Strength: Ability to demonstrate clinical benefits of combination therapy.

Limitation: Only a single dose of both medicines were used. Risk of harm: Minimal, ASA I-II patients included. Feasibility of use: Adequate conclusion supported by sufficient data.

Reducing opioid consumption in surgical units.


Double-blind randomized-controlled test involving 40 patients. First group received a 0.5 lgkg-1 dose of dexmedetomidine within 10 minutes, then an additional 0.5 lgkg-1 infused throughout the entire surgery. The second group received normal saline.

40 patients (ASA I-III) aged between 18-15 years expecting a knee arthroplasty. The study was carried out in a hospital setting.
## Major Variables Studied and Their Definitions

- Height, weight, age ASA physical status, BMI, duration of surgery and gestational age

## Measurement and Data Analysis

- Visual analogue scale (VAS) was used to measure pain levels.

## Findings

Dexmedetomidine is an effective anesthesia for patients undergoing caesarian section.

## Results

Intravenous DEX led to reduced requirement for postoperative opioid in patients.

## Conclusions

Dex infusion is an effective anesthesia and sedative.

## Appraisal: Worth to Practice/Level

- **Strength:** adequate sample size.
- **Limitation:** Level of patient sedation not measured.
- **Risk of harm:** low.
- **Feasibility of use:** can be applied in clinical setup.

## THEME

Safety and efficacy of Dexmedetomidine in Caesarian section patients.

### Evaluation table 9

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</tr>
</thead>
<tbody>
<tr>
<td>Design/Method</td>
<td>Randomized test involving total knee arthroplasty (TKA) patients categorized into 2 groups: Control and dexmedetomidine.</td>
</tr>
<tr>
<td>Sample/Setting</td>
<td>80 pediatric patients (ages 20-80) going through TKA</td>
</tr>
<tr>
<td>Major Variables Studied and Their Definitions</td>
<td>Age, sex, height, weight, ASA classification, surgery duration</td>
</tr>
</tbody>
</table>
PASS 2008 was utilized in calculating the sample size.

There was a considerable difference in the amount of fentanyl needed after surgery between the two groups.

DEX reduced the need of fentanyl post operation in TKA patients.

DEX prolongs analgesic period hence reduces the requirement for fentanyl use after surgery.

Strength: Adequate sample to provide bias-free results. Limitation: taking two sequential blood samples from one patient. Risk of harm: low. Feasibility of use: can be applied in clinical practice.

Effect of DEX on administration of fentanyl post-surgery.


300 parturients due for caesarian section being treated to spinal anaesthesia were grouped into 3 categories:

- Group B: 9.0 mg of bupivacaine (0.75%) together with 1 ml saline
- Group FB: 9.0 mg of bupivacaine (0.75%) together with 1 ml fentanyl (20 μg)
- Group DB: 9.0 mg of bupivacaine (0.75%) together with 5 μg of DEX (1 ml).

300 patients under spinal anesthesia.
| Major Variables Studied and Their Definitions | Height, weight, age ASA physical status, BMI, duration of surgery and gestational age |
| Measurement and Data Analysis | PASS 15.0 software was used in the analysis of data. |
| Findings | Dexmedetomidine 0.5 µg/kg has a block effect on which reduces the need for analgesics after surgery. |
| Results | There was no major difference in postoperative levels of pain across the three groups, including period of surgery, peak sensory level, and blood loss. Groups FB and DB demonstrated prolonged periods of sensory block compared to Group B; Group B (108.4 min), Group FB (122.0 min), and Group DB (148.2 min). |
| Conclusions | Dex has the potential to improve the quality of parturients’ recovery by causing a block effect particularly in a 5 µg DEX combination. |
| Appraisal: Worth to Practice/Level | Strength: use of ANOVA software left limited room for error. Limitation: the sample was too small. Risk of harm: low. Feasibility of use: results from study can be applied in clinical settings. |
| THEME | Efficacy and safety of Dex for patients experiencing caesarian section. |

| Citation | Chan, I. A., Maslany, J. G., Gorman, K. J., O’Brien, J. M., & McKay, W. P. (2016). Dexmedetomidine during total knee arthroplasty performed under spinal anesthesia decreases opioid use: a randomized-controlled |
| **Design/Method** | Randomized test involving ASA I or II patients categorized into two groups: D (bupivacaine plus 5mg Dex) and C (bupivacaine plus equal amount of saline). Subsequent dose of bupivacaine depended upon the enhanced up-down allocation process. The starting bupivacaine dose for both groups was 4 mg and was increased subsequently based on the probability of the present dose. |
| **Sample/Setting** | 90 patients (ASA I or II) going through caesarean section in spinal anesthesia. |
| **Major Variables Studied and Their Definitions** | Height, weight, age ASA physical status, BMI, duration of surgery; (that is, the period from the onset of the surgery until its completion), and period until recovery. |
| **Measurement and Data Analysis** | Logistic regression model was used to calculate ED95. Normal distribution was estimated using the Kolmogorov-Smirnov test. |
| **Findings** | Group C recorded higher ED95 and 95% CI (confidence interval) than Group D |
| **Results** | Intrathecal 5mg DEX increases the efficacy of spinal bupivacaine by at least 24%. |
| **Conclusions** | DEX prolongs analgesic period in and enhances efficacy of spinal bupivacaine in patients undergoing caesarian section. |
| **Appraisal: Worth to Practice/Level** | Strength: Adequate sample to provide bias-free results. Limitation: small sample size, and absence of measurements to determine neurological deficit. Risk of harm: minimal. Feasibility of use: can be applied in clinical practice. |
| **THEME** | Effect of DEX on spinal bupivacaine. |

**Evaluation table 12**

| **Citation** | Fares, K. M., Mohamed, S. A. B., Abd El-Rahman, A. M., AbdeLemam, R. M., & Osman, A. M. M. (2020). Analgesic Effect of Intrathecal Fentanyl vs... |
Dexmedetomidine as Adjuvants to Bupivacaine Following Abdominal Surgery for Cancer in Children, a Randomized Trial. *Pain Medicine, 21*(11), 2634-2641.

<table>
<thead>
<tr>
<th>Design/Method</th>
<th>Randomized double-blind test involving ASA I or II malignancy patients categorized into 3 groups: C (2ml bupivacaine); F (2mg bupivacaine plus fentanyl 0.2 mg/kg); and D (2 ml bupivacaine + dexmedetomidine 0.2 lg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample/Setting</td>
<td>60 pediatric patients (ages 3-13) going through malignancy treatment</td>
</tr>
<tr>
<td>Major Variables</td>
<td>Systolic blood pressure (SBP), Diastolic blood pressure, heart rate, sedation score</td>
</tr>
<tr>
<td>Study and Their Definitions</td>
<td>Pain score was measured using the Face, Legs, Activity, Crying, and Consolability (FLACC).</td>
</tr>
<tr>
<td>Measurement and Data Analysis</td>
<td>Intrathecal narcotics can be effective anesthesia during surgery</td>
</tr>
<tr>
<td>Findings</td>
<td>Systolic blood pressure (SBP) was lower in group D than in C and F</td>
</tr>
<tr>
<td>Results</td>
<td>DEX prolongs analgesic period in and enhances efficacy of spinal bupivacaine in patients undergoing surgery</td>
</tr>
<tr>
<td>Conclusions</td>
<td>Strength: Adequate sample to provide bias-free results. Limitation: small sample size, and absence of measurements to determine neurological deficit. Risk of harm: minimal. Feasibility of use: can be applied in clinical practice.</td>
</tr>
<tr>
<td>Appraisal: Worth to Practice/Level</td>
<td>Effect of DEX on spinal bupivacaine.</td>
</tr>
</tbody>
</table>
Appendix C:

MEMORANDUM

To: Dr. Vicente Gonzalez
CC: Jillian Gil

From: Maria Melendez-Vargas, MIBA, IRB Coordinator

Date: June 3, 2021

Protocol Title: “The Utilization of Dexmedetomidine as and Anesthetic Adjunct in Spinal Anesthesia to Reduce Perioperative Consumption of Opioids”

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-21-0202  IRB Exemption Date: 06/03/21
TOPAZ Reference #: 110236

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.

MMV/cm
Appendix D:

Pretest and Posttest Questionnaire:

The Utilization of Dexmedetomidine as an Anesthetic Adjunct in Spinal Anesthesia to Reduce Perioperative Consumption of Opioids

INTRODUCTION

The primary aim of this QI project is to improve the knowledge of CRNAs pertaining to the utilization of dexmedetomidine as an anesthetic adjunct in spinal anesthesia in order to reduce perioperative consumption of opioids.

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format and are meant to measure knowledge and perceptions on the utilization of dexmedetomidine as an anesthetic adjunct in spinal anesthesia to reduce perioperative consumption of opioids.

PERSONAL INFORMATION

1. Gender: Male    Female    Other________

2. Age: ________

3. Ethnicity:
   Hispanic   Caucasian   African American   Asian
   Other______________

4. Position/Title: ____________________________________________

5. Level of Education: Associates     Bachelors    Masters    Other
   __________

6. How many years have you been an anesthesia provider?
   Over 10     5-10 years     2-5 years     1-2 year

Page 69 of 74
1. 6% of previously opioid naïve surgical patients continued taking opioids _____ post-surgery:
   a. 2-4 weeks
   b. 1-2 months
   c. 3-6 months
   d. 1-2 years

2. Adverse effects of chronic opioid consumption include:
   a. Urinary retention
   b. hyperalgesia
   c. respiratory depression
   d. bradycardia
   e. somnolence
   f. all of the above

3. In 2018, it was reported that _____ Americans 12 years and older partook in the misuse of opioids:
   a. 5.2 million
   b. 10.3 million
   c. 15 million
   d. 18.4 million

4. Since 1999, more than _________ Americans have died from an opioid overdose:
   a. 120,000
   b. 250,000
   c. 500,000
   d. 760,000

5. Dexmedetomidine is a:
a. $\alpha_2$-adrenergic receptor agonist
b. $\alpha_2$-adrenergic receptor antagonist
c. $\beta_1$-adrenergic receptor agonist
d. $\beta_2$-adrenergic receptor antagonist

6. The benefits of Dexmedetomidine include:
   a. Causes minimal respiratory depression
   b. Has analgesic properties
   c. Prevents postoperative delirium
   d. All of the above

7. Select the true statement:
   a. Dexmedetomidine increases the need of opioid administration
   b. Dexmedetomidine increases MAC and response to intubation
   c. Dexmedetomidine can cause hypotension, hypertension, nausea, bradycardia, anemia, and hypothermia
   d. Coadministration of dexmedetomidine with anesthetics, sedatives, hypnotics, and opioids is likely to lead to a decrease of their effects

8. Dexmedetomidine given at 1 µg/kg IV loading dose over 10 minutes, followed by 0.4 µg/kg/h reduces total morphine consumption by at least _____.
   a. 15%
   b. 20%
   c. 35%
   d. 50%

9. How likely are you to use dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia?
   a. Most likely
   b. Somewhat likely
c. Somewhat unlikely

d. Most unlikely

10. How likely are you to recommend utilizing dexmedetomidine as an anesthetic adjunct in patients receiving spinal anesthesia?

   a. Most likely
   b. Somewhat likely
   c. Somewhat unlikely
   d. Most unlikely
Appendix F: Poster

The Utilization of Dexmedetomidine as an Anesthetic Adjuvant in Spinal Anesthesia to Reduce Perioperative Consumption of Opioids

Jillian Gil, MSN, RN; Fernando Alfonso, DNP, CRNA; Anika Dianez, DNP, CRNA
Florida International University Nicole Wertheim College of Nursing and Health Sciences

INTRODUCTION

Nearly all US patients are prescribed and receive opioids during surgery. However, their widespread use has had a devastating effect. Patients prescribed opioids often require higher doses of opioids to maintain analgesia with adverse effects such as opioid-induced endocrinopathy, hyperalgesia, respiratory depression. Moreover, opioid abuse is considered a public health emergency due to an alarming incidence of overdose-related deaths, sexual abuse, nutritional neglect, and children born to opioid-dependent mothers following opioid abuse. These side effects have attracted debates on whether they are indisputable and continuously prompt further consideration of alternative approaches. Recent studies have suggested that dexmedetomidine (Dex) has a good analgesic profile and can reduce opioid consumption. Therefore, more research is required to establish whether dexmedetomidine as an adjuvant therapy can influence opioid consumption in surgical units.

PURPOSE

This literature review aimed to evaluate the current randomized controlled trials (RCTs) on the impact of dexmedetomidine as an adjunct therapy on opioid consumption and further recommend best available practices on the current issue.

RESEARCH OBJECTIVES

1. To explore opioid-sparing modalities that can produce comparable analgesic effects.
2. To assess the viability of dexmedetomidine as a pain management adjunct.
3. To propose recommendations that would reduce the perioperative consumption of opioids and help combat the opioid epidemic.

RESEARCH OBJECTIVES

1. To acquire knowledge on the use of dexmedetomidine in spinal anesthesia
2. To recognize the core issues surrounding the opioid epidemic and dexmedetomidine use
3. To demonstrate a willingness to administer dexmedetomidine during spinal anesthesia and reduce opioid administration

METHODOLOGY

- Research articles were obtained by searching the following databases: Medline, Embase, Pubmed, and Google Scholar
- Keywords: dexmedetomidine, opioids, spinal anesthesia, opioid consumption, and syringe
- Inclusion criteria: Studies published after 2019, RCTs, published in English, dexmedetomidine as the treatment, and opioid consumption as the primary outcome.
- Exclusion criteria: Meta-analysis and systematic review focus on opioid consumption as the primary outcome, and dexmedetomidine not used in treatment.
- Implementation involved delivering an educational module to CRNAs on the perioperative management of patients receiving Dex during spinal anesthesia aligned with the learning objectives.
- Survey instrument was used to collect pre and post-implementation data on provider understanding of the educational module.

RESULTS

- The evidence search and screening resulted in 7 RCTs. Three studies demonstrated Dex infused at the induction of anesthesia to reduce post-operative and perioperative opioid consumption. Four studies demonstrated Dex would reduce cumulative opioid consumption when administered before induction of anesthesia. One study demonstrated Dex intranasal to impact cumulative opioid consumption.

LIMITATIONS

The literature review was limited by the small number of studies reviewed (7) as there is no wide scholarship on the subject. Moreover, the reviewed studies exhibited a lack of heterogeneity and limited a standardized approach to Dex use, producing a generalized limitation. Regarding implementation, recruitment had a low response rate (36%) contributing to a small sample size (n=30). It was only administratively online, which contributed to the small sample.

PRE & POST DEMOGRAPHICS

The demographics are similar in the pre and post-test as there were no attrition among participants. They are summarized in the table shown:

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Pre (%)</th>
<th>Post (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32%</td>
<td>32%</td>
</tr>
<tr>
<td>Female</td>
<td>68%</td>
<td>68%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>37%</td>
<td>37%</td>
</tr>
<tr>
<td>40-55</td>
<td>22%</td>
<td>22%</td>
</tr>
<tr>
<td>&gt;55</td>
<td>41%</td>
<td>41%</td>
</tr>
</tbody>
</table>

REFERENCES

Available upon request. Contact gil@fiu.edu

*This project was IRB exempt.