Cost-Efficiency of Sugammadex Versus Neostigmine/Robinul in Reversing Neuromuscular Blockade

Joel Fryfogle

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COST-EFFICIENCY OF SUGAMMADEX VERSUS NEOSTIGMINE/ROBINUL IN REVERSING NEUROMUSCULAR BLOCKADE

by

Joel Daniel Fryfogle

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

Approved by:

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ABSTRACT

As healthcare costs in the United States continue to rise, healthcare providers must do their part to negate the expenses incurred by hospitals and patients. However, some treatments or medications may be more beneficial than others but come at a higher price. Such is the case with sugammadex, a medication approved for use in 2015 that can effectively and reliably reverse paralysis brought about by aminosteroidal induced neuromuscular blockade with rocuronium. Neostigmine/robinul combinations have traditionally been used for neuromuscular blockade reversal but with less efficient results than sugammadex (Abad-Gurumeta et al., 2015). Hence, a cost analysis was conducted at a facility in North Mississippi with a 9-bed operating room to compare the price difference between these two methods of reversing neuromuscular blockade. After prices for each medication were retrieved from the facility, a mean number of cases requiring neuromuscular blockade for surgery was calculated per month. The cost of sugammadex was applied to the average case number and then added over a 6-month period. The same was also done for the neostigmine/robinul combination. The calculation resulted in sugammadex totaling $63,416.64 over six months and neostigmine/robinul combination totaling $12,485.76 over six months. A difference of $50,930.88, which results in 80.3% cost-savings, was noted between the two reversal methods in favor of neostigmine/robinul. The results were shared with anesthesia providers at the facility along with an extensive literature review describing the benefits and complications of both sugammadex and neostigmine/robinul.
ACKNOWLEDGMENTS

I would like to express my gratitude to The University of Southern Mississippi Nurse Anesthesia Program for offering me such an exciting opportunity. Dr. Michong Rayborn and Dr. Nina McLain played a necessary and instrumental role in the completion of this project. My achievements would not have been possible without the patience, support, and guidance of the program’s staff.
DEDICATION

I would like to dedicate this project to my wife, Brooke, and my two children, Blakelee and Kohen. They are the inspiration in my life that leads me to succeed. Brooke has provided support and encouragement throughout my time in the program despite attending The University of Southern Mississippi’s Family Nurse Practitioner Program concurrently. No task was too great for Brooke to handle. I can only hope to provide for my family as well as they have for me. I love each one of you dearly.
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LIST OF ABBREVIATIONS

AACN  American Association of Colleges of Nursing
ACH  Acetylcholine
AMP  Average Manufacturer Price
AWP  Average Wholesale Price
CMS  Centers for Medicare and Medicaid Services
CRNA  Certified Registered Nurse Anesthetist
DSH  Disproportionate Share Hospital
FDA  Food and Drug Administration
GPO  Group Purchasing Organization
IRB  Institutional Review Board
NMB  Neuromuscular Blocker
OR  Operating Room
PACU  Post Anesthesia Care Unit
PONV  Post-Operative Nausea and Vomiting
PORC  Post-Operative Residual Curarization
PTC  Post-Tetanic Count
TOF  Train of Four
WAC  Wholesale Acquisition Cost
CHAPTER I - INTRODUCTION

Healthcare expenditure in the United States has increased steadily over the years and is currently projected to increase further (Centers for Medicare and Medicaid Services [CMS], 2016). The cost is expected to increase to as much as $5.7 trillion by the year 2026, consuming 19.7% of the gross domestic product of the United States (CMS, 2016). Costs in 2016 were estimated at $3.3 trillion with $328.6 billion (10%) owed to drug costs (CMS, 2016). Efforts are being made nationwide to decrease these costs while simultaneously providing high-quality health care to those in need.

These efforts extend into the operating room, where competent anesthesia providers must balance costs, risks, and benefits of any drug to be administered to a patient. Some of the drugs used in anesthesia practice accomplish similar goals. However, the drugs can vary in price and also affect the operating room (OR) time, post-anesthesia care unit (PACU) time, and the general wellness of the patient. All of these variables can increase or decrease the cost of health care and must often be weighed together to provide the most cost-effective, high-quality care that can be afforded.

Sugammadex was approved in 2015 as an alternative neuromuscular blocker (NMB) reversal agent. Anesthesia providers have deliberated Sugammadex’s cost against the traditional use of other reversal agents. However, costs can differ greatly for NMB reversal agents from institution to institution. Identifying the actual difference in price between NMB reversal agents when deliberating about their use is prudent.

Background and Significance

Different classes of NMBs exist with respect to how they work and how they are metabolized. Commonly used paralytics include rocuronium and vecuronium,
intermediate-acting aminosteroidal NMBs, and cisatracurium, an intermediate-acting benzylisoquinolone. Benzylisoquinolones are eliminated by the pH and temperature of the body and reversed with NMB reversal agents (Carron, Baratto, Zarantonello, & Ori, 2016). Aminosteroidal NMBs, like rocuronium, must either be metabolized and excreted over time or antagonized with reversal medications (Carron et al., 2016).

Neostigmine and robinul combinations are hallmark medications used by anesthesia providers to reverse neuromuscular blockade. Sugammadex was recently approved in 2015 by the U.S. Food and Drug Administration (FDA) and provides a rapid and reliable alternative to neostigmine/robinul for rocuronium NMB reversal (Cada, Levien, & Baker, 2016). Abad Gurumeta et al. (2015) state that sugammadex was associated with a significantly lower incidence of side effects and postoperative residual curarization (PORC) when compared with neostigmine for NMB reversal. However, concerns over the cost of sugammadex, as compared to neostigmine/robinul, have limited its use among anesthesia providers.

PICO/Project Question

Is a full dose neostigmine/robinul NMB reversal more cost-effective than full dose sugammadex reversal for neuromuscular blockade when evaluated by cost analysis? The cost of a full dose reversal of rocuronium with neostigmine/robinul will be compared to a full dose reversal with sugammadex to assess the estimated costs of both. The known benefits and complications of sugammadex and neostigmine/robinul will be discussed along with general pharmaceutical pricing information.
Problem Statement

Healthcare professionals all have a shared responsibility to decrease costs in the United States. Therefore, anesthesia providers must do their part in selecting medications that will benefit the patient to the greatest degree within financially reasonable means. NMB reversal agents are no different in this aspect.

Sugammadex has been proven effective in minimizing complications, hastening recovery, and having fewer side effects in comparison with neostigmine/robinul (Abad-Gurumeta et al., 2015; Carron et al., 2016; Chambers et al. 2010; Ledowski et al., 2012; Unal et al., 2015). The cost has been the factor limiting the use of sugammadex in many institutions. Ledowski et al. (2010) confirmed cost as the limiting factor in their study after prices were negotiated at Royal Perth Hospital in Australia.

However, sugammadex and neostigmine/robinul prices can vary in different regions depending on how the drugs are purchased. Rebates, discounts, group purchasing organizations (GPOs), average wholesale prices (AWPs), manufacturer costs, and other factors make labeling one drug with a specific price difficult (Mattingly, 2012). Understanding these terms and how they are used can aid the anesthesia provider in choosing the most appropriate NMB reversal agent.

Purpose of the Project

The project purpose was to establish the cost efficiency of full dose sugammadex in comparison with full dose neostigmine/robinul for NMB reversal at a single facility. The results were shared with the anesthesia staff at the facility. Disseminating the results aided in appropriate selection of an NMB reversal agent and maximized cost savings and patient benefits.
Needs Assessment

The needs assessment was established after a discussion with the chief certified registered nurse anesthetist (CRNA) at a hospital in north Mississippi. Questions had been raised by the anesthesia staff over the cost of sugammadex versus neostigmine/robinul for NMB reversal. The CRNA requested that a cost analysis be conducted to evaluate the cost-efficiency of sugammadex compared to the traditional use of neostigmine/robinul at the facility.

Conceptual Framework

The Donabedian Model was utilized as the framework for this project. Donabedian’s model is the most commonly used theoretical framework among health services research (Ancker et al., 2012). The Donabedian model evaluates healthcare quality by dividing the systems approach into three groups. These divisions are structure, processes, and outcomes.

The structure includes the organizational, material, and human resources that exist within the health care system (Ancker et al., 2012). These components of structure greatly influence the quality of care given. The anesthesia personnel and pharmacy at the health care facility were the structure for this project.

Processes are actions carried out by the system and personnel within it (Ancker et al., 2012). Therefore, selection of the NMB reversal agent by the anesthesia provider is the most prominent action applicable to this project. Pharmacy purchasing options also influence the cost.

Lastly, outcomes refer to the end result that can be measured or quantified in some way (Ancker et al., 2012). The outcome assessed refers to the difference in cost of
full dose reversal of NMB with sugammadex as opposed to neostigmine/robinul. Benefits were established by means of a literature review, to aid in the selection of the appropriate NMB reversal agent.

DNP Essentials

The American Association of Colleges of Nursing (AACN) has established eight essentials necessary for DNP graduates to prove competent in for credentialing purposes (AACN, 2006). The eight essentials are complemented by actions performed during the project as follows:

- Essential I, Scientific Underpinnings for Practice, was performed by conducting a literature review of the cost, benefits, and risks of both sugammadex and neostigmine/robinul.
- Essential II, Organizational and Systems Leadership for Quality Improvement and Systems Thinking, was performed by establishing the cost efficiency of full dose reversal of NMB with sugammadex versus neostigmine/robinul and presenting evidence of the benefits and risks of each.
- Essential III, Clinical Scholarship and Analytical Methods for Evidence-Based Practice was performed by applying information gathered from the literature review and creating an analyzed cost comparison between NMB reversal agents.
- Essential IV, Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care were performed by conducting a literature review using information databases and accessing hospital resources for cost estimation.
• Essential V, Health Care Policy for Advocacy in Health Care, was performed by forming results and presenting the results with anesthesia staff at the health care facility to improve health care delivery.

• Essential VI, Inter-professional Collaboration for Improving Patient and Population Health Outcomes was performed by interacting with anesthesia staff at the healthcare facility regarding cost efficiency of NMB reversal selection and known risks and benefits of each type.

• Essential VII, Clinical Prevention and Population Health for Improving the Nation’s Health was performed by reviewing current literature regarding benefits and risks of NMB agents as it relates to cost efficiency so safe, quality health care delivery can be given.

• Essential VIII, Advanced Nursing Practice, was performed by presenting results of the cost efficiency analysis of sugammadex versus neostigmine/robinul to the CRNAs with respect to the benefits and risks provided by current literature.

Review of the Evidence

The literature review was conducted via electronic databases including the Cumulative Index to Allied and Nursing Health Literature (CINAHL), Google Scholar, Pub Med, Academic Search Premier, and the Cochrane Library. The keywords, phrases, and combinations used to acquire the results on these databases included neostigmine, sugammadex, sugammadex versus neostigmine, cost of sugammadex, cost of neostigmine, pharmaceutical pricing, group purchasing organizations, wholesale acquisition costs, and cost-efficiency. All literature included in this project was limited to English-language literature published from 2010 to present.
Neuromuscular Blockers

NMBs can be divided into two broad categories which are depolarizing and nondepolarizing NMBs. Succinylcholine is a depolarizing NMB that acts on acetylcholine (ACh) receptors at the motor endplate causing depolarization of the cells (Nagelhout & Elisha, 2018). By depolarizing the cells, succinylcholine causes a prolonged refractory period in which muscle cannot be stimulated again until the resting membrane potential returns to normal (Nagelhout & Elisha, 2018). Succinylcholine still has its place among anesthesia providers because of its ultrashort action and is commonly used even though it is host to many potential adverse effects. However, succinylcholine’s mechanism of action and elimination differs from nondepolarizers. Succinylcholine does not require NMB reversal agents for the cessation of action. Therefore, succinylcholine’s relevance is limited in this report.

Nondepolarizing NMBs are subdivided into benzylisoquinolines and steroidalcs. Benzylisoquinolines (atracurium, cisatracurium) act by binding to ACh receptors, thereby, inhibiting the ability of ACh to cause an action potential (Nagelhout & Elisha, 2018). Inhibiting the action potential results in muscular relaxation. Benzylisoquinolines are degraded by physiologic temperature and pH, also known as Hoffman’s elimination. This class of NMBs is not antagonized by sugammadex, so its relevance is limited. Steroidalcs also act by binding to ACh receptors and blocking ACh, ultimately leading to muscle relaxation. Types of steroidalcs include rocuronium, vecuronium, and pancuronium. Each of these NMBs are eliminated by both renal and hepatic excretion (Nagelhout & Elisha, 2018). Rocuronium and vecuronium both fall into the intermediate-acting group with a duration of action of 30-60 minutes. Pancuronium is a long-acting
NMB with a duration of action lasting 60-90 minutes. The effects of these NMBs are antagonized by anticholinesterases, such as neostigmine and edrophonium, which allows for greater quantities of ACh in the neuromuscular junction (Nagelhout & Elisha, 2018). The ACh then competes with the NMBs for ACh receptor binding. The effects of rocuronium and vecuronium can also be reversed with sugammadex.

Train of four (TOF) ratios, tested with a nerve stimulator to cause four successive twitches, are often used by anesthesia practitioners to assess the depth of neuromuscular blockade. The response of the first twitch to the fourth twitch during nerve stimulation determines the designated ratio (Nagelhout & Elisha, 2018). Upon nerve stimulation prior to NMB administration, four equal twitch responses should be elicited. When nondepolarizing NMBs are administered, a dose-dependent decrease in muscle twitch response should be noted. TOF ratios during recovery from NMBs are then graded according to twitch response. TOF fade is noted when the strength of the contraction is weaker and weaker with each twitch. If the fourth twitch is visible but much weaker than the first twitch, the TOF ratio is likely less than 0.5 (Nagelhout & Elisha, 2018). If the fourth twitch is almost equal to the first twitch, the TOF is likely 0.9 or greater.

Sugammadex

Sugammadex (Bridion) is a selective NMB reversal agent that was approved by the FDA in 2015 (Cada et al., 2016). This medication is selective for steroidal NMBs, rendering it ineffective for use with benzylisoquinolines and succinylcholine. Sugammadex was originally designed to reverse the effects of rocuronium, but it has also been shown to counteract vecuronium as well (Cada et al., 2016).
Sugammadex is a γ-cyclodextrin derivative that forms a 1:1 complex with rocuronium by encapsulating the molecule and inhibiting its ability to interact with ACh receptors (Cada et al., 2016; Carron et al., 2016; Ledowski et al., 2012). This method of NMB reversal differs from anticholinesterase/antimuscarinic combinations in that it works directly on the NMB molecule. Sugammadex’s sequestering of rocuronium causes a rapid onset of action with reliable reversal of steroidal neuromuscular blockade with a much lower incidence of residual postoperative paralysis, which can lead to harmful consequences (Ledowski et al., 2012).

Sugammadex is supplied in 100 mg/ml concentrations in 2 ml and 5 ml vials. Current recommendations for reversal of rocuronium with sugammadex are based on TOF responses. Current recommendations state that sugammadex be given at doses of 2 mg/kg for 2 twitches, 4 mg/kg for no twitches or a post-tetanic count (PTC) of 1 to 2, and 16 mg/kg for emergency reversal (Cada et al., 2016; Nagelhout & Elisha, 2018). However, rocuronium reversal with as little as 0.5 mg/kg of sugammadex when a second twitch was observed has resulted in a 0.9 TOF ratio (Cada et al., 2016).

TOF ratios used to assess effectiveness of aminosteroidal NMB reversal agents consistently showed a rapid return to a ratio of 0.9 or greater with sugammadex as compared to neostigmine (Abad-Gurumeta et al., 2015; Carron et al, 2016; Chambers et al. 2010; Ledowski et al., 2012; Unal et al., 2015). The difference in time to recovery of a TOF ratio of 0.9 or greater during a deep blockade with use of sugammadex as opposed to neostigmine is even greater. Cada et al. (2016) refer to a study in which reversal during a PTC of 1 to 2 resulted in a return to TOF ratio of 0.9 in 2.9 minutes with sugammadex in contrast to 50.4 minutes with neostigmine.
Although less adverse effects are associated with sugammadex, the γ-cyclodextrin derivative has been speculated to be the cause of unanticipated consequences such as anaphylaxis, bradycardia, nausea, vomiting, and drug interactions (Cada et al., 2016; Nakanishi, Ishida, Utada, Yamaguchi, & Matsumoto, 2016). Nakanishi et al. (2016) report two previous positive hypersensitivity skin prick tests to sugammadex and one positive skin prick test they conducted themselves on a patient suspected to have hypersensitivity to the drug. During this study, diluted and undiluted concentrations of sugammadex alone and sugammadex mixed with rocuronium were administered via skin prick test. Their findings suggest that hypersensitivity is due to the amounts of free molecules of sugammadex and that sugammadex-rocuronium complexes that have been formed do not cause a reaction (Nakanishi et al., 2016).

Drug interactions with sugammadex have also been noted. Toremifene, a drug used during breast cancer treatment, can bind to sugammadex because of its affinity for it which can delay NMB reversal (Cada et al., 2016). Sugammadex is thought to also bind to progesterone, which may render birth control ineffective. Ondansetron, ranitidine, and verapamil are physically incompatible to mix with sugammadex (Cada et al., 2016).

As far as elimination, sugammadex binds with rocuronium and is excreted renally. The complex formed by rocuronium and sugammadex is eliminated unchanged. Therefore, sugammadex has been detected for up to 7 days when administered to patients with severe renal impairment (Cada et al, 2016).

*Neostigmine/Robinul*

Neostigmine, an anticholinesterase, and robinul, an antimuscarinic, have often been given in conjunction for reversal of NMBs. In contrast to sugammadex, reversal
with this combination can be used in benzyliisoquinoline reversal or aminosteroidal reversal. Neostigmine’s anticholinesterase effects are primarily responsible for the reversal of NMBs because they inhibit the degradation of ACh by acetylcholinesterase (Nagelhout & Elisha, 2018). Robinul’s antimuscarinic effects are necessary to counteract side effects produced by the administration of neostigmine (Abad-Gurumeta et al., 2015; Nagelhout & Elisha, 2018).

Neostigmine, when used as a reversal agent, forms a complex with acetylcholinesterase that inhibits the breakdown of ACh (Nagelhout & Elisha, 2018). A larger amount of ACh is then available in the neuromuscular junction to compete with NMBs for ACh receptor sites. The process ultimately leads to a greater possibility of eliciting an action potential. Because neostigmine does not directly act on nondepolarizing NMBs and depends on increased ACh to displace NMB molecules, the incidence of PORC is of greater concern (Abad-Gurumeta et al., 2015). If PORC is present after surgery, it can lead to atelectasis, pneumonia, respiratory failure, and possible re-intubation.

When neostigmine is administered, side effects related to the inherent parasympathetic action of increased ACh will occur. The side effects include decreased heart rate, low blood pressure, postoperative nausea and vomiting (PONV), bronchoconstriction, hypersalivation, and arrhythmias (Nagelhout & Elisha, 2018). To offset these effects when administering neostigmine for NMB reversal, an antimuscarinic is given in conjunction with it.

Robinul, an antimuscarinic, is usually given along with neostigmine for NMB reversal. Antimuscarinics are responsible for competitively blocking postganglionic
muscarinic receptors (Nagelhout & Elisha, 2018). Some types of these muscarinic receptors reside in cardiac and smooth muscle, which offsets the effects of increased ACh on organs innervated by parasympathetic nerves (Nagelhout & Elisha, 2018). Because skeletal muscle tissue is not innervated by these parasympathetic nerves, it is spared the antimuscarinic actions of robinul. Therefore, ACh continues to bind to ACh receptors on skeletal muscle tissue and reversing the NMBs, while it is also competitively blocked from binding to muscarinic receptors on cardiac and smooth muscle cells. This pharmacologic action attempts to reverse NMBs and avoid adverse events.

Neostigmine is concentrated from 0.5 mg/ml to 1 mg/ml and robinul concentrated as 0.2 mg/ml. The recommended dose of robinul to neostigmine is 0.2 mg robinul to 1 mg neostigmine (Nagelhout & Elisha, 2018). Neostigmine is supplied as 10 ml vials and robinul is supplied as 1 ml, 2 ml, 5 ml, and 20 ml vials.

**Pharmaceutical Pricing**

Drug pricing is a convoluted subject that greatly interferes with large scale estimations of cost across individual pharmacies and hospitals in the United States. Prices can vary greatly from one institution to another due to rebates, discounts, wholesaler purchasing, GPOs, and AWPs among other things (Mattingly, 2012). Therefore, one drug may cost a hospital a great deal more to supply and administer than another. The average manufacturer price (AMP) is the estimated price paid by a wholesaler or direct purchaser for a drug with rebates and discounts included. The wholesale acquisition cost (WAC) is the actual price of the drug that the manufacturer is selling without rebates or discounts included. Manufacturers offer rebates and discounts often, so the AMP is a better estimate after rebates and discounts are calculated (Mattingly, 2012).
Hospitals and pharmacies can purchase medications from a wholesaler for the average wholesale price (AWP) or from the manufacturer directly for the average manufacturer price (AMP) (Mattingly, 2012). However, the location of the manufacturer and supply of the medications directly impacts the ability of facilities to purchase directly from the manufacturers. Hospitals typically purchase drugs from wholesalers, but the price is usually marked up from the WAC or AMP by a certain percentage (Mattingly, 2012). Wholesalers can also offer discounts and state Medicaid programs will reimburse pharmacies for carrying certain medications, which produces further variation in medication cost (Mattingly, 2012).

With the steadily increasing costs of medications in the United States, GPOs have grown in number and size to improve buyer purchasing power (Graf, 2014). GPOs are made up of healthcare providers, hospitals, hospital staff, pharmacies, and other affiliates in which the supply of medication directly impacts their business (Dobson, Heath, Reuter, & DeVanzo, 2014). The GPOs negotiate with multiple wholesalers and manufacturers to establish the most competitive price to include rebates, discounts, and list price. In 2012, the savings estimated from GPOs for its members and consumers was around $22 billion and $55.2 billion (Dobson et al., 2014). Therefore, the formation and use of GPOs can decrease healthcare costs and increase consumer power (Dobson et al., 2014; Graf, 2014).

Summary

The purpose of this project is to evaluate the cost of sugammadex versus neostigmine/robinul. The literature review reflects the benefits and risks of these medications and how they should be balanced with the cost that the facility is incurring.
for their use. Benefits of sugammadex include rapid, reliable reversal of NMBs and lower incidence of PORC. On the other hand, sugammadex has been associated with rare, but serious, adverse effects. Neostigmine/robinul combination has traditionally been used for NMB reversal, so it is trusted by anesthesia providers. Rates of PORC and associated complications are higher with neostigmine/robinul, however. Limited information exists on the exact cost of these medications due to drug purchasing economics. However, estimating the cost at a single facility between the use of sugammadex and neostigmine/robinul for NMB reversal is feasible.
CHAPTER II – METHODOLOGY

Target Outcome

The target outcome of this study was to determine the cost-efficiency of full dose sugammadex in comparison with full dose neostigmine/robinul for NMB reversal. The cost analysis, in conjunction with a relevant literature review of risks and benefits of the medications, was meant to guide the selection of these NMB reversal agents in clinical practice. The long-term goal was cost savings and safe, quality healthcare. To insert an additional chapter(s) in this template follow these steps:

Population and Setting

The population included any operations for patients requiring NMBs. The setting was at a hospital in North Mississippi. This hospital has a 9-bed OR that is responsible for performing arthroscopic, endoscopic, orthopedic, cardiovascular, and general surgery cases.

Design

The medication costs for a full dose reversal with sugammadex alone and neostigmine/robinul combination were collected and analyzed. The data was compiled into an excel spreadsheet to illustrate and organize the costs accrued for comparison. Findings were then communicated with the CRNAs at the hospital.

Barriers

A barrier present in this analysis is the variation of costs associated with these drugs. The price of these drugs is subject to variability among not only other hospitals, but within the hospital, the study occurred in as well. No variations in price occurred during data collection in this project, however. Research data of cost-related material in
regard to sugammadex versus neostigmine/robinul was also limited. The FDA approved sugammadex in 2015, so information regarding its cost is limited.

Methodology

The chief CRNA provided a letter of approval from the hospital and The University of Southern Mississippi Institutional Review Board (IRB) also approved the project (IRB-19-88, Appendix B). The hospital pharmacy was then contacted to obtain information related to the expenses of sugammadex, neostigmine, and robinul. Information regarding the quantity of cases for the 6 months prior to project implementation, requiring NMBs and subsequent NMB reversal agents, was gathered from the chief CRNA. An average number of cases was calculated per month. The full dose reversal cost of sugammadex was applied to the average monthly caseload to determine the estimated expense for the month. The full dose reversal cost of neostigmine/robinul was also applied to the average monthly cases to estimate the monthly expenditure. The estimated monthly expense for both NMB reversal agents was then projected over a 6-month period to identify the estimated cost difference over time based on average monthly case numbers. All information was placed in excel format. The costs were compared and analyzed with an estimated difference calculated. A cost-efficiency analysis report was written and prepared for review. The report was reviewed by a panel of experts before presenting the results to anesthesia staff at the hospital where this project was conducted. A recommendation based off of the report for selection of an NMB reversal agent for cases requiring NMB was given to the chief CRNA. This information was stored in a password-protected computer for a 6-month period following the presentation and erased thereafter.
Summary

This project identified the cost efficiency of sugammadex versus neostigmine/robinul and provided enlightenment regarding the known risks and benefits of each. The data was gathered, quantified, and analyzed for presentation. The project was conducted at a hospital with a 9-bed OR. Approval was received from both the facility and the IRB.
CHAPTER III - RESULTS

Analysis

Purchasing information for neostigmine, robinul, and sugammadex was obtained from the pharmacy. The prices were represented as cost per vial, and the concentrations of the NMB reversal agents were also provided. Prices and concentrations for the medications are listed in Table 1.

Table 1

Cost of NMB Reversals by Vial

<table>
<thead>
<tr>
<th>Medication</th>
<th>Concentration</th>
<th>Cost per vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugammadex</td>
<td>100mg/mL, 2mL</td>
<td>$94.37</td>
</tr>
<tr>
<td>Neostigmine</td>
<td>1mg/mL, 10mL</td>
<td>$5.95</td>
</tr>
<tr>
<td>Robinul</td>
<td>0.2mg/mL, 2mL</td>
<td>$4.21</td>
</tr>
</tbody>
</table>

The hospital belongs to a GPO and purchases its medications almost exclusively through a wholesaler. The hospital is also a disproportionate share hospital (DSH), which enables it to receive special pricing on the robinul along with a 2.5% rebate through the GPO. The sugammadex and neostigmine are only subject to GPO contract pricing with no included rebates or discounts.

Average case numbers requiring NMB reversals per month were calculated by using billing information retrieved from the pharmacy and chief CRNA. All cases that involved NMB reversals from January 1, 2019, to June 30, 2019, were included during this calculation. The information was recorded in excel format and can be viewed in Table 2.
The cost of neostigmine/robinul combination versus sugammadex alone was then applied to the average case number per month to yield the final results. The 200 mg single-dose vial of sugammadex was applied to the 112 cases as the vial contains an average full dose reversal. The maximum full dose reversal of neostigmine is 5 mg given concomitantly with 1 mg of robinul (Nagelhout & Elisha, 2018). The neostigmine available at the hospital is multidose vials with the concentration supplied as 10 mg per vial. However, even multidose vials should be dedicated to single patient use when in a patient treatment area, such as the OR. Therefore, the cost of 1 vial of neostigmine and 3 vials of robinul were used for a single reversal dose and applied to the 112 cases. The data was compiled into an excel spreadsheet and can be seen in Table 3.

Table 3

**Cost of Neostigmine/Robinul Combination Versus Sugammadex at 1 Month and 6 Months**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Unit of Measure</th>
<th>Cost</th>
<th>Monthly Usage</th>
<th>Monthly Expense</th>
<th>6-Month Expense</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugammadex</td>
<td>1 Vial</td>
<td>$94.37</td>
<td>112</td>
<td>$10,569.44</td>
<td>$63,416.64</td>
</tr>
<tr>
<td>Neostigmine/Robinul</td>
<td>1 Vial/3 Vials</td>
<td>$18.58</td>
<td>112</td>
<td>$2,080.96</td>
<td>$12,485.76</td>
</tr>
</tbody>
</table>

Results

The costs were calculated for both neostigmine/robinul combination and sugammadex, then projected over a 6-month period. The results were analyzed and
compared to show that neostigmine/robinul combination is the more cost-efficient option. As Table 3 shows, the cost of sugammadex at the end of the 6 months shows a total of $63,416.64, as compared to $12,485.76 for neostigmine/robinul combination. This totals out for a difference of $50,930.88, which results in 80.3% costs-savings. Variables specific to this hospital regarding pricing and drug usage may not apply to other facilities. These variables will be discussed as limitations to this study in the next chapter.

Summary

The project purpose was to establish the cost difference between neostigmine/robinul combination and sugammadex for reversing NMB. Based upon pricing information received from the facility’s pharmacy and subsequent evaluation of the results, the neostigmine/robinul combination was the more cost-efficient choice. The results were then communicated to the chief CRNA and anesthesia staff at the hospital, which will be discussed in Chapter IV.
CHAPTER IV – DISCUSSION

Presentation of Results to Anesthesia Providers

The results were disseminated to anesthesia staff at the facility. Six of the CRNAs at the facility voluntarily participated in the panel of experts questionnaire after reviewing the results. The questionnaire can be viewed in Appendix C. All respondents agreed that the presentation of results adequately reflected the cost evaluation of sugammadex and neostigmine/robinul. All respondents also agreed that they were not encouraged to select an alternative reversal agent based on the information provided. Therefore, they did not consider a practice change to sugammadex alone over neostigmine/robinul. Some of the anesthesia providers did state in the comments section that sugammadex would be a good alternative to prevent complications of residual paralysis when neostigmine/robinul combination was not adequate. In an effort to minimize cost, the CRNAs could give sugammadex to completely reverse NMB after neostigmine/robinul had already been given.

Limitations

Many limitations exist in terms of extrapolating the data from this project to another facility. Rebates, discounts, reimbursement, price negotiating organizations, and other factors specific to other healthcare institutions can affect the pricing of each drug. Some anesthesia providers at the facility the project was conducted in may choose to use half doses of neostigmine/robinul for reversal. Although using half doses would not affect neostigmine use per vial, only one or two robinul vials may be used. Another potential limitation to this project is the anesthesia providers’ concomitant use of...
sugammadex when neostigmine/robinul reversal is inadequate which would further alter results.

Future Implications

Projects executed at this facility in the future related to cost efficiency of sugammadex versus neostigmine/robinul should prioritize units of OR time, recovery room time, and postoperative complications. Evaluating units of OR time, recovery room time, and postoperative complications would expand the amount of cost-related data that could be collected. Cost to the patient cost to the hospital and efficacy of the drugs in preventing complications could be assessed. Preventing complications during the postoperative period would also decrease cost by avoiding use of other medical supplies needed during intervention.

Discussion

The chief CRNA at a hospital in North Mississippi contacted this DNP student to compare the cost of sugammadex versus neostigmine/robinul combination for NMB reversal. This DNP student accepted the proposal. An extensive literature review related to the cost of these NMB reversal agents was performed. The pharmacy was contacted regarding the pricing of the NMB reversal agents. The costs were applied to the mean number of general anesthetic cases requiring NMB reversal per month and then extended over the course of 6 months. All information was placed in excel format. A difference of $50,930.88 at the end of a 6-month period was calculated in favor of neostigmine/robinul. The difference results in 80.3% cost-savings for the facility. Neostigmine/robinul combination, when compared to sugammadex by cost analysis, appears to be the more cost-efficient option at this facility.
Summary

The literature review and cost analysis indicate an imbalance between medication efficiency and cost. At the hospital, the project was conducted, neostigmine/robinul is much more cost-efficient for NMB reversal. However, recent research would suggest that avoiding complications and decreasing OR time with sugammadex will also aid in avoiding unnecessary costs. Therefore, this DNP student recommends continuing the use of neostigmine/robinul due to the lower cost of these medications at the facility the project was conducted. If there is inadequate reversal of NMB with neostigmine/robinul combination, then it would be prudent to administer sugammadex to avoid postoperative complications and increased hospital time. This DNP student would also recommend investigation into the cost of OR time, recovery room time, and postoperative complications at this facility with regard to each of the NMB reversal agents.
## Table A1. DNP Essentials

<table>
<thead>
<tr>
<th>Essential I</th>
<th>Scientific Underpinnings for Practice</th>
<th>Performed a literature review of the cost, benefits, and risks of both sugammadex and neostigmine/robinul.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential II</td>
<td>Organizational and Systems Leadership for Quality Improvement and Systems Thinking</td>
<td>Established the cost efficiency of full dose reversal of NMB with sugammadex versus neostigmine/robinul and presenting evidence of the benefits and risks of each.</td>
</tr>
<tr>
<td>Essential III</td>
<td>Clinical Scholarship and Analytical Methods for Evidence-Based Practice</td>
<td>Applied information gathered from the literature review and created an analyzed cost comparison between NMB reversal agents.</td>
</tr>
<tr>
<td>Essential IV</td>
<td>Information Systems/Technology and Patient Care Technology for the Improvement of Transformation of Health Care</td>
<td>Conducted a literature review by using information databases and by accessing hospital resources for cost estimation.</td>
</tr>
<tr>
<td>Essential V</td>
<td>Health Care Policy for Advocacy in Health Care</td>
<td>Formed results and presented the results to anesthesia staff at the health care facility to improve health care delivery.</td>
</tr>
<tr>
<td>Essential VI</td>
<td>Inter-professional Collaboration for Improving Patient and Population Health Outcomes</td>
<td>Interacted with anesthesia staff at the healthcare facility regarding cost efficiency of NMB reversal selection and known risks and benefits of each type.</td>
</tr>
<tr>
<td>Essential VII</td>
<td>Clinical Prevention and Population Health for Improving the Nation’s Health</td>
<td>Reviewed current literature regarding the benefits and risks of NMB agents as it relates to cost efficiency so</td>
</tr>
<tr>
<td>Essential VIII</td>
<td>Advanced Nursing Practice</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
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<td></td>
</tr>
<tr>
<td>Presented results of the cost efficiency analysis of sugammadex versus neostigmine/robinul to the CRNAs with respect to the benefits and risks provided by current literature.</td>
<td>safe, quality health care delivery can be given.</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX B – IRB Approval Letter

Notice of Institutional Review Board Action

The project below has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 21, 111), Department of Health and Human Services regulations (45 CFR Part 49), and University Policy to ensure:

- The risks to subjects are minimized and 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 involving risks to subjects must be reported immediately. Problems should be reported to OR via the incident template on Cayuse IRB.
- The period of approval is twelve months. An application for renewal must be submitted for projects exceeding twelve months.

Protocol Number: IRB-13-88
Project Title: Cost Efficiency of Vecuronium Versus Vecuronium-R依托泊酚 in Reversing Neuromuscular Blockade
School/Program: School of LANP, Leadership & Advanced Nursing
Researchers: Joel Fryogle, Michong Rayborn

IRB Committee Action: Exempt
Category: Exempt

Category 4: Secondary research for which consent is not required. Secondary research uses identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501(a) or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 206(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note. If all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq. APPROVED

Starting: May 7, 2019

Donald Sacco, Ph.D.
Institutional Review Board Chairperson
APPENDIX C – Panel of Experts of Questionnaire

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 cost evaluation between sugammadex and neostigmine/robinul reversal agents for patients undergoing general anesthesia?
   a. Yes
   b. No

2) Did the information provided in this presentation encourage you to reconsider your current selection of reversal agents?
   a. Yes
   b. No

3) Would you consider changing your practice based on the information presented if given the option to provide sugammadex?
   a. Yes
   b. No

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

_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________
_____________________________________________________________________

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REFERENCES


