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Intraoperative Ketamine Administration: An Adjunctive Therapy That Reduces Postoperative Pain for Patients Undergoing Spinal Surgery

Brittany Pierce

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INTRAOPERATIVE KETAMINE ADMINISTRATION: AN ADJUNCTIVE
THERAPY THAT REDUCES POSTOPERATIVE PAIN FOR PATIENTS
UNDERGOING SPINAL SURGERY

by

Brittany Pierce

A Doctoral Project
Submitted to the Graduate School,
the College of Nursing and Health Professions
and the School of Leadership and Advanced Nursing Practice
at The University of Southern Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Doctor of Nursing Practice

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ABSTRACT

In 2017, the United States Department of Health and Human Services declared that the country was experiencing an opioid crisis (U.S. Department of Health and Human Services, 2018). As a result of this phenomenon, healthcare providers are examining how they are managing pain and researching new avenues for the treatment of pain. Anesthesia providers are in a unique position to help reduce postoperative pain and ultimately the development of chronic pain. This doctoral project was conducted in order to write an evidence-based policy that directs and educates anesthesia providers in the administration of intraoperative ketamine to reduce postoperative pain in patients undergoing spinal surgery. A review of the evidence and collaboration with a physician anesthesiologist contributed to the creation of the policy. A presentation of the evidence and policy was given to a panel of experts. The policy was evaluated using a survey provided to the experts. The feedback provided by the panel of experts revealed that the policy provided the information needed to inform the anesthesia providers about the current best practice regarding intraoperative ketamine administration for reducing postoperative pain. The panel also agreed that the information provided changed their practice in regard to adding ketamine as an adjunct therapy. An executive summary was completed after reviewing the feedback provided by the panel of experts and presented to the key participating members.

ACKNOWLEDGMENTS

First, I would like to sincerely thank my Committee Chair, Dr. Michong Rayborn, for her tireless support and encouragement throughout this process. I could not have succeeded in this endeavor without her guidance. I also wish to thank my Committee Members, Drs. Mary Jane Collins and Bonnie Harbaugh, for their feedback. Your points of view gave this project the depth that was needed. Finally, I would like to extend my gratitude to Dr. Edmund Bagingito for taking the time to collaborate with me. The time and resources you provided were very valuable to the development of this project.

DEDICATION

I would like to dedicate this project directly to my paternal grandmother, Barbara Mills Pierce. May she rest in peace. She taught me that the only obstacle I have to overcome is myself, and as long as I believe I can achieve something I will. I also wish to dedicate this project to my parents, Bradley and Tamra Pierce. Their encouragement gave me the strength to continue on my path to success and complete this project. Lastly, I would like to dedicate this project to the Society for Opioid Free Anesthesia (SOFA) for providing the inspiration for the development of my DNP project.

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LIST OF ABBREVIATIONS

AANA – American Association of Nurse Anesthetists

ASA – American Society of Anesthesiologists

APS – American Pain Society

CDC – Center for Disease Control and Prevention

CRNA – Certified Registered Nurse Anesthetist

DNP – Doctor of Nursing Practice

HHS – Department of Health and Human Services

SOFA – Society of Opioid Free Anesthesia

NMDA - N-Methyl-D-aspartate

CHAPTER I - INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), the State of Mississippi is among the top 10 in the United States in the number of opioid prescriptions written each year. In 2014, 120 opioid prescriptions were written per 100 Mississippi residents (CDC, 2017). Acute postoperative pain that is poorly controlled within the first three postoperative days is considered to be a trigger for chronic pain, so it is important for anesthesia providers to utilize multimodal pain management strategies in an effort to prevent chronic pain. Spinal surgery patients are at a greater risk for having suboptimal pain control after surgery for two reasons. First, spinal surgery patients are more likely taking opioids for pain management at home due to preexisting chronic back pain (Bajwa & Haldar, 2015). Second, the surgery itself is also known to be very painful due to the extensive incision and tissue retraction (Bajwa & Haldar, 2015). The addition of ketamine into a multimodal pain management plan reduces centralized excitability and decreases opioid tolerance, which effectively decreases postoperative pain. The purpose of this Doctor of Nursing Practice (DNP) project was to create a policy that guides anesthesia providers in the timing, dosage, and exclusion criteria for administration of intraoperative ketamine.

Background and Significance

Ketamine is an N-Methyl-D-aspartate (NMDA) noncompetitive antagonist that directly affects the central nervous system by preventing sensitization of the nociceptive pathway (Bajwa & Haldar, 2015). In essence, ketamine's mechanism of action can prevent the severe pain expected from surgery as well as the development of chronic pain that arises from central sensitization and hyperalgesia (Gao, Rejaei, & Liu, 2016). As an

NMDA receptor antagonist, ketamine also reduces previous opioid tolerance, which decreases the amount of narcotics the patient requires to achieve the same level of pain control (Bajwa & Haldar, 2015). The American Pain Society Practice Guideline for the Management of Acute Postoperative Pain (Chou et al., 2016) suggested the use of intraoperative ketamine as part of a multimodal pain management plan which is specifically useful in painful surgical procedures as well as for those patients who have opioid tolerance. In order to achieve the best results, timing and dosage of intraoperative ketamine are essential. A bolus dose of ketamine between induction and skin incision followed by a low dose maintenance infusion to be stopped upon wound closure provide the most optimal effect (Chou et al., 2016).

Spinal surgeries were recently named in the top six most painful surgical procedures; therefore, creating a high quality, multimodal pain management plan is essential for improving patient care (Bajwa & Haldar, 2015). Unlike other orthopedic procedures, spinal surgery patients cannot benefit from the use of neuraxial or regional anesthesia to reduce postoperative pain. Patients who undergo spinal surgery are already more likely to be experiencing chronic pain and have an increased tolerance to narcotics. Patients with poorly managed postoperative pain have a delay in surgical recovery, hospital readmissions for pain management, and decreased patient satisfaction.

In order to best address the methods by which providers are treating postoperative pain, the American Pain Society (APS) suggested that specific policies, which are focused on safe and evidence-based treatments, should be created (Chou et al., 2016). Clinical policies standardize care amongst patients as well as provide a reliable reference for providers to use within their practice. Pain management strategies should be

procedure-specific because each surgical procedure affects the body in different ways, and procedure-specific pain management would take into account the expectations for recovery after the surgery (Kehlet, Wilkinson, Fischer, & Camu, 2007). The American Society for Anesthesiologists (ASA) recommends anesthesia providers develop institutional policies and protocols to standardize care, improve patient outcomes, and reduce anesthesia care gaps (ASA Task Force on Acute Pain Management, 2012). Currently, the use of intraoperative ketamine varies from provider to provider. A policy will establish an institutionally preferred dose range, administration time, and exclusion criteria.

Problem Statement

According to the CDC (2017), the number of opioid prescriptions written in 2013 was equal to the number of American adults. The opioid problem is not just invading metropolitan areas of the country, but some of the most rural states (e.g., Mississippi) are the most affected. Prescription opioid abuse is tied to badly managed postoperative pain and the development of chronic pain. Anesthesia providers are in a unique position to help decrease the intensity of postoperative pain, adequately manage acute pain, and possibly prevent the development of chronic pain all by using a multimodal pain management strategy. Intraoperative ketamine has been shown to be an effective puzzle piece within multimodal pain management. As it currently stands, ketamine administration varies from provider to provider. The development of an intraoperative ketamine policy will standardize ketamine administration among providers and supply a useful resource for providers to use in the development of their anesthesia plan.

Purpose of the Project

The purpose of this project was to create an intraoperative ketamine infusion policy using evidence-based practice and best practice recommendations to reduce postoperative pain in spinal surgery patients at an orthopedic specialty hospital in southeast Mississippi. Ketamine was first introduced to the market in the 1970s, but using low dose intraoperative ketamine as an adjunctive therapy for pain management is still a relatively new concept that is gaining favor among anesthesia providers nationwide (Bell, Dahl, Moore, & Kalso, 2015). A policy provided a straightforward reference for dosage and timing of administration as well as patient exclusion criteria. A policy, along with anesthesia provider education, should increase the provider receptiveness to adding intraoperative ketamine for spinal surgery patients to their pain management plan.

Needs Assessment

A needs assessment was performed at a south Mississippi orthopedic surgery center in the fall of 2017. A gap in knowledge among providers was found about dosing and timing recommendations for intraoperative ketamine during spinal surgery. After surveying, it was evident that anesthesia providers were also unaware of the benefits that low-dose ketamine provides to spinal surgery patients and felt that it was a hassle to prepare. A clear and concise policy that details the timing, dosage, and type of administration may well increase the consistency with which intraoperative ketamine is administered as well as increase the likelihood of administration.

Conceptual Framework

The conceptual framework of this study was Bardach's eightfold model for policy analysis. Bardach (2012) stated that policy analysis requires as much intuition as science

and, therefore, is an art which merely requires straightforward steps as a guide, which is how he developed his eight-step model. The eight steps are as follows: define the problem, assemble evidence, construct alternatives, select criteria, project outcomes, confront the trade-offs, evaluate, and present the findings. According to Bardach (2012), the process starts by defining your problem and inevitably ends by presenting the results. The other steps do not necessarily need to happen in the exact order he presented them. The benefit to Bardach's model is flexibility. The user can apply Bardach's model to his or her own plan and easily make changes to better fit the problem.

Steps 1 through 4 were the foundation for the current proposed policy. First, the problem must be defined. The problem is the lack of knowledge, understanding, and consistency behind the administration of ketamine intraoperatively to reduce pain for spinal surgery patients in the postoperative period. The next step is to gather and assemble evidence to educate and construct a policy that will guide anesthesia providers in the administration of ketamine for spinal surgery patients. The policy will detail patient selection and exclusion criteria. Steps 5 through 8 will define the outcomes, assess for barriers, and evaluate the policy. The ultimate outcome for this project was to create a policy for the administration of intraoperative ketamine for spinal surgery patients. Before the policy can be evaluated, barriers must be addressed that will define the practice of the anesthesia providers. Barriers may include the perception of intrusion in the anesthesia provider's personal practice, a provider's disbelief in the effectiveness of ketamine for postoperative pain relief, and the current national shortage of the ketamine supply. The initial policy was presented to the anesthesia providers who were the most affected by the policy for their evaluation and input. A survey was provided for

feedback on the policy. After reviewing the feedback within the surveys that were submitted, a finalized policy was created. Finally, the policy was presented to the stakeholders at the orthopedic specialty hospital for consideration as best practice for intraoperative ketamine.

DNP Essentials

The American Association of the Colleges of Nursing outlined eight essential elements for completion of a DNP (DNP Essentials Task Force, 2006). This project will meet each essential; each essential is listed as follows:

- *Essential I, Scientific Underpinnings for Practice* (Chism, 2015).

A review of current literature for practice recommendations associated with intraoperative ketamine dosage and timing satisfied Essential I. The informational data gathered included practice recommendations and best practice guidelines that provide recommendations for intraoperative ketamine administration.

- *Essential II, Organizational and Systems Leadership for Quality Improvement and Systems Thinking* (Chism, 2015). Essential II was met by creating a policy to anesthesia providers who will standardize intraoperative ketamine administration for spinal surgery, which will ultimately improve the quality of anesthetic provided by the anesthesia staff. Before implementing the policy, anesthesia provider education shed light on the need and importance of the policy.

- *Essential III. Clinical Scholarship and Analytical Methods for Evidence-Based Practice* (Chism, 2015) A literature review included gathering practice guidelines supported by evidence which included recommendations for intraoperative ketamine

- infusions. Analyzing the best practice guidelines and comparing their evidence to the evidence that the current literature review revealed met Essential III.
- *Essential IV. Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care* (Chism, 2015) The project intervention was created with information technology, and the project intervention was created with information technology. Patient care technology was utilized as part of the policy. An intraoperative ketamine infusion requires an intravenous (IV) infusion pump for accurate administration.
 - *Essential V. Health Care Policy for Advocacy in Health Care* (Chism, 2015). Multimodal pain management was created to address the healthcare problem that was created by using just one method for pain management. The ultimate inspiration for this project was to provide an effective alternative to manage pain specifically to a population that usually has difficulty achieving adequate pain relief. Essential V was met with the creation of a policy with the intention of improving health care.
 - *Essential VI. Interprofessional Collaboration for Improving Patient and Population Health Outcomes* (Chism, 2015). Collaboration with the anesthesia providers, stakeholders, and nurse anesthesia program faculty met Essential VI.
 - *Essential VII. Clinical Prevention and Population Health for Improving the Nation's Health* (Chism, 2015). A secondary goal of the policy created was to reduce postoperative pain and the amount of narcotics required to treat pain during a patient's recovery from spinal surgery. By educating providers about the benefits of intraoperative ketamine, this DNP project may foster the understanding that anesthesia can benefit a patient far outside of the operating room and past the end of

- anesthesia time. Essential VII was met by educating providers about the potential long-term benefits a patient can receive by using intraoperative ketamine.
- *Essential VIII. Advanced Nursing Practice* (Chism, 2015). Advanced practice nurses were expected to analyze current best practice and implement those guidelines in their practice. Analyzing best practice guidelines and educating current providers about the recommendations specific to their practice met Essential VIII.

Review of Evidence

An evidence search was performed to explore the available evidence demonstrating that a perioperative dose of ketamine decreases pain in the postoperative period and how the researchers were able to prove ketamine's effectiveness. Several databases, including CINAHL with Full Text, Medline, PubMed, Cochrane, and Google Scholar, were searched for relevant articles. The following key search terms were utilized: ketamine, perioperative, spine surgery, acute pain, and opioid sparing. An initial search with limitations to full text only and publication dates between 2001 and 2018 returned 98 articles after duplications were removed. Upon further review of all databases accessed, a total of eight articles were selected because they were strongly applicable to this project. An evidence matrix is included with information from each of the included articles (see Appendix A).

Pain Management and Spinal Surgery

“Due to the extensive damage of soft tissues and muscles surrounding the vertebral column” (Garg et al., 2016, p. 1), patients who undergo spinal surgery can experience intense pain postoperatively. The mismanagement of acute postoperative pain in spinal surgery patients leads to poor outcomes, such as a “delayed recovery, poor

rehabilitation, and progression to chronic pain” (Garg et al., 2016, p. 1). Therefore, it is imperative for anesthesia providers to be mindful of the increased risk for spinal surgery patients to experience inadequate pain management and to be aggressive in treating the known causes of pain to prevent poor surgical outcomes. According to Garg et al. (2016), low-dose ketamine provides analgesia with limited side effects due to the inhibition of the NMDA receptor and also is shown to occupy opiate receptors in the brain and spinal cord. The centrally acting analgesia ketamine provided lends itself to be especially effective in spinal surgery cases.

A study comparing the effects of ketamine and dexmedetomidine on postoperative pain in spinal surgery found that the patients who received a bolus dose of ketamine at induction (0.25 mg/kg) followed by an infusion (0.25 mg/kg/hr) reported the lowest pain scores postoperatively (Garg et al., 2016). Garg et al. (2016) also reported that the patients who received ketamine intraoperatively had a 74% reduction in opioid requirements after surgery. Loftus et al. (2010) studied the effect of using low-dose ketamine intraoperatively to reduce opioid requirements after spinal surgery in patients with chronic back pain. The patients received a bolus dose of ketamine at induction (0.5 mg/kg) followed by an infusion (10 mcg/kg/min) initiated before skin incision and maintained until wound closure (Loftus et al., 2010). The study’s results showed a decrease in intraoperative opioid requirements by 24%, a 37% decrease in opioid consumption up to 48 hours postoperatively, and a 26% decrease in pain intensity postoperatively that lasted up to a 6-week follow-up visit (Loftus et al., 2010). In July 2018, a joint effort by the American Society of Regional Anesthesia, American Academy of Pain Medicine, and the American Society of Anesthesiologists released the consensus

guidelines for using ketamine as an adjunctive therapy to treat pain (Schwenk et al., 2018). According to Schwenk et al. (2018), ketamine is most useful in reducing acute postoperative pain in patients who are undergoing painful surgery, such as spinal surgeries, as well as for patients who are opioid-tolerant.

Low Dose Ketamine and Pain

When ketamine was released into the market in 1970, it was believed to quickly replace other induction agents because it provided amnesia, analgesia, and anesthesia while maintaining a patient's hemodynamic stability (Gao et al., 2016). After a few years on the market, patients experienced the severe neurological symptoms, such as hallucinations, more frequently than initially expected when given the full anesthetic dose of ketamine (Gao et al., 2016). The anesthetic dose or induction dose of ketamine is 1-2 mg/kg (Gao et al., 2016). The increase in the incidence of hallucinations and other neurological symptoms make providers wary of using full-dose ketamine unless the patient's hemodynamically stability is in question. Within the last decade, alternative uses for ketamine have surfaced. Sub-anesthetic doses of ketamine are being used to treat chronic pain, acute pain, mood disorders, and post-traumatic stress disorder without the side effects seen in a full-anesthetic dose (Gao et al., 2016).

Ketamine attenuates pain by “decreasing central excitability, decreasing acute postoperative opiate tolerance, and modulation of opiate receptors” (Loftus et al., 2010., p. 639). A low-dose ketamine infusion, when administered at 10 mcg/kg/min intraoperatively, has been shown to reduce the amount of opioids required after surgery to manage pain (Loftus et al., 2010.). The opioid-sparing effect of ketamine is beneficial because by reducing the need for opioids there is also a reduction in the opioid-related

side effects, such as respiratory depression, nausea and vomiting, and hyperalgesia (Garg et al., 2016). Adjunctive doses of ketamine intraoperative are helpful to patients who are most at risk for developing opioid-related respiratory depression, such as patients with obstructive sleep apnea (Schwenk et al., 2018).

Recommendations for Multimodal Pain Management

According to a United States (U.S.) survey to discover the incidence in postoperative pain in 2014, nearly half of postoperative surgical patients reported undermanaged pain during their recovery, and 75% of postoperative surgical patients rated their pain as high or severe (Gan et al., 2014). Unmanaged acute, postoperative pain can lead to the development of chronic pain. The APS released an updated guideline for the management of postoperative pain. APS “strongly recommends the use the multimodal analgesia, using a variety of medication and technique to have a more synergistic, effective approach to pain relief than single-modality intervention” (Chou et al., 2016, p. 254).” Despite evidence that a multimodal pain management reduces acute postoperative pain, opioids are still the main method of pain management in the operating room (White & Kehlet, 2010). Anesthesia providers need to be more mindful of how they are treating postoperative pain now more than ever because they can either be the cause of a problem or the solution to it. White and Kehlet (2010) suggested the best way to reduce postoperative pain is to implement best practice recommendations for multimodal pain management techniques supplemented with opioids if needed. Ketamine, among other therapies, is recommended.

Summary

Chapter 1 included the background, significance, project purpose, problem statement, needs assessment, and DNP Essentials. This chapter also included a review of current evidence that supported the development of this project. Chapter II discusses the methods utilized in the completion of this DNP project.

CHAPTER II - METHODOLOGY

Target Outcome

The objective of this doctoral project was to create a policy on intraoperative ketamine administration for spinal surgery for a healthcare facility in southeastern Mississippi that specializes in orthopedic surgery. The policy was created in collaboration with a physician anesthesiologist, who chiefly oversees anesthesia care at the facility, followed by a thorough review of the evidence and current practice guidelines. A copy of the policy is provided in Appendix B. The policy included specific dosing and timing of administration guidelines to facilitate the use of intraoperative ketamine among anesthesia providers within the facility. An executive summary of the doctoral project, as well as the initial draft of the policy, were presented to a panel of experts (e.g., the physician anesthesiologist, CRNAs, hospital administrators, and pharmacists). The panel of experts was chosen to provide feedback on each aspect of the policy from the structure to the content. The anesthesia providers and pharmacists selected were able to comment on the content of the policy, and the hospital administrators were able to give feedback on the structure of the policy itself. Once the panel of experts had reviewed the executive summary as well as the policy, they were provided feedback via a survey. A copy of the survey is provided in Appendix C. The survey was used to gather evidence on how to improve the policy for future implementation at the facility. The short-term goal of this doctoral project was to establish a policy based on evidence-based practice for the administration of intraoperative ketamine. The long-term goal of this doctoral project was to provide a

reference for anesthesia providers to elevate their care to standardized evidence-based practice.

Population

For this doctoral project, the main focused population included patients who were undergoing spinal surgery at the specialty orthopedic facility in southeastern Mississippi unless they met exclusion criteria. The exclusion criteria for this project included patients with a known intolerance or allergy to ketamine, over 70 years old, an increased intraocular pressure (IOP), uncontrolled hypertension (HTN), increased intracranial pressure (ICP), pregnancy, and history for seizure disorder. Prior to implementation of this study, approval was obtained from The University of Southern Mississippi's Institutional Review Board (Protocol # 18070602) (see Appendix D).

Design

A policy was created after a thorough review of the evidence and best practice guidelines. The DNP student collaborated with a physician anesthesiologist who wished to develop a policy for his facility. The policy delineated the correct dosage as well as the timing of administration of intraoperative ketamine supported by the evidence. The policy provided administration guidelines, such as patient exclusion criteria to promote safe administration. In order to promote the use of the policy, a short explanation of the evidence that supported the policy's guidelines was included in the form of an executive summary. The executive summary is included in Appendix E. A panel of experts, including pharmacists, CRNAs, and the physician anesthesiologist was presented with the initial policy. A survey was provided to give feedback to the DNP student. The survey essentially asked the following questions:

1. Did this project presentation provide you with information regarding intraoperative ketamine administration that reduces postoperative pain for patients undergoing spinal surgery?
2. Did the information provided in this presentation encourage you to reconsider your current anesthesia practice?
3. Would you consider changing your practice based on the information presented if given the option of utilizing ketamine as an adjunctive therapy?

The last question asked for comments and suggestions regarding the policy. The DNP student collected data via surveys. After analyzing data provided by the surveys, the DNP student evaluated the changes against current best practice and information gathered during the literature review. The findings were included in the executive summary. Once data were evaluated, the DNP student altered the policy per the recommendations provided through the surveys and evidence. Once the final policy was approved by the collaborating physician anesthesiologist, the DNP student presented the finalized policy to the panel of experts and DNP committee members to evaluate the project by the DNP essentials and validate the project as doctorate level work. During the final presentation, the DNP student provided recommendations and an executive summary to the orthopedic specialty facility based on data, evidence review, the facility's anesthesia providers, and a panel of experts' opinions.

Limitations

In order to effect positive change, it was important to understand the challenges that surfaced during the process. The first barrier realized was institutional culture. If the institution was unwilling to allow a change, it would immediately halt progress. By

collaborating with a physician anesthesiologist who is willing to support this doctoral project, the institution was more willing to allow this change. A future barrier was the implementation of the policy due to provider culture. The providers needed to accept change and be willing to change their practice in order for this project's long-term goals to be fulfilled. This barrier was addressed during the creation of the policy. The feedback provided by the experts led to creation of a policy appropriate and user-friendly.

Summary

Chapter II detailed the target outcome of this DNP project. Also included in Chapter II were the population of interest, design, and limitations. The results of the project are outlined in Chapter III.

CHAPTER III - RESULTS

A combination of a thorough literature review of current best practice recommendations and a 5-question survey that provided feedback from a panel of experts about the initial policy was employed for this DNP project. Those individuals on the panel of experts included a hospital administrator, pharmacist, chief physician anesthesiologist, and 9 CRNAs who routinely provide care for patients undergoing spinal surgery at the orthopedic specialty facility. The panel was constructed of members who possess the most knowledge and influence over the care of patients undergoing spinal surgery. The panel members also were most affected by policy implementation. Therefore, the experts chosen provided influential feedback on the policy structure and included information within the policy. Members of the panel were presented with the best practice information regarding the timing, dosage, and administration of intraoperative ketamine and were instructed to review the policy afterward. Once they had reviewed the policy, the panel asked for feedback using the 5-question survey. Each participant agreed that the policy provided them with information on how intraoperative ketamine administration reduces postoperative pain for spinal surgery patients. Only one participant answered, "No," when asked if the information provided encouraged them to reconsider changing their current practice. Within the comments section of the survey, it was revealed that this participant already uses ketamine intraoperatively for specific spinal surgery cases; therefore, the presentation reaffirmed this participant's practice. Finally, each participant agreed that based on the information provided they would change their practice if given the opportunity of utilizing ketamine as an adjunctive therapy.

The survey results revealed that the information within the policy adequately explained the evidence for the use of intraoperative ketamine to reduce postoperative pain in spinal surgery patients as well as the evidence-based method for administration. Participants also revealed a willingness to change their practice to incorporate intraoperative ketamine administration which tackles one of the proposed future barriers to the implementation of the policy. In the comments and suggestions section of the survey, one participant recommended a way to combat the ketamine shortage was involving the perioperative pharmacists that manage the distribution of medication trays, antibiotics, and infusions. The pharmacist can separate a vial of ketamine into individual infusions and bolus doses, which decreases waste and cost of the adjunctive therapy. Once the intraoperative ketamine policy was implemented, including the change suggested above, the practices in this facility improved.

Summary

In Chapter III, the results from the survey of the panel of experts were reviewed and analyzed. The data revealed that the policy created for this DNP project met the target outcomes outlined in Chapter II. Chapter IV will present the findings of this project.

CHAPTER IV – CONCLUSION

Summary

Multimodal pain management has been hailed as the gold standard by the ASA (2012), yet many providers rely heavily on a single treatment modality to treat pain. The purpose of this DNP project was to create a policy which outlines the best practice for intraoperative ketamine administration for spinal surgery patients in order to facilitate the use of ketamine as an adjunctive treatment. By providing all the information required to include ketamine into the anesthesia plan, the policy made integrating the adjunctive therapy easier for the providers. The data revealed that the information provided within the policy increased the willingness to incorporate ketamine into their anesthesia practice. This information may lead the way for future policies that enhance postoperative outcomes.

Interpretation

The evidence is clear that the anesthetic provided to spinal surgery patients has an effect on patients well into the postoperative period. Policies such as the one created for this DNP project give anesthesia providers the tools necessary for developing a multimodal anesthetic that ensures the best recovery possible for each patient. In order to successfully implement a policy, the institutional culture must be amenable to change. Based on the information gathered by this project, once an institution is ready to incorporate changes into their practice, all that is required is a policy which provides evidence-based practice for the intervention.

Implications for Future Practice

Once the intraoperative ketamine policy was implemented, a retrospective analysis comparing patients' pain scores as well as the opioid consumption postoperatively was performed. The retrospective analysis was performed after using intraoperative ketamine policy for 6 months in order to gather adequate evidence to compare the two data sets. This doctoral student believes that having the patient data that proves the effectiveness of intraoperative ketamine for the population of south Mississippi will lead to the creation of similar policies in other facilities in the area as well as reinforce the evidence that already exists within the literature. Intraoperative ketamine administration as an adjunct was shown to be effective in reducing postoperative pain for several types of procedures. The doctoral student recommends that the policy should be extended to include other procedures similar to spinal surgeries which limit the use of regional anesthesia for postoperative pain control.

Conclusions

Despite the opioid epidemic that is affecting the nation, patients are still experiencing inadequate pain control after surgery. Improperly managed pain postoperatively increases the length of hospital stay and can lead to the development of chronic pain. Anesthesia providers are uniquely placed to preemptively treat the expected pain from surgery and reduce postoperative pain by using a multimodal pain management technique that includes intraoperative ketamine. The objective of this DNP project was to create a policy, in collaboration with a physician anesthesiologist and a thorough review of the current evidence, that details the timing, dosage, and administration of intraoperative ketamine for the purpose of reducing postoperative pain.

The participants agreed once presented with the policy that they would change their practice to include intraoperative ketamine, and the policy that was created adequately provides them with the information required to use the technique.

APPENDIX A – LITERATURE MATRIX

Author/Year/Title	Level/Grade	Sample/Data Collection	Finding	Recommendations
Bajwa, & Haldar, 2015 Pain management following spinal surgeries: An appraisal of the available options”	Level II Literature review	N/A	Spinal surgery is in the top six most painful procedures for patients. Aggressive pain control improves the success of the surgery and the outcomes for the patients. Experts suggest that multimodal therapy is the best way to manage pain in patients undergoing spinal surgery.	Effective pain control is shown to improve the outcomes in spinal surgery patients. Using multimodal treatments to attack pain in various pathways versus just one is the best method of treatment and provides a better outcome for the patients.
Chou, Gordon, de Leon-Casasola, Rosenberg, Bickler, Brennan, et al. 2016 “Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists’ Committee on Regional Anesthesia, Executive Committee, and Administrative Council”	Level I Systemic Review of Evidence		Facilities in which surgery is performed should have an organizational structure to oversee the development, implementation, and evaluation of policies and practices to assure safe, evidence-based, and effective post-operative pain and the development of chronic pain.	The Panel recommends that facilities in which surgery is performed have an organizational structure in place to develop and refine policies and processes for safe and effective delivery of postoperative pain control. The Panel recommends that clinicians consider ketamine as a component of multimodal analgesia in adults.

Author/Year/Title	Level/Grade	Sample/Data Collection	Finding	Recommendations
Garg, Panda, Gandhi, Bhagat, Batra, Grover, & Chhabra, 2016 “Comparison of Small Dose Ketamine and Dexmedetomidine Infusion for Postoperative Analgesia in Spine Surgery—A Prospective Randomized Double-Blind Placebo-Controlled Study”	Level II Double-blind placebo controlled study	Mean pain-free periods in the ketamine group (860 min) and the dexmedetomidine group (580 min) were longer than in the saline group (265 min) ($p < 0.002$) during the observation period of 48 hours. There was a significant decrease in the rescue analgesic requirements in both ketamine and dexmedetomidine group ($p < .05$) (cumulative morphine requirement at 24h—Group C (15.64 ± 9.31 mg, group D 6.89 ± 5.88 mg, group K 2.45 ± 2.06 mg; at 48 h—group C 21.09 ± 12.88 mg, group D 7.98 ± 7.72 mg, group K 2.59 ± 1.97 mg)	Low-dose ketamine provides good postoperative analgesia with minimal side effects. The group that received intraoperative ketamine scored their pain the lowest but providing they achieved the best pain control. The patients who received ketamine also took the longest to require breakthrough pain treatment.	

Author/Year/Title	Level/Grade	Sample/Data Collection	Finding	Recommendations
Loftus, Sengupta, Abdu, Beach, Clark, Brown, & Yeager, 2010 “Does Intraoperative Ketamine Reduce Acute Postoperative Pain in Opiate-Dependent Chronic Back Pain Patients Undergoing Spinal Surgery? A Prospective Randomized Placebo-Controlled Double-Blind Study”	Level II	In the treatment group, patients received 37% fewer opioids within 48 hours after surgery than patients who received the placebo, 30% fewer opioids within the first 24 hours postoperatively, and showed a 26% reduction in pain intensity.	Intraoperative ketamine reduces opiate consumption in the 48-h postoperative period in opiate-dependent patients with chronic pain. Ketamine may also reduce opioid consumption and pain intensity throughout the postoperative period in this patient population. This benefit is without an increase in side effects.	Intraoperative ketamine administration is beneficial for both opiate-naïve and opioid-tolerant patients for reducing postoperative pain after spinal surgery.
Practice Guidelines for Acute Pain Management in the Perioperative Setting: An Updated Report by the American Society of Anesthesiologists Task Force on Acute Pain Management	Level I Systematic Review of Evidence			The consultants and ASA members strongly agree that anesthesiologists offering perioperative analgesia services should provide, in collaboration with other healthcare professionals as appropriate, ongoing education and training of hospital personnel regarding the effective and safe use of the available treatment options within the institution. They should participate in developing standardized institutional policies and procedures. Whenever possible, anesthesiologists should use multimodal pain management therapy.

Author/Year/Title	Level/Grade	Sample/Data Collection	Finding	Recommendations
<p>Schwenk, Viscusi, Buvanendran, Hurley, Wasan, & Narouze, et al. 2018 “Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists.”</p>			<p>Findings support the use of a bolus dose and infusion for perioperative pain management with the benefit of reducing postoperative pain and opioid consumption. The published evidence demonstrates a clear short-term, opioid-sparing effect when ketamine is used in subanesthetic doses as a perioperative adjunct.</p>	<p>Evidence supports the use of Ketamine for acute pain in a variety of contexts, including as a stand-alone treatment, as an adjunct to opioids, and, to a lesser extent, as an intranasal formulation. Contraindications for acute pain are similar to those for chronic pain, partly based on the observation that the dosage ranges are similar.</p>

APPENDIX B – CLINICAL POLICY

Clinical Policy

PERIOPERATIVE KETAMINE ADMINISTRATION FOR SPINE SURGERY

1. Policy Statement

This document details guidelines for the administration of Ketamine in the perioperative period for patients undergoing spine surgery. The addition of Ketamine into a multi-modal pain management regimen will provide an effective decrease in postoperative pain.

2. Background

Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, has been shown to reduce pain by decreasing central excitability and opioid tolerance. The reduction in pain is demonstrated by a reduced amount of opioids consumed by the patient during their recovery. Ketamine is considered a dissociative anesthetic and may produce hallucinations. A pre-operative 1-2 mg dose of a benzodiazepine, Midazolam, exponentially decreases the risk of the dissociative effects of Ketamine.

3. Responsibilities

CRNA
MD/DO
SRNA

4. Plan of Care

Patient Selection

- Patients undergoing spinal surgery at the [REDACTED] of Forrest Health, unless they meet any of the criteria for exclusion.

Exclusion Criteria

- Known Intolerance or Allergy to Ketamine
- Increased Intraocular Pressure (IOP)
- Uncontrolled Hypertension (HTN)
- Increased Intracranial Pressure (ICP)
- Pregnancy
- History of a Seizure Disorder

Preparation

- Midazolam 1-2 mg pre-operative dose
- Ketamine 0.5 mg/kg for a bolus dose at induction
- Infusion: mix 250 mg Ketamine in a 250 mL bag of 0.9% Normal Saline, making the infusion concentration 1 mg/mL. Set up and program the IV pump for 10 mcg/kg/min administration.

Administration

Before bringing the patient back for their surgery, administer 1-2 mg Midazolam.

In addition to the patient-specific anesthetic plan for induction, add a bolus dose of Ketamine 0.5 mg/kg. Maintain the patient on the volatile inhalation agent or intravenous agent of choice, in accordance with surgical requirements and patient's needs. Before the surgical incision is made, connect the Ketamine infusion tubing onto a port on the main IV fluid line. Start the Ketamine infusion at 10 mcg/kg/min. At the time of wound closure, turn off the Ketamine infusion.

5. References

- Gorlin, A. W., Rosenfeld, D. M., & Ramakrishna, H. (2016). Intravenous sub-anesthetic ketamine for perioperative analgesia. *Journal of Anaesthesiology, Clinical Pharmacology*, 32(2), 160–167. <http://doi.org/10.4103/0970-9185.182085>
- Loftus, R. W., Sengupta, D. K., Abdu, W. A., Beach, M. L., Clark, J. A., Brown, J. R., & Yeager, M. P. (2010). Does intraoperative ketamine reduce acute postoperative pain in opiate-dependent chronic back pain patients undergoing spinal surgery? A prospective randomized placebo-controlled double-blind study. *Spine Journal*, 10(9). doi:10.1016/j.spinee.2010.07.012
- Garg, N., Panda, N. B., Gandhi, K. A., Bhagat, H., Batra, Y. K., Grover, V. K., & Chhabra, R. (2016). Comparison of small dose ketamine and dexmedetomidine infusion for postoperative analgesia in spine surgery: A prospective randomized double-blind placebo-controlled study. *Journal of Neurosurgical Anesthesiology*, 28(1), 27-31. doi:10.1097/ana.000000000000193

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04/08/18

Edmund M Bagingito, M.D.
Orthopedic Institute
27 Southern Pointe Parkway
Hattiesburg, MS 39401

Dear IRB Members:

I have read over Brittany Pierce's project proposal for a Doctor of Nursing Practice (DNP) project. I understand that this student is conducting this project as part of their requirements for the Nurse Anesthesia's DNP program at the University of Southern Mississippi, and will have the opportunity to present their findings in other venues.

I understand that the Institutional Review Board for the Use of Human Subject's in Research (IRB) at the University is concerned with protecting the confidentiality, privacy, and well-being of research participants. Further, it is my understanding that the student will additionally be advised in this project by their project chair Dr. Michong Rayborn along and committee members Dr. Bonnie Harbaugh and Dr. Mary Jane Collins, both of whom will have regular contact with this student.

I do not have concerns about the project the student has proposed based on conversations with the student and after reviewing their project proposal. The agency supports this student's plan and approves of the project.

Should you have additional questions or concerns, you may contact me.

Sincerely,


Edmund M Bagingito M.D.

APPENDIX C – EVALUATION TOOL

Participation in this anonymous questionnaire is voluntary. There are no repercussions for nonparticipation. Thank you for your time.

Please answer the following questions with a *Yes* or *No* response.

1. Did this project presentation provide you with information regarding intraoperative ketamine administration that reduces postoperative pain for patients undergoing spinal surgery?
 - a. Yes
 - b. No

2. Did the information provided in this presentation encourage you to reconsider your current anesthesia practice?
 - a. Yes
 - b. No

3. Would you consider changing your practice based on the information presented if given the option of utilizing ketamine as an adjunctive therapy?
 - a. Yes
 - b. No

4. Please provide any comments or suggestions regarding this practice recommendation

APPENDIX D – IRB APPROVAL



INSTITUTIONAL REVIEW BOARD

118 College Drive #5147 | Hattiesburg, MS 39406-0001

Phone: 601.266.5997 | Fax: 601.266.4377 | www.usm.edu/research/institutional.review.board

NOTICE OF COMMITTEE ACTION

The project has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services (45 CFR Part 46), and university guidelines to ensure adherence to the following criteria:

- The risks to subjects are minimized.
- The risks to subjects are reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
- Appropriate additional safeguards have been included to protect vulnerable subjects.
- Any unanticipated, serious, or continuing problems encountered regarding risks to subjects must be reported immediately, but not later than 10 days following the event. This should be reported to the IRB Office via the "Adverse Effect Report Form".
- If approved, the maximum period of approval is limited to twelve months.
Projects that exceed this period must submit an application for renewal or continuation.

PROTOCOL NUMBER: 18070602

PROJECT TITLE: Intraoperative Ketamine Administration: An Adjunctive Therapy that Reduces Postoperative Pain for Patients Undergoing Spinal Surgery

PROJECT TYPE: New Project

RESEARCHER(S): Brittany Pierce

COLLEGE/DIVISION: College of Nursing and Health Professions

DEPARTMENT: School of Leadership and Advanced Nursing Practice

FUNDING AGENCY/SPONSOR: N/A

IRB COMMITTEE ACTION: Exempt Reivew Approval

PERIOD OF APPROVAL: 07/27/2018 to 07/26/2019

Edward L. Goshorn, Ph.D.

Institutional Review Board

APPENDIX E - EXECUTIVE SUMMARY

Despite a shift in focus within the last 20 years towards providing adequate and achievable postoperative pain relief, approximately 70% of patients can still expect to wake up in recovery with moderate to severe pain. The American Pain Society (APS), American Society of Anesthesiologists (ASA), and the American Association of Nurse Anesthetists (AANA) all agree that the best method for postoperative pain management is through a multimodal approach aimed at treating multiple pathways for pain.

Unfortunately, despite the evidence proving that a multimodal pain management approach is most effective, many anesthesia providers are still using strictly opioids as their main method for treating postoperative pain. Postoperative pain carries many risks, such as a decrease in recovery time, increased length of stay in a facility, and the increased likelihood of developing chronic pain. As the nation fights the current opioid epidemic, anesthesia providers have an opportunity to decrease the amount of narcotics that patients require after surgery by using a multimodal technique. Spine surgery is known for being one of the most painful surgeries for patients, and due to the location of incision regional techniques are not beneficial. Using an intraoperative ketamine infusion reduces postoperative pain and is specifically beneficial in the population who receive spine surgery. The majority of spine surgery patients either have chronic back pain and/or take opioids to manage their pain preoperatively. As an N-methyl-D-aspartic acid (NMDA) receptor antagonist, by nature ketamine provides a strong neuropathic pain relief, but at low doses ketamine also reduces pain sensitivity and opioid tolerance. An intraoperative ketamine infusion reduces acute postoperative pain and decreases the amount of opioids required to manage pain after surgery.

In collaboration with a physician anesthesiologist who is currently utilizing intraoperative ketamine during spinal surgery cases, I created a policy to facilitate the increase in usage of intraoperative ketamine for spine surgery. The policy includes correct dosage, the timing of administration, patient exclusion criteria, and administration guidelines. After the policy was completed, I presented it to a panel of experts that included the collaborating physician anesthesiologist, CRNAs, a pharmacist, and a hospital administrator. I provided them with a survey that included questions, such as the following: Did this project presentation provide you with information regarding intraoperative ketamine administration that reduces postoperative pain for patients undergoing spinal surgery? Did the information provided in this presentation encourage you to reconsider your current anesthesia practice? And would you consider changing your practice based on the information presented if given the option of utilizing ketamine as an adjunctive therapy? This doctoral student collected data from their surveys that detailed their expert opinion and analyzed the feedback they provided. I revised my policy using information I gathered from their feedback. Finally, I included the recommendations and the finalized policy based on data, literature review, and a panel of experts to the physician anesthesiologist at the Orthopedic Institute for his use.

The survey results revealed that the policy was effective in providing the information needed to explain the evidence for the use of intraoperative ketamine to reduce postoperative pain in spinal surgery patients. The participants' responses revealed that they were willing to change their practice to include intraoperative ketamine as an adjunctive therapy if the opportunity presents itself. My recommendation is to implement the policy at the facility. Once the policy is initiated, a retroactive analysis

should be performed between the patients who received intraoperative ketamine to those in the past who had not received ketamine for their spinal surgery to compare the amount of opioids required for pain control and patient satisfaction after the procedure. By comparing the amount of opioids required for pain control postoperatively between patients before and after policy implementation, the facility can prove the benefit of intraoperative ketamine for their patient population.

REFERENCES

- American Society of Anesthesiologists Task Force on Acute Pain Management. (2012). Practice guidelines for acute pain management in the perioperative setting. *Anesthesiology*, 116(2), 248-273. doi:10.1097/aln.0b013e31823c1030
- Bajwa, S. J., & Haldar, R. (2015). Pain management following spinal surgeries: An appraisal of the available options. *Journal of Craniovertebral Junction and Spine*, 6(3), 105–110. Retrieved from <http://doi.org/10.4103/0974-8237.161589>
- Bardach, E. (2012). *A practical guide for policy analysis: The eightfold path to more effective problem solving* (4th ed.). Los Angeles, CA: Sage.
- Bell, R., Dahl, J., Moore, R., & Kalso, E. (2015). Perioperative ketamine for acute postoperative pain. *Cochrane Database of Systematic Reviews*, 7. doi:10.1002/14651858.cd004603.pub3
- Centers for Disease Control and Prevention (CDC). (2017). Prescription opioid data / drug overdose / CDC Injury Center. Retrieved from <https://www.cdc.gov/drug-overdose/data/prescribing.html>
- Chism, L. (2015). *The doctor of nursing practice: A guidebook for role development and professional issues* (3rd ed.). Burlington, VT: Jones & Bartlett Learning.
- Chou, R., Gordon, D. B., Leon-Casasola, O. A., Rosenberg, J. M., Bickler, S., Brennan, T., . . . Wu, C. L. (2016). Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *The Journal of Pain*, 17(2), 131-157. doi:10.1016/j.jpain.2015.12.008

- DNP Essentials Task Force. (2006). *The essentials of doctoral education for advanced nursing practice*. Washington, DC: Ebook. Retrieved from <http://www.aacnnursing.org/Portals/42/Publications/DNPEssential.pdf>
- Gan, T. J., Habib, A. S., Miller, T. E., White, W., & Apfelbaum, J. L. (2014). Incidence, patient satisfaction, and perceptions of post-surgical pain: Results from a US national survey. *Current Medical Research and Opinion*, 30(1), 149-160. doi:10.1185/03007995.2013.860019
- Gao, M., Rejaei, D., & Liu, H. (2016). Ketamine use in current clinical practice. *Acta Pharmacologica Sinica*, 37(7), 865-872. Doi:10.1038/aps.2016.5
- Garg, N., Panda, N. B., Gandhi, K. A., Bhagat, H., Batra, Y. K., Grover, V. K., & Chhabra, R. (2016). Comparison of small dose ketamine and dexmedetomidine infusion for postoperative analgesia in spine surgery: A prospective randomized double-blind placebo-controlled study. *Journal of Neurosurgical Anesthesiology*, 28(1), 27-31. doi:10.1097/ana.0000000000000193
- Kehlet, H., Wilkinson, R. C., Fischer, H. B. J., & Camu, F. (2007). *PROSPECT: Evidence-Based, Procedure-Specific Postoperative Pain Management*. doi: <https://doi.org/10.1016/j.bpa.2006.12.001>
- Loftus, R. W., Sengupta, D. K., Abdu, W. A., Beach, M. L., Clark, J. A., Brown, J. R., & Yeager, M. P. (2010). Does intraoperative ketamine reduce acute postoperative pain in opiate-dependent chronic back pain patients undergoing spinal surgery? A prospective randomized placebo-controlled double-blind study. *Spine Journal*, 10(9). doi:10.1016/j.spinee.2010.07.012

- Schwenk, E. S., Viscusi, E. R., Buvanendran, A., Hurley, R. W., Wasan, A. D., Narouze, S., . . . Cohen, S. P. (2018). Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. *Regional Anesthesia and Pain Medicine*, 43(5), 1. doi:10.1097/aap.0000000000000806
- Staneva, M., Dobbs, T., Pearson, M., Preacely, N., & Byers, P. (2017, May 11). *The Mississippi opioid epidemic: Data Brief*. Jackson, MS: Mississippi State Department of Health.
- U.S. Department of Health and Human Services. (2018). *What is the U.S. opioid epidemic?*. Retrieved from <https://www.hhs.gov/opioids/about-the-epidemic/index.html>
- White, P., & Kehlet, H. (2010). Improving postoperative pain management: What are the unresolved issues? *Anesthesiology*, 112, 220-225.