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In the Postoperative Cardiothoracic Surgical Patient Being Mechanically Ventilated, is There a Difference in Outcomes When Comparing Sedation with Dexmedetomidine Versus Propofol?

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IN THE POSTOPERATIVE CARDIOTHORACIC SURGICAL PATIENT BEING MECHANICALLY VENTILATED, IS THERE A DIFFERENCE IN OUTCOMES WHEN COMPARING SEDATION WITH DEXMEDETOMIDINE VERSUS PROPOFOL?

by

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ABSTRACT

IN THE POSTOPERATIVE CARDIOTHORACIC SURGICAL PATIENT BEING MECHANICALLY VENTILATED, IS THERE A DIFFERENCE IN OUTCOMES WHEN COMPARING SEDATION WITH DEXMEDETOMIDINE VERSUS PROPOFOL?

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Patients undergoing a cardiothoracic operation typically require mechanical ventilation in the postoperative phase. Each year approximately 395,000 of these operations are performed in the United States alone. As many as 10% of these patients require reoperation within the first few hours of recovery due to complications (Barash & Cullen, 2013). This comprehensive review of the literature was performed to determine whether postoperative sedation with dexmedetomidine leads to better patient outcomes than sedation with propofol. Inclusion criteria included publications written in the English language, articles available in full text, articles written within the last 10 years, and publications with a focus on a population over the age of 18. Exclusion criteria included articles not written in the English language, articles not available in full text, articles not from peer-reviewed journals, and articles focused on pediatric populations. A comprehensive review of the literature was performed and the results from the included studies were analyzed regarding patient outcomes in the postoperative cardiothoracic surgery patient being mechanically ventilated. The results of these studies were compiled and disseminated via a practice change proposal.

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I would like to take this opportunity to thank my committee chair Dr. Marjorie Geisz-Everson, and my other committee members, Dr. Michong Rayborn and Dr. Melanie Gilmore. Without their endless support and guidance this capstone project would not have been possible.

DEDICATION

First and foremost, I would like to thank God for allowing me to fulfill my dream of obtaining my Doctorate degree. I would also like to thank my wonderful wife Jennifer, my amazing son Aiden and my beautiful daughter Hadley; they have sacrificed so much during these past few years and without them none of this would have been possible. Last but certainly not least I would like to thank my parents, my family, and my friends for always being there for me.

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LIST OF ABBREVIATIONS

AVR	Aortic Valve Replacement
AVP	Aortic Valvuloplasty
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
CABG	Coronary Artery Bypass Graft
CK-MB	Creatinine Kinase MB Isoenzyme
DNP	Doctor of Nursing Practice
FDA	Food and Drug Administration
FGH	Forrest General Hospital
Fi02	Fraction of Inspired Oxygen
GABA	Gamma Aminobutyric Acid
HCAPHS	Hospital Consumer Assessment of - Healthcare providers and Systems
ICU	Intensive Care Unit
MVR	Mitral Valve Replacement
MVP	Mitral Valvuloplasty
RSBI	Rapid Shallow Breathing Index
US	United States
VAP	Ventilator Associated Pneumonia

CHAPTER I - INTRODUCTION

Statement of the Problem

According to the centers for disease control and prevention (CDC) there are approximately 395,000 cardiothoracic operations performed annually in the United States (US) alone (Centers for Disease Control and Prevention, 2015). It is estimated that up to 10 % of these patients experience complications following surgery that necessitate them being brought back to the operating room for additional surgery (Barash & Cullen, 2013). Examples of complications that can arise are uncontrolled bleeding, graft rupture, aortic dissection, cardiac tamponade, myocardial infarction, and poor cardiac performance (Barash & Cullen, 2013).

Patients that have undergone cardiothoracic procedures are brought to the intensive care unit (ICU) still intubated and placed on mechanical ventilation until they are deemed stable enough to be extubated. Post-operative mechanical ventilation after cardiothoracic surgery can be a stressful event for not only the patient but also the nurse caring for the patient. Sedative agents are commonly used to keep these patients comfortable until they can be weaned from mechanical ventilation. It is the responsibility of the healthcare team to ensure that the transition from mechanical ventilation to extubation goes as smoothly as possible for the patient.

In this new era of modern healthcare, advances have been made to reduce patient length of stay in the hospital. As a result, many patients are now placed on "fast track" recovery protocols. The goal of these protocols is to get these patients extubated within six hours of being in the ICU (Kiessling et al., 2013). Having patients remain on mechanical ventilation for long periods of time has numerous deleterious effects such as:

decrease in patient satisfaction, increased cost to the hospital and the patient, and increased incidence of pneumonia. Since the goal is a rapid recovery, anesthesia providers have had to change the way these patients are anesthetized for their operations. Newer sedative medications with shorter duration of actions and fewer side effects are often being utilized. It is increasingly common for the anesthesia provider to initiate an intravenous sedative infusion in the operating room and have it continued in to the postoperative period (Barash & Cullen, 2013).

Clinical Question

Because of the increased postoperative risk that cardiothoracic operations bring with them, anesthesia providers must carefully tailor all interventions to maximize positive patient outcomes. A clinical question was prepared to establish if the administration of dexmedetomidine for postoperative sedation leads to better outcomes than utilizing propofol for sedation. Does the use of dexmedetomidine lead to better overall outcomes than with the use of propofol in patients being mechanically ventilated following cardiothoracic surgery?

Purpose of the Project

The purpose of this capstone project was to assess if overall outcomes improve due to the use of dexmedetomidine for sedation of mechanically ventilated patients following cardiothoracic surgery when compared to sedation with propofol. The short term goal of this project was to influence a clinical practice change and improve patient outcomes at a level II trauma facility in Mississippi. The long-term goal of this project is to improve patient outcomes for anyone undergoing a cardiothoracic operation in the United States.

CHAPTER II - METHODOLOGY

A comprehensive review of the literature was conducted using electronic databases. The following databases were utilized for this review: Nursing OVID, CINAHL, Google Scholar, and PubMed. Key words that were incorporated into this systematic review were: cardiac surgery, dexmedetomidine, cardiovascular surgery, cardiothoracic surgery, postoperative, and sedation. Outcomes from the literature that were analyzed included: postoperative time spent on mechanical ventilation, incidence of ventilator associated pneumonia, cost effectiveness of dexmedetomidine, and mortality and morbidity associated with postoperative sedation. The outcomes listed above were measured in patients who were receiving either dexmedetomidine or propofol for postoperative sedation. Findings from the review of these articles will be assembled and used as the basis of a practice change proposal. This practice change proposal was presented to a group of Anesthesiologists at a level II trauma hospital in Mississippi. The intent of this practice change proposal was to attempt to help guide a practice change in order to help improve patient outcomes for those patients undergoing cardiothoracic surgery.

Expected Outcomes

The purpose of this DNP project was to assess whether the use of dexmedetomidine or propofol for sedation of postoperative cardiothoracic surgical patients led to better outcomes. The anticipated outcome was to improve patient outcomes as a result of a practice change brought about by the formulation, distribution, and presentation of a practice change proposal. This practice change proposal was presented to the Anesthesiologists at a level II trauma hospital in Mississippi with the aid

of a formal PowerPoint presentation. After the initial presentation was completed, a short questionnaire was given to the Anesthesiologists to assess their willingness to adopt a practice change; the practice change proposal was then made available to the department with the intent that better patient outcomes would ensue.

Barriers to Implementation

A number of barriers were identified during the course of this DNP project. There were a limited number of studies performed utilizing dexmedetomidine as a sedative agent. Uncertainty whether the Anesthesiologists at the local level II trauma facility would be hesitant to try this newer technique of postoperative sedation was also present.

Target Population

Articles reviewed for this DNP project included patient populations that were over the age of 18, had undergone a cardiothoracic surgery, and were on a mechanical ventilator in the postoperative phase. Cardiothoracic surgery, for the purposes of this capstone, includes coronary artery bypass grafting, mitral valve replacement, and aortic valve replacement. Inclusion criteria for articles to be reviewed were: the articles had to be published within the last 10 years or be seminal articles, and the articles had to be in the English language. Seminal works are of central importance to a topic; often they are the first publications written on a specific topic and offer new insight into an area. Exclusion criteria therefore included articles published more than 10 years ago that were not seminal articles, and articles published in any language other than English.

The Importance of Time Spent on Mechanical Ventilation

Reducing the amount of time the patients spend on mechanical ventilation greatly improves their chance of having a successful, uneventful recovery period. The mainstay of cardiothoracic surgical patient recovery now is the "fast track" route; this route aims to have the patient weaned from the mechanical ventilator within six hours (Kiessling et al., 2013). Patients on mechanical ventilation for a prolonged period of time are at risk for developing ventilator-associated pneumonia (VAP). Signs and symptoms associated with VAP include: (a) temperature greater than 38 degrees Celsius, (b) white blood cell count greater than 12,000, (c) new onset purulent drainage from the endotracheal tube, or worsening oxygen requirements (Craven & Hjalmarson, 2010). VAP carries with it a nearly 40% mortality rate and an average cost of $40,000 per occurrence (Craven & Hjalmarson, 2010).

Lack of Knowledge regarding Dexmedetomidine

Dexmedetomidine is a newer sedative agent that was approved for use by the Food and Drug Administration (FDA) in 1999. Because it is a relatively new medication, healthcare providers' knowledge base regarding the drug may not always be vast. Dexmedetomidine has a different mechanism of action than most sedative agents and it does not depress the respiratory center in the brain (Wanat, Fitousis, Boston, & Masud, 2014). Since it does not depress the central respiratory center it does not have to be discontinued prior to weaning a patient from the mechanical ventilator, this is a major advantage of this medication over conventional sedative agents. If the patient can be left adequately sedated while still being arousable to verbal stimuli, which is the key benefit

to using dexmedetomidine, then tracheal extubation can occur in such a way that it is comfortable for the patient while still being safe (Karaman et al., 2015).

Clinical Use of Sedative Agents

Sedative agents can help facilitate an uneventful transition from mechanical ventilation to extubation. Patients can be kept in a quiescent state until vital signs, hemodynamic values, volume status, and postoperative bleeding are all normalized. Most institutions use a protocol that contains criteria that help guide the ICU nurse's decision to start weaning the patient from mechanical ventilation. Some examples of criteria that must be met may include the following: fraction of inspired oxygen (Fi02) less than 50%, hemodynamically stable, awake and alert, able to maintain airway reflexes, negative inspiratory force of 30 cm water, and a rapid shallow breathing index (RSBI) of less than 100 (Hensley, Martin, & Gravlee, 2013). The fraction of inspired oxygen is the concentration of oxygen that is set on the ventilator to be delivered to the patient; the concentration that is available in the atmosphere is 21%, for the purposes of weaning ventilatory support a concentration of 50% or less is desirable (Stoelting & Hillier, 2006). Negative inspiratory force is a test of respiratory muscle strength, during spontaneous respiration the diaphragm descends causing a negative pressure within the chest that causes air to rush into the lungs. The negative inspiratory force is simply a way to quantify how negative the pressure is that the diaphragmatic movement creates, 30 cm of water pressure is an ideal measurement for this test (Barash & Cullen, 2013). The rapid shallow breathing index is a ratio that is used to assess whether the patient is taking breaths that are of adequate depth. The ratio is obtained by dividing the patients breaths per minute by their tidal volume, so a patient breathing 25 times per minute with a tidal

volume of 250cc would have a RSBI of 100 (Barash & Cullen, 2013). After these criteria have been met the patient can start the process of being weaned from mechanical ventilation. Depending on the type of sedative agent being used, it may or may not have to be weaned as well.

Propofol versus Dexmedetomidine

Propofol is an isopropylphenol that is administered intravenously in order to cause rapid sedation. Propofol exerts its sedative action via activation of the gamma aminobutyric acid (GABA) receptors. Activation of this receptor causes negatively charged chloride ions to hyperpolarize the postsynaptic cell membrane of the neuron and therefore inhibit neuronal excitation (Stoelting & Hillier, 2006). In other words, Propofol creates an environment within the neuron that makes it more difficult for the cell to send and receive signals. Propofol is rapidly redistributed to body tissues and the lungs and then it is metabolized by the oxidative enzyme cytochrome P-450 (Nagelhout & Plaus, 2014). Due to the rapid redistribution of Propofol, patients awaken quickly from a single bolus dose therefore a continuous infusion is typically utilized. This drug works in a dose-dependent manner in which a higher dose can be used to provide surgical anesthesia or a lower dose can be used for sedation in the intensive care unit (ICU). Typical doses for sedation in the ICU range from 25 to 100 micrograms per kilogram per minute and can be delivered via a continuous infusion pump (Stoelting & Hillier, 2006). Propofol produces anesthesia without analgesia and also exhibits a profound respiratory depressant effect (Nagelhout & Plaus, 2014).

Dexmedetomidine is a sedative agent that works by stimulating the presynaptic alpha-2 receptor. Presynaptic alpha-2 receptors work as auto regulatory receptors.

Physiologically, norepinephrine normally binds to this receptor and causes a negative feedback loop to be initiated. When the receptor is bound, it signals to the presynaptic neuron that the synapse has an adequate concentration of norepinephrine and no more is needed. When the drug dexmedetomidine mimics this effect it results in a decreased level of norepinephrine in the synapse and this in turn leads to sedation (Nagelhout & Plaus, 2014). In addition to sedation, other physiologic effects can be seen with administration of dexmedetomidine such as hypotension and bradycardia (Barash & Cullen, 2013). Dexmedetomidine is metabolized via glucoronidation in the liver and also by the oxidative enzyme cytochrome P-450. Dexmedetomidine produces sedation at doses ranging from 0.2 to 1 microgram per kilogram per hour; a loading dose of 1 microgram per kilogram can also be used to rapidly achieve an adequate plasma concentration. Dexmedetomidine mainly exerts its actions in the locus ceruleus of the brain stem, therefore it does not depress respiration. One of the main functions of the locus ceruleus is the maintenance of the sleep-wake cycle. Additionally, dexmedetomidine exerts some action at the spinal cord level, which is not well understood, this accounts for its analgesic properties (Nagelhout & Plaus, 2014).

Cost Reduction

Dexmedetomidine use for sedation has been shown to actually decrease that patient's hospital bill by an average of $9679 (Wanat et al., 2014). The reason for this reduction in cost is attributed to a lesser time spent on mechanical ventilation, shortened hospital stay, and less adjunct medication use such as morphine. The use of dexmedetomidine has also been shown to decrease incidence of VAP, which can carry with it a $40,000 cost increase. If the figures provided earlier are extrapolated then there

are an estimated 39,500 patients at increased risk of contracting VAP; this could possibly lead to a cost increase of $1,580,000,000.00 and 15,800 deaths nationwide.

Research Strategy

A comprehensive review of the literature was conducted to determine whether dexmedetomidine used for sedation of postoperative cardiothoracic surgical patients led to better patient outcomes than when the drug propofol was used for the same purpose. Once the systematic review is complete and a conclusion is reached, a practice change proposal will be made. The intent of this practice change proposal was to influence a practice change and improve patient outcomes at a level II trauma facility in Mississippi.

CHAPTER III - COMPREHENSIVE REVIEW OF THE LITERATURE

There is a vast amount of literature that has recently been published supporting the use of dexmedetomidine for postoperative sedation, specifically for patients that have undergone cardiothoracic surgery. While reviewing the literature a number of barriers to the use of dexmedetomidine were identified; they included: (a) concern whether dexmedetomidine could reduce postoperative ventilation time without increasing adverse events; (b) concern over total cost-effectiveness of dexmedetomidine vs. propofol; (c) lack of knowledge regarding advantages and disadvantages of dexmedetomidine for sedation. This review of the literature will seek to determine whether dexmedetomidine when used for sedation of postoperative cardiothoracic surgery patients leads to better patient outcomes than when sedation with propofol is used.

Search Methods

The search of the literature was conducted using the following evidence-based databases: CINAHL, Nursing OVID, and Pub Med; in addition to the evidence-based databases already mentioned, Google Scholar was also used as a preliminary search measure. Search terms that were utilized included cardiac surgery, dexmedetomidine, cardiovascular surgery, cardiothoracic surgery, postoperative, and sedation. In addition to the aforementioned search terms, inclusion criteria consisted of articles in the English language, articles available in full text, articles written within the last 10 years, and articles that dealt with populations over the age of 18. Exclusion criteria included articles not written in the English language, articles not available in full text, articles not from peer-reviewed journals, and articles dealing with pediatric populations. Patient outcomes that were examined in these articles included time spent on mechanical ventilation,

incidence of ventilator associated pneumonia, cost effectiveness of dexmedetomidine, and mortality and morbidity associated with postoperative mechanical ventilation.

Dexmedetomidine to reduce Postoperative Ventilation Time

The length of time spent on mechanical ventilation in the immediate postoperative period is crucial. In years past, cardiothoracic surgical patients in the postoperative period would be sedated and left intubated for up to 24 hours while their fluid status, hemodynamic parameters, cardiac function, electrolytes, and temperature were being normalized (Klineberg, Geer, Hirsh, & Aukburg, 1977). Hemodynamic parameters that are typically monitored in these patients include central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, blood pressure, stroke volume, cardiac output, and cardiac index (Barash & Cullen, 2013). It was discovered that leaving these patients on the ventilator overnight was not exactly leading to the best patient outcomes. The cardiac surgery community started looking for a better way of approaching postoperative care for cardiothoracic surgery patients. During the period from the mid 1970's to the late 1990's major advances were made in the intraoperative and postoperative care of these patients. Some of these advances included the utilization of transesophageal echocardiography, movement away from use of long acting paralytics such as pancuronium, and use of a balanced anesthetic technique instead of a primarily narcotic based approach (Stoelting & Hillier, 2006).

Now the goal in the early postoperative period is to stabilize the patient and wean them from the ventilator as quickly as possible (Barash & Cullen, 2013). The new trend in cardiac anesthesia is to "fast-track" cardiothoracic surgical patients. The goal of fast-track ventilator weaning is to have the patient extubated within six hours (Karaman et al.,

2015). Having these patients extubated within six hours reduces the overall incidence of ventilator-associated pneumonia (VAP). Reducing the incidence of VAP not only improves patient outcomes but it has also been shown to improve patient satisfaction scores (Craven & Hjalmarson, 2010). VAP has been shown to be up to 20 times more common in mechanically ventilated patients. It has been associated with a crude mortality rate of 20% to 40% and carries with it an average cost of $40,000 per incident (Craven & Hjalmarson, 2010).

A retrospective observational trial was conducted by Wanut and colleagues (2014) in which time spent on mechanical ventilation was compared with a group receiving dexmedetomidine and a group receiving propofol for postoperative sedation. The patients included in this study had undergone coronary artery bypass grafting (CABG), mitral valve replacement (MVR), or aortic valve replacement (AVR). Patients were excluded from the study if they were under the age of 18, were pregnant, had a prior organ transplant, or were receiving infusions of both dexmedetomidine and propofol. There was no randomization to the groups, patients received either dexmedetomidine or propofol for sedation based on the ordering physician preference. The results of the study showed that patients that received dexmedetomidine (N=33) had a statistically significant reduction in time spent on the ventilator when compared to patients that received propofol (N=319), mean ventilation times were 7.4 hours and 12.5 hours respectively (p value <.042) (Wanat et al., 2014).

Karaman et al. (2015) conducted a randomized controlled trial in patients undergoing CABG comparing dexmedetomidine to propofol with regard to extubation time as well as hemodynamic and respiratory parameters, complication rates, and patient

satisfaction scores. The study included 70 patients and exclusion criteria included patients with chronic renal failure, liver failure, congestive heart failure, valvular heart disease, respiratory system disorders, propofol or dexmedetomidine allergies, Alzheimer's disease or dementia, ejection fraction of less than 40%, body mass index of >30, and a bypass time of >120 minutes. The patients were randomized to receive either dexmedetomidine or propofol for sedation in the postoperative phase. Dexmedetomidine was infused at a rate of 0.2-1.0 micrograms per kilogram per hour and propofol was infused at a rate of 1-3 milligrams per kilogram per hour. The typical infusion rate for dexmedetomidine is 0.2-0.7 micrograms per kilogram per hour, and the typical infusion rate for Propofol is 1-3 milligrams per kilogram per hour (Nagelhout & Plaus, 2014). The study showed that patients that received dexmedetomidine (N=31) had statistically significant reductions in ventilator time when compared to patients that received propofol (N=33). Times for the two groups were 266 minutes vs. 323 minutes respectively (p value <.001) (Karaman et al., 2015). The goal of fast track ventilator weaning in these patients is 360 minutes (Karaman et al., 2015).

Park et al. (2014) performed a randomized controlled trial on patients undergoing CABG, aortic valvuloplasty (AVP), mitral valvuloplasty (MVP), and combined CABG and valve procedures. In this trial dexmedetomidine was compared to remifentanil with regard to neurological, hemodynamic, and sedative differences. The study included 142 patients that were randomized into either the dexmedetomidine group or the remifentanil group. Remifentanil is a potent synthetic opioid that is administered via a continuous infusion; it is broken down in the plasma by red blood cell esterases and as such it has a half-life of approximately four minutes (Nagelhout & Plaus, 2014). Dexmedetomidine

infusion rates were between 0.2-0.8 micrograms per kilogram per hour and remifentanil infusion rates were between 1-2.5 milligrams per hour. The typical dose of remifentanil when administered as a continuous infusion is between 0.05-2 milligrams per hour (Nagelhout & Plaus, 2014). The study failed to demonstrate a reduction in postoperative ventilation time with dexmedetomidine when compared to remifentanil ($p > .05$). However, the study did conclude that the dexmedetomidine group had a statistically significant reduction in overall incidence of postoperative delirium 8.96% compared to 22.67% ($p < .05$) (Park et al., 2014). This study also pointed out that it has been shown that a prolonged amount of time on mechanical ventilation can itself lead to increased risk of developing delirium by as much as 790% ($p < .05$) (Park et al., 2014).

Cost Effectiveness

Providing patients with cost effective, safe healthcare is in everyone's best interest. There are a number of studies that have been published elucidating the cost effectiveness of using dexmedetomidine for postoperative sedation. Wanut et al. (2014) found in their retrospective observational trial that, on average, using dexmedetomidine for postoperative sedation reduced the hospital bill by $9679.00. This amount of savings was due to a combination of things such as: decreased length of time on ventilator, decreased incidence of pneumonia and stress ulcers, decreased length of stay in the hospital, and less use of adjunct medications such as morphine, beta blockers, and epinephrine (Wanat et al., 2014).

Ji et al. (2013) conducted a single-center, retrospective cohort study that included 1260 patients that underwent CABG, MVR, or AVR surgery; the aim of their study was to determine whether perioperative use of dexmedetomidine reduced the incidence of

adverse complications and mortality following surgery. Exclusion criteria for this study included emergency operations, off-pump surgery, robotic surgery, circulatory arrest, and surgery involving the thoracic aorta. The study showed a decrease in the mortality rate while in the hospital, 1.23% vs. 4.59% ($p < 0.0001$). The study also showed a decrease in the 30 day and 1-year mortality rates, 1.76% vs. 5.12% and 3.17% vs. 7.95% respectively ($p < 0.0001$ for both) (Ji et al., 2013). A perioperative infusion of dexmedetomidine was also shown to decrease the overall incidence of complications (stroke, MI, sepsis, cardiac arrest, acute renal failure) from 54.06% to 47.18% ($p = 0.0136$). By decreasing the likelihood that these patients will experience adverse complications both shortly after surgery and even up to one year out from surgery, readmission to the hospital in this time period is decreased. Reimbursement from the Centers for Medicare and Medicaid Services (CMS) is now tied to readmission rates (Centers for Medicare and Medicaid Services, 2014), so anything that can be proven to reduce these rates is of great benefit to an organization and the patient.

Patients are now being given a survey to fill out upon discharge called the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS), the results of this survey factor into reimbursement for the institution (Centers for Medicare and Medicaid Services, 2014). Karaman et al. (2015) found that not only did using dexmedetomidine reduce time spent on mechanical ventilation, it also had a statistically significant impact of patient satisfaction scores. The average satisfaction score for the dexmedetomidine group was 9 whereas the mean score for the propofol group was 7 (p value <.001) (Karaman et al., 2015).

Knowledge Deficit Regarding Dexmedetomidine

It was found during this review of the literature that there is a generalizable knowledge deficit regarding the advantages to using dexmedetomidine in the perioperative setting. The advantages of dexmedetomidine over conventional sedative agents are numerous. Possibly the most underutilized and unknown benefit of dexmedetomidine is that the infusion can be continued for up to 24 hours after extubation (Wanat et al., 2014). Unlike most conventional sedatives that work on the GABA receptors, dexmedetomidine exerts its action on the presynaptic alpha-2 adrenergic receptors (Nagelhout & Plaus, 2014). Since its action is mediated through the alpha-2 receptors, which causes sedation by ultimately reducing the amount of norepinephrine in the synaptic cleft and not by mimicking the body's own sedative mechanism, the respiratory center in the brain is not affected. Because of the unique mechanism of action that dexmedetomidine possesses, it can safely be continued in the period following tracheal extubation.

Ren et al. (2013) performed a randomized control trial with the aim of evaluating the impact that dexmedetomidine had on myocardial injury in the postoperative period. This trial included 162 patients that were undergoing off-pump coronary artery bypass. Patients were randomized into two groups, one received dexmedetomidine in the perioperative period while the other received propofol. The study found that using a dexmedetomidine in the postoperative period led to a decreased serum level of both norepinephrine and cortisol ($p < .05$). Norepinephrine and cortisol are both associated with an increased stress response that is initiated by surgery or trauma. In an already weakened heart it is important that this stress response be allayed as much as possible.

The trial also determined that dexmedetomidine infusions led to a decreased creatinine kinase MB isoenzyme (CK-MB) levels ($p < .05$), and a decreased number of myocardial ischemic events ($p < .05$) (Ren et al., 2013). Myocardial ischemia ensues when oxygen demand by the heart outweighs the oxygen supply from the blood (Barash & Cullen, 2013) CK-MB is the isoenzyme of creatinine kinase that is released when myocardial cells are irreversibly injured (Kumar et al., 2013).

In addition to its sedative effects, dexmedetomidine also offers patients some analgesic properties. The analgesic properties of dexmedetomidine are due to its alpha-2 adrenergic agonist activity at the level of the spinal cord (Barash & Cullen, 2013). Herr et al. (2003) conducted a randomized trial spanning 25 hospitals in the United States and Canada investigating differences in analgesic use, beta blocking agents, antiemetic use, epinephrine, and diuretics in patients receiving either dexmedetomidine or propofol for sedation in the ICU after CABG surgery. The study consisted of 295 patients that were randomized into either the dexmedetomidine group, or the propofol group. It was found that in the dexmedetomidine group, only 28% of patients required morphine for break through pain whereas 69% of the patients in the propofol group received morphine ($p < 0.001$) (Herr et al., 2003). It was also shown that the propofol group received, on average, four times the amount of morphine that the dexmedetomidine group received while in the ICU. The dexmedetomidine group also received fewer doses of beta blockers, antiemetic drugs, epinephrine, and diuretics while in the ICU (Herr et al., 2003).

Doctor of Nursing Practice Essentials

Doctor of Nursing Practice (DNP) Essential I is the scientific underpinning for practice (Zaccagnini & White, 2014). This essential allows the researcher to integrate the science of nursing along with a nursing theory or concept in order to determine a need for, and be able to implement a change within a healthcare organization. Nursing theories are classified according to their philosophy, scope, scale, or perspective (Zaccagnini & White, 2014). I plan to utilize a middle range theory into this DNP project. Middle range theories are "specific descriptions, explanations, or predictions about a phenomenon of interest" which are narrower in scope than grand theories (Zaccagnini & White, 2014, p. 14). The specific theory that will be incorporated into this DNP project is the comfort theory by Katherine Kolcaba. The comfort theory has a few basic assumptions that one must be familiar with in order to apply the theory. The first basic assumption is that people experience holistic responses to complicated situations. The second basic assumption is that comfort is indeed a desirable outcome that is pertinent to nursing. Finally, the third basic assumption is that all people will strive to have their basic need for comfort met (Kolcaba, 1994). These three assumptions provide the foundation for the comfort theory and give practitioners a vantage point from which to view their project. The use of this theory will help to ascertain whether the use of dexmedetomidine leads to increased comfort when compared to propofol.

DNP Essential II is organizational and systems leadership for quality improvement and systems thinking (Zaccagnini & White, 2014). This essential assists the researcher in developing methods to improve healthcare delivery for current and future patient populations. According to this essential, scientific as well as economic

findings can be utilized to develop new care delivery approaches. The aim of this project is to determine whether dexmedetomidine leads to better patient outcomes when compared to propofol. The main variable that will determine which of these sedative agents leads to better outcomes is the difference in time to extubation between these two drugs. Another variable that will be examined in this capstone is the monetary benefit of utilizing one drug over the other. Both sedative agents provide safe and reliable sedation of postoperative cardiothoracic surgery patients; however, it is the aim of this capstone to determine which medication produces better patient outcomes and from there a clinical practice change will be made with the goal of improving patient safety.

DNP Essential III is clinical leadership and analytical methods for evidence-based practice (Zaccagnini & White, 2014). This essential helps the researcher to critically appraise existing literature and determine what is the best evidence for practice. This capstone project will contain a systematic review of the current literature regarding the use of dexmedetomidine for the sedation of postoperative cardiothoracic surgery patients. This review of the literature will be synthesized into a practice change proposal and presented to a group of local Anesthesiologists in Mississippi with the intent of influencing a clinical practice change that will improve patient safety.

DNP Essential IV is information systems/technology and patient care technology for the improvement and transformation of healthcare (Zaccagnini & White, 2014). This essential is of the utmost importance in today's healthcare field. Not only is an understanding of technology and information systems important when performing actual patient care or performing a retrospective chart review, but it is also essential to be able to navigate through the electronic databases that contain most of today's research. To

perform the systematic review of the literature that will be tantamount to the completion of this DNP project, multiple electronic sources will need to be navigated in order to find the relevant material.

DNP Essential V is healthcare policy for advocacy in healthcare (Zaccagnini & White, 2014). This essential is important for the researcher since it prepares them to develop policies at the institutional, local, state, and federal levels. It also prepares the nursing researcher to educated policy makers regarding safety and patient outcomes. A practice change proposal was written and given to a local anesthesia department with the hope that it would influence a practice change and improve both patient safety and patient outcomes.

DNP Essential VI interpersonal collaboration for improving patient and population health outcomes (Zaccagnini & White, 2014). This essential is vital to the nursing researcher because the DNP prepared nurse must be able to collaborate with other professionals in order to establish a meaningful practice change. Interpersonal relationships must be established by the researcher with this capstone project in order to influence a change in policy and practice. Also, the presentation of the practice change proposal relied on interpersonal communication between the researcher and the Anesthesiologists in order to be effective.

DNP Essential VII is clinical prevention and population health for improving the nation's health (Zaccagnini & White, 2014). The DNP prepared nurse must be able to analyze scientific data related to their population of interest and synthesize that data into meaningful, easy to use information that can be utilized to help implement and evaluate a change in practice. Dexmedetomidine used as a postoperative sedative agent for patients

that have undergone a cardiothoracic operation can help reduce time spent on mechanical ventilation in this patient population. By reducing the amount of time spent on mechanical ventilation, the incidence of pneumonia is decreased, the patient satisfaction levels are increased, cost is decreased to the patient and facility, and there are less postoperative myocardial ischemic events. So by implementing the latest evidence based findings with regard to postoperative sedation of cardiothoracic surgery patients, patient outcomes can be greatly enhanced.

DNP Essential VIII is advanced nursing practice (Zaccagnini & White, 2014). It is essential to develop and maintain relationships with other healthcare professionals in order to provide better patient care and improve patient outcomes. Professional relationships that are made within the anesthesia department at the local level II trauma hospital will be nurtured in order to obtain a lasting, significant practice change at this facility. Also, it is imperative to be able to demonstrate a superior ability to be able to evaluate research to ascertain what the best evidence-based practice is. Within this DNP project there is a comprehensive review of the literature that contains the latest research on the issue of utilizing dexmedetomidine for sedation of postoperative cardiothoracic surgery patients. At the conclusion of the literature review section it is clear what the best evidence for this particular topic is. With this evidence in hand, a practice change proposal was written and given to the local anesthesia department for consideration for implementation.

Practice Change Proposal

According to the centers for disease control and prevention (CDC) there are approximately 395,000 cardiothoracic operations performed annually in the United States

alone (Centers for Disease Control and Prevention, 2015). It is estimated that up to 10% of these patients experience complications following surgery that necessitate them being brought back to the operating room for additional surgery (Barash & Cullen, 2013). Examples of complications that can arise are uncontrolled bleeding, graft rupture, aortic dissection, cardiac tamponade, myocardial infarction, and poor cardiac performance (Barash & Cullen, 2013).

These patients are brought from the operating room to the intensive care unit and placed on a mechanical ventilator until they are strong enough to be weaned from ventilator support. This period is particularly stressful for the patient as they make the transition from being ventilated to maintain their own airway. The majority of these patients require some type of sedation until their hemodynamics stabilize to the point that they can start to be weaned from the ventilator. The typical sedative that is used for ventilated patients in the ICU is propofol.

Propofol is an isopropylphenol that is administered intravenously in order to cause rapid sedation. Propofol exerts its sedative action via activation of the gamma aminobutyric acid receptors. Activation of this receptor causes negatively charged chloride ions to hyperpolarize the postsynaptic cell membrane of the neuron and therefore inhibit neuronal excitation (Stoelting & Hillier, 2006). In other words, Propofol creates an environment within the neuron that makes it more difficult for the cell to send and receive signals. Propofol is rapidly redistributed to body tissues and the lungs and then it is metabolized by the oxidative enzyme cytochrome P-450 (Nagelhout & Plaus, 2014). Due to the rapid redistribution of Propofol, patients awaken quickly from a single bolus dose therefore a continuous infusion is typically utilized.

An alternative drug is also available for sedation of these patients, dexmedetomidine. Dexmedetomidine is a sedative agent that works by stimulating the presynaptic alpha-2 receptor. Presynaptic alpha-2 receptors work as auto regulatory receptors. Physiologically, norepinephrine normally binds to this receptor and causes a negative feedback loop to be initiated. When the receptor is bound, it signals to the presynaptic neuron that the synapse has an adequate concentration of norepinephrine and no more is needed. When the drug dexmedetomidine mimics this effect it results in a decreased level of norepinephrine in the synapse and this in turn leads to sedation (Nagelhout & Plaus, 2014). In addition to sedation, other physiologic effects can be seen with administration of dexmedetomidine such as hypotension and bradycardia (Barash & Cullen, 2013). Dexmedetomidine is metabolized via glucoronidation in the liver and also by the oxidative enzyme cytochrome P-450. Dexmedetomidine produces sedation at doses ranging from 0.2 to 1 microgram per kilogram per hour; a loading dose of 1 microgram per kilogram can also be used to rapidly achieve an adequate plasma concentration. Dexmedetomidine mainly exerts its actions in the locus ceruleus of the brainstem, therefore it does not depress respiration. One of the main functions of the locus ceruleus is the maintenance of the sleep-wake cycle. Additionally, dexmedetomidine exerts some action at the spinal cord level, which is not well understood, this accounts for its analgesic properties (Nagelhout & Plaus, 2014).

The purpose of this DNP project was to determine whether sedation with dexmedetomidine leads to better patient outcomes when compared to sedation with propofol. A comprehensive review of the literature was performed and outcomes were compared between propofol and dexmedetomidine. The results of the literature review

were taken to a level II trauma center in Mississippi and discussed with the staff Anesthesiologists there. The Anesthesiologists were given a short questionnaire inquiring whether or not they would be willing to change their practice based on the current literature. Eighty percent (4/5) of the Anesthesiologists that were presented with this information said that they would consider a practice change, the only one that did not say yes instead said "maybe".

Some findings from the review of the literature are as follows. Dexmedetomidine use was found to lead to a shorter duration of time spent on mechanical ventilation when compared to propofol (Wanat et al., 2014). Patients who spend less time on the ventilator are less susceptible to acquiring VAP, which carries with it a 40% crude mortality rate (Craven & Hjalmarson, 2010). The use of dexmedetomidine was proven to reduce the overall hospital bill by approximately $9679 (Wanat et al., 2014); this was due to a number of variables such as decreased time spent on mechanical ventilation, decreased length of stay in ICU and decrease in adjunct medication given (morphine, epinephrine, beta blockers). In hospital, 30 day, and 1 year mortality rates were also all proven to be lower in the dexmedetomidine patients (Ji et al., 2013).

Based on the information gleaned from the review of the literature and compiled within this DNP project, dexmedetomidine is a superior sedative agent when compared to propofol for postoperative sedation of cardiothoracic surgery patients. The recommendation of this capstone project is that dexmedetomidine be used for sedation in this patient population. Furthermore, is it also recommended that the changes proposed within this capstone project be tested for accuracy to determine whether a real world practice change should take place.

CHAPTER IV – SUMMARY

The goal of this DNP project was to determine whether sedation with dexmedetomidine leads to better outcomes when compared to sedation with propofol in the postoperative cardiothoracic surgical patient population. Outcomes in several areas were focused on when the review of the literature was conducted. These areas included: postoperative time spent on mechanical ventilation, incidence of VAP, cost effectiveness of dexmedetomidine, and mortality and morbidity associated with postoperative sedation.

A comprehensive review of the literature was conducted and the results from these randomized controlled trials and retrospective studies were compiled within this capstone project. These results were then presented to the staff Anesthesiologists at a level II trauma hospital in Mississippi with a subsequent survey on whether or not they would consider a practice change based upon the evidence from the literature.

Summary of Findings

The most influential finding of this systematic review of the literature was that the use of dexmedetomidine lead to a decreased amount of time spent on mechanical ventilation. Due to the reduced amount of time spent on the ventilator the patients' risk of acquiring VAP were also reduced; VAP carries with it a 40% mortality rate and a cost of up to $40,000. This literature review also showed that the patients receiving dexmedetomidine were discharged from the intensive care unit faster and required significantly less pain medication.

The use of dexmedetomidine for postoperative sedation of cardiothoracic surgical patients was also shown to decrease mortality rates. The in-hospital mortality rate decreased from 4.59% to 1.23%, the 30-day and 1-year mortality rates both also

decreased by a significant amount (5.12% to 1.76% and 7.95% to 3.17% respectively). Lastly, the cost effectiveness of utilizing dexmedetomidine was analyzed. One study found that patients receiving dexmedetomidine postoperatively had a reduction in their hospital bills by an average of $9679. This cost reduction was attributed to less time spent on mechanical ventilation, less time in the ICU and fewer adjunct medications administered.

Following the completion of the review of the literature and after IRB approval was obtained, the results of this literature review were presented to the staff Anesthesiologists at a local level II trauma facility. Of the 5 Anesthesiologists that were presented with these results, 4 of them stated that they would consider a practice change and the other one stated "maybe" when asked about a practice change.

Recommendations

This review of the literature showed that the use of dexmedetomidine for sedation of postoperative cardiothoracic surgical patients leads to better patient outcomes and overall decreased cost to the patient. The next step in the process of implementing this practice change proposal will be to get surgeon approval; without their help this proposal will not be successful. The recommendation of this DNP project is that someone take this literature review a step further and present these results to the cardiothoracic surgeons at the level II trauma hospital in Mississippi. The results of this capstone project should then be tested to determine if the results are significant enough to warrant a clinical practice change.

Conclusion

The aim of this DNP project was to determine whether sedation with dexmedetomidine lead to better patient outcomes when compared with propofol sedation. The ultimate desire is to influence a practice change based upon the evidence discovered in the literature. It is my sincere belief that the results found within this DNP project and the practice change proposal will help clinicians make better decisions regarding sedation for their patients and ultimately will improve patient outcomes.

APPENDIX A – IRB Approval Letter

THE UNIVERSITY OF
SOUTHERN MISSISSIPPI

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: 16071802
PROJECT TITLE: In the postoperative cardiothoracic surgical patient being mechanically ventilated, is there a difference in outcomes when comparing sedation with dexmedetomidine versus propofol?
PROJECT TYPE: New Project
RESEARCHER(S): Benjamin Riebesel
COLLEGE/DIVISION: College of Nursing
DEPARTMENT: Advanced Practice
FUNDING AGENCY/SPONSOR: N/A
IRB COMMITTEE ACTION: Exempt Review Approval
PERIOD OF APPROVAL: 07/19/2016 to 07/18/2017
Lawrence A. Hosman, Ph.D.
Institutional Review Board

APPENDIX B – Letter of Support

July 8, 2016

I, Dr. Joe Campbell, MD support Benjamin Riebesel's capstone project focusing on postoperative sedation of cardiothoracic surgical patients.

Sincerely,

Dr. Joe Campbell, MD

APPENDIX C – Consent Form

Letter of Consent

Dear Participant,

I invite you to participate in a research study entitled: *In The Postoperative Cardiothoracic Surgery Patient Being Mechanically Ventilated, Is There A Difference In Outcomes When Comparing Sedation With Dexmedetomidine Versus Propofol*. I am currently enrolled in the Nurse Anesthesia program at the University of Southern Mississippi in Hattiesburg, MS and am in the process of writing my DNP Capstone paper. The purpose of the research is to determine whether patient outcomes can be improved by utilizing dexmedetomidine.

The enclosed questionnaire has been designed to collect information on 1.) whether or not you plan to alter your current practice based on the literature provided and 2.) if you do plan on altering your practice, in what way would that be.

Your participation in this research project is completely voluntary. You may decline altogether, or leave blank any questions you don't wish to answer. There are no known risks to participation beyond those encountered in everyday life. Your responses will remain confidential and anonymous. Data from this research will be kept under lock and key for 6 months and then destroyed; data will be reported only as a collective combined total. No one other than the researchers will know your individual answers to this questionnaire.

If you agree to participate in this project, please answer the questions on the questionnaire as best you can. It should take approximately 5 minutes to complete. Please return the questionnaire to me at the end of the presentation.

If you have any questions about this project, feel free to contact Dr Marjorie Geisz-Everson, Capstone Chair, at 601-266-5500, or via email at Marjorie.GeiszEverson@usm.edu.

Thank you for your assistance in this important endeavor.

Sincerely yours,

Benjamin Riebesel BSN, RN, CCRN, CEN

My signature below indicates that I understand the procedures to be used in this study, all my questions concerning the study have been answered to my satisfaction, and I agree to be a participant in this study. I also agree to allow the researcher to present his findings publicly or privately, in written and or oral form.

Participant's Signature

_____

Date

_____

APPENDIX D Evaluation Tool

Benjamin Riebesel Evaluation Tool

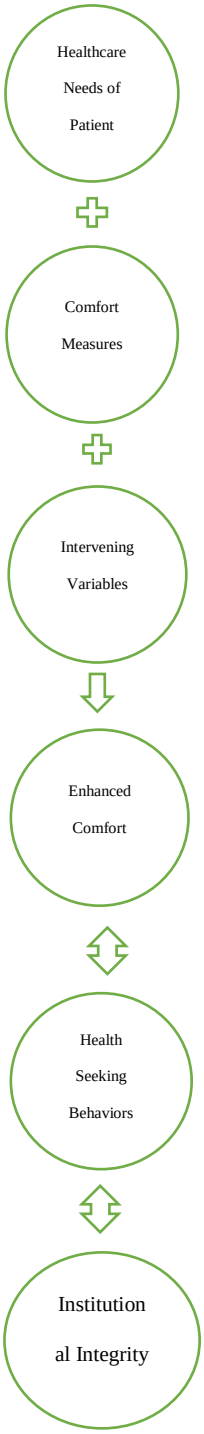
1. Are you over the age of 18? **YES** or **NO**

2. Do you consent to the use of the results of this questionnaire being included in the Capstone project by Benjamin Riebesel? **YES** or **NO**

3. Would you consider a practice change based on the information that was provided today? **YES** or **NO**

4. If you answered YES to question 3, what would your practice change include? Please answer in a few sentences below.

APPENDIX E – Comfort Theory Framework



REFERENCES

Barash, P. G., & Cullen, B. F. (2013). *Clinical anesthesia.* Philadelphia, PA: Lippincott Williams & Wilkins

Centers for Disease Control and Prevention. (2015, April 25). *Inpatient Surgery.* Retrieved from http://www.cdc.gov/nchs/fastats/inpatient-surgery.htm

Centers for Medicare and Medicaid Services. (2014, August 4). *Readmissions Reduction Program: Centers for Medicare and Medicaid Services* . Retrieved from Centers for Medicare and Medicaid Services: http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program.html

Centers for Medicare and Medicaid Services. (2014, September 25). *HCAHPS: Patients' Perspectives of Care Survey: Centers for Medicare and Medicaid Services* . Retrieved from Centers for Medicare and Medicaid Services : http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/HospitalQualityInits/HospitalHCAHPS.html

Craven, D. E., & Hjalmarson, K. L. (2010). Ventilator-associated tracheobronchitis and pneumonia: thinking outside the box. *Clinical Infectious Diseases*, *51*(S1), S59-S66.

Hensley, F. A., Martin, D. E., & Gravlee, G. P. (2013). *A practical approach to cardiac anesthesia* . Philadelphia, PA: Lippincott, Williams & Wilkins.

Herr, D. L., Sum-Ping, J., & England, M. (2003). ICU sedation after coronary artery bypass graft surgery: Dexmedetomidine-based versus propofol-based sedation regimens. *Journal of Cardiothoracic and Vascular Anesthesia*, *17*(5), 576-584.

Ji, F., Li, Z., Nguyen, H., et al. (2013). Perioperative dexmedetomidine improves outcomes of cardiac surgery. *Circulation*, *127*(15), 1576-1586.

Karaman, Y., Abud, B., Tekgul, Z. T., et al. (2015, January 4). Effects of dexmedetomidine and propofol on sedation in patients after coronary artery bypass graft surgery in a fast-track recovery room setting. *Journal of Anesthesia*, *29*(4), 1-7.

Kiessling, A. H., Huneke, P., Reyher, C., et al. (2013). Risk factor analysis for fast track protocol failure. *Journal of Cardiothoracic Surgery*, *47*(8), 47-53.

Klineberg, P. L., Geer, R. T., Hirsh, R. A., et al. (1977, November/December). Early extubation after coronary artery bypass graft surgery. *Critical Care Medicine*, *5*(6), 272-274.

Kolcaba, K. Y. (1994). A theory of holistic comfort for nursing . *Journal of Advanced Nursing*, *19*(6), 1178-1184.

Kumar, V., Abbas, A. K., & Aster, J. C. (2013). *Robbins Basic Pathology.* Philadelphia, PA: Elsevier Saunders .

Nagelhout, J. J., & Plaus, K. L. (2014). *Nurse Anesthesia.* St. Louis, MO: Elsevier Saunders.

Park, J. B., Bang, S. H., Chee, H. K., et al. (2014). Efficacy and safety of dexmedetomidine for postoperative delirium in adult cardiac surgery on cardiopulmonary bypass. *Korean Journal of Thoracic and Cardiovascular Surgery*, *47*(3), 249-254.

Ren, J., Zhang, H., Huang, L., et al. (2013). Protective effect of dexmedetomidine in coronary artery bypass grafting surgery. *Experimental and Therapeutic Medicine, 6*(2), 497-502.

Stoelting, R. K., & Hillier, S. C. (2006). *Pharmacology & physiology in anesthestic practice* . Philadelphia, PA: Lippincott, Williams & Wilkins.

Wanat, M., Fitousis, K., Boston, F., et al. (2014). Comparrison of dexmedetomidine versus propofol for sedation in mechanically ventilated patients after cardiovascular surgery. *Methodist DeBakey Cardiovascular Journal*, *10*(2), 111-117.

Zaccagnini, M. E., & White, K. W. (2014). *The doctor of nursing practice essentials.* Burlington, VT: Jones & Bartlett Learning.