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Review of Incidence of Postoperative Events after Muscle Paralysis Reversal Utilizing Sugammadex (Bridion) In Comparison to Anticholinesterase and Anticholinergic Combination Therapy

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Abstract

Sugammadex was critiqued over multiple postoperative outcomes and the results from the studies listed showed that sugammadex resulted in improved outcomes in most studies when compared to neostigmine. In all of the studies assessed and the multiple outcomes assessed within each, there was no outcome that showed neostigmine to be superior to sugammadex with statistical significance. The results on PONV showed in multiple studies that sugammadex decreases PONV in the first hours postoperatively[1,2]. Multiple studies looked at the reversal time from neuromuscular blockade and showed substantial decrease in recovery time from neostigmine groups[3,4]. These same results ultimately led to other studies on discharge times. The results on discharge times showed improved discharge and discharge readiness times compared to neostigmine[5]. Results on postoperative pulmonary complications showed that residual curarisation was the greatest outcome decreased[6,3]. With the decrease in residual curarisation this led to results of decreased complications associated with residual curarisation such as postoperative desaturations and mechanical ventilation[7,8]. The conclusion of this study resulted in an understanding that sugammadex has a greater efficacy with more rapid and complete reversal of neuromuscular blockade and decrease in side effects and complications related to the side effects predominantly seen with the use of neostigmine.

Introduction

A patient's successful postoperative recovery predicates upon holistic management of the patient's condition prior to, during, and after an invasive surgical procedure as well as active prevention of factors that cause or increase events that lead to complications that extend the duration of patient stay. Adverse postoperative events can occur from sources related to the patient and surgical procedure, as well as caused by risk factors associated with several variables pertaining to general anesthesia[8]. Postoperative complications including but not limited to delayed emergence or extubation, postoperative residual curarisation (PORC), respiratory or cardiovascular complications, nausea and vomiting, and unmanaged pain cause extended stays in the post anesthesia care unit (PACU); duration of PACU stay greater than the average one hour have been shown to be associated with poor patient recovery[6,9]. Furthermore, unplanned admissions and extended PACU stays are costly events that pose a challenge in maintaining balance between patient safety and hospital efficiency[10]. The use of neuromuscular blockade during general anesthesia has shown to be a primary culprit implicated in critical postoperative events that necessitate intervention in 0.8% and 6.9% of patients after extubation including upper airway obstruction, inefficient ventilation and or perfusion leading to hypoxia or respiratory failure, evidence or suspicion of postextubation aspiration, and reintubation[11]. Muscle relaxants

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are routinely reversed at the culmination of a surgical case in an effort to prevent these complications, however inefficiencies and ineffectiveness of medications used for this purpose has spurred investigation of alternatives that exert a more positive impact on post-surgical patient outcomes.

Purpose

This review aims to integrate the evidence regarding the efficacy of selective muscle relaxant binding and reversal agent Bridion (sugammadex) and the implications of the use of this medication on adverse events and outcomes in postoperative patients compared to an anticholinesterase/anticholinergic combination. Standard procedure regarding reversal of muscle relaxant includes the use of a cholinesterase inhibitor such as neostigmine, in combination with an anticholinergic medication such as glycopyrrolate or atropine to offset side effects of anticholinesterase use including bradycardia, increased secretions, and bronchospasm[8]. The limitations of this practice in both efficacy and safety are evident in studies revealing unresolved neuromuscular blockade or even worsening muscle function, as well as properties such as slow onset, short duration, variable results, ceiling effect, and unsuitability for reversal of deep neuromuscular blockade[12]. This integrative review is intended to determine if common practice is best based on examination of literature analyzing the medications used to reverse muscle paralysis, as well as randomized controlled trials and retrospective observational studies of post-surgical patient outcomes identifying the variables associated with adverse events in relation to the use of anticholinesterase and anticholinergic treatment. Identifying the factors associated with muscle relaxant reversal that affect increased PACU stays and investigating methods to prevent these is important in the effort to improve patient stability, recovery, and fiscal use of facility resources[9].

Variables

Variables studied in this integrative review are relative to complications associated with the use reversal of neuromuscular blocking agents (sugammadex versus anticholinesterase medications such as neostigmine) and their implications on postoperative patient recovery. These include a comparison of time to moderate and deep neuromuscular blockade recovery, which has been shown to directly correlate with patient stability and positive postsurgical outcomes[13,14]. In addition, operating room to PACU discharge times are examined and also directly reflect a distinction between reversal medications' efficacy[5]. Additional variables examined include those associated with the reversal medications' direct effects and side effects such as cardiovascular compromise and muscular weakness[14]. Major determinants of patient comfort and duration of PACU stays are investigated in this review and include the presence of residual paralysis and the implications of this complication, the incidence of nausea and vomiting in the immediate postoperative period and during the first 24 hours in the post surgical patient, and pulmonary complications especially in special populations such as the elderly[1]. A comprehensive analysis of the variables listed above as well as time to TOF, operating time, PACU stay duration, desaturation after extubation, reintubation, and reversal cost/complication treatment cost/total cost allows for a thorough understanding of the efficacy and appropriateness of sugammadex (Bridion) in comparison to anticholinesterase and anticholinergic treatment and provides rationale for the pursuit of change to current practice[8].

Search Criteria

The literature search for this integrative review included utilization of multiple databases such as PubMed, CINAHL complete, MEDLINE, ProQuest, and Cochrane library. A search was conducted using keywords sugammadex, bridion, neostigmine and postoperative complications. The search was then narrowed by title and abstract to make sure it fit within the review guidelines. Publications that compare the efficacy, safety, and risk of complications of sugammadex (Bridion) and anticholinesterase treatment are used to synthesize a cumulative overview of the disadvantages of current clinical practice and follow evidence showing how the use of sugammadex (Bridion) remedies many common postoperative complications[14]. Data and discussion for this review was gleaned from randomized controlled trials of adequate sample size, retrospective observational studies of postoperative patient outcomes, prior literature reviews, and texts utilized to investigate objective differences between the two treatments for muscle relaxant reversal.

Outcomes Measured

This integrative review focuses on post-surgical patients; various specific groups within this population were considered such as patients with obstructive sleep apnea (OSA), patients undergoing gynecological procedures, those classified as obese, patients of ASA status 1-4, and multiple age groups beginning at age 18. The primary intervention examined in this study is reversal of neuromuscular blockade utilizing sugammadex (Bridion). Comparison of patient outcomes after treatment with sugammadex (Bridion) rather than commonly utilized anticholinesterase and anticholinergic combination treatment was achieved by identifying variables that affect postoperative recovery. Outcomes that are measured include factors associated with patient recovery and specific adverse events occurring in the postoperative period and their incidence relative to the use of sugammadex (Bridion) versus anticholinesterase/anticholinergic treatment such as neostigmine and glycopyrrolate. The time frame in which the majority of data yielded usable results is the immediate postoperative as well as within a 24 hour period after surgical procedure.

Organization of Data

The primary method of organization utilized during this study is a collaborative drive and labeled folders to sort journal articles and ongoing/completed works. Data acquired from literature relative to this study was analyzed and placed in an evidence table that is categorized by participants, research design, methods used, and results to allow for efficient and thorough review of acquired information.

Methods

Population Elements and Demographics

The population examined in the studies included in this review is comprised of surgical patients of ASA status 1-3 undergoing procedures requiring general anesthesia and neuromuscular block-

ade including but limited to laparoscopic gynecological procedures, extremity operations, obstructive sleep apnea surgery, elective inpatient operations, and same-day surgeries. In addition, the population considered only included patients who were able to be recovered in the post anesthesia care unit (PACU); patients that required intensive care admission were not considered since objective assessment of neuromuscular blockade recovery and isolation of affecting variables could not be accurately conducted in these patients. The majority of studies conducted regarding the use of the reversal agent Bridion (sugammadex) compared to an anticholinesterase/anticholinergic combination included patients greater than 18 years of age, but less than 65 in order to eliminate or decrease age related factors of the pediatric and elderly population that may decrease the representativeness of the sample. All studies except one included in this review, utilized both men and women. Patients of ASA status IV, V, and VI were not considered due to inability to isolate postoperative outcomes related to neuromuscular blockade reversal from those associated with presenting comorbidities. Each article explained who was participating in the studies, who was excluded, and why they chose the given population allowing for a cumulative review that assesses a sample population that is congruent with the general population.

Source Range

As a group we decided that outdated literature would not be relevant to our research analysis. As we looked through journal articles, the oldest article that we reviewed was from 2012. Three articles were from 2018, three from 2017, two from 2015, and one from 2014. This makes all of the information gained on our topic within the past six years. We felt that having a range of only six years from the current that this would allow that our research would be more valid.

Sources Reviewed

The foundational knowledge for this review was obtained from academic texts in order to objectively define the two treatment modalities and properties of each medicine relevant to this study. Subsequent research included articles from academic journals focused on clinical anesthesia. Data and discussion for this review was gleaned from randomized controlled trials of adequate sample size, retrospective observational studies of postoperative patient outcomes, prior literature reviews, and texts utilized to investigate objective differences between the two treatments for muscle relaxant reversal. Comparison of sugammadex (Bridion) and anticholinesterase/anticholinergic treatment was guided by reported results of studies conducted to more accurately delineate differences in patient outcomes based on administered treatment with reduced variability in light of patient related factors. Retrospective review of outcomes without standardized muscle relaxant protocol were also considered as means to identify prospective consequences of treatment based on individual case reports and circumstances. Neither government nor grey literature was utilized for this review.

Search Strategies

The literature search for this integrative review included utilization of multiple databases such as PubMed, CINAHL complete, MEDLINE, ProQuest, and Cochrane library. A search was conducted using keywords sugammadex, neostigmine and postoperative complications. The search was then narrowed by title and abstract. Publications that compare the efficacy, safety, and risk of complications of sugammadex (Bridion) and anticholinesterase treatment are used to synthesize a cumulative overview of the disadvantages of current clinical practice and follow evidence showing how the use of sugammadex (Bridion) remedies many common postoperative complications[14].

Inclusion Criteria: The selection of studies for inclusion in this review was made by establishing parameters to remove or decrease the influence of confounding variables and utilize sample populations that accurately represent the general population. Furthermore, the goal in creating these parameters is to understand the representativeness of the sample population(s) and take this into consideration when incorporating reported results into discussion or recommendations for the use of sugammadex (Bridion). To be included in this review, studies must have utilized an unbiased, random sample with a minimum sample size of 70 participants for an original trial or 500 participants/case reports for a systematic review or meta analysis. Studies must have included surgical patients, ASA 1-3, undergoing general anesthesia requiring neuromuscular blockade and reversal of muscle relaxant at culmination of operation. Inclusion of studies limited to a single surgery type or population type was allowed but this was taken into consideration while drawing conclusions from the reported patient outcomes.

Exclusion Criteria: Studies that utilized patients with comorbidities that directly affect responsiveness to treatment with neuromuscular blocking agents or muscle relaxant reversal agents in a manner that would skew results positively or negatively, i.e. conditions such as neuromuscular disease, extreme respiratory compromise, ASA 4-6, where excluded from this review. Studies demonstrating low internal validity were also excluded - these contained threats to internal validity including but not limited to maturation due to patient progress or decline due to factors unrelated to neuromuscular blockade or muscle relaxant reversal, instrumentation due to health care provider and medication administration dose and timing variability, and selection due to a large disparity in patient health status or demographic especially if present in the control group[15]. Studies that used methods of self report such as the Likert scale were not considered due to the subjective nature of the results. Any presence of Type I or Type II errors whether due to inadequate sample size specific to the study or skewed sampling resulting in adequate representation of the population were also considered cause for exclusion[16].

Data Quality

Literature acquired for this review was evaluated based on level of congruence with inclusion criteria as well as strength of reported results as reflected by sample size and associated symmetry of distribution. Studies utilizing controlled trials or otherwise acquired data were evaluated for statistical significance and subsequent implied clinical significance. Each article and source was evaluated for degree of contributory information leading to synthesis of discussion or drawing of conclusion. With use of an evidence table to organize acquired data, we were able to as-

sign a numerical value to all articles/texts denoting the degree of relevance to the review. Data quality was ranked statistically and clinically by heterogeneity. Statistical heterogeneity was assessed by looking at p values and I2 values when available. Values were assessed to determine if heterogeneity was statistically significant for the study. Values greater than p >.05 were excluded from the study. Clinical heterogeneity was also subjectively assessed and compared to similar studies.

Approach to Analysis

Analysis of treatment modalities utilized for reversal of neuromuscular blockade during general anesthesia gained impetus after introduction of the use of modified cyclodextrin agent sugammadex (Bridion) into clinical practice[17]. Understanding of the role of sugammadex (Bridion) in the clinical setting has increased with the publication of studies investigating the outcomes associated with its use in specific populations, side effects and adverse events associated with its administration, and the implications of the use of sugammadex on expenditure of time, money, and resources[8]. Our analysis takes into consideration numerous publications of this type in an effort to develop a true understanding of this treatment modality in comparison to those that are already established and challenge common practice in light of the incidence of postoperative events associated with neuromuscular blockade reversal (or inadequate reversal). In order to conduct this comparison, we first identified the current common practice regarding reversal of paralytic agents after neuromuscular blockade during general anesthesia as being an anticholinesterase/anticholinergic combination and defined the parameters of its use in the clinical setting. We next identified sugammadex(Bridion) as an alternative method for muscle relaxant reversal and established understanding of mechanism of action, onset, duration, etc. of the individual drugs as well as reviewed associated outcomes, side effects, and postoperative events associated with each treatment modality.

Utilizing publications that demonstrated an inferential statistical approach, we conducted a comparison of incidence of adverse postoperative events based on treatment modality. This consisted of identification of continuous measures such as operating time, recovery time, age, and summarized using standard deviations as well as identification of variables (categorical and binary) such as desaturation, nausea, etc. presented as percentages in order to quantify evidence in a manner that would support our ability to draw conclusions regarding best practice[4]. We conducted a thorough search of literature to verify, duplicate, and affirm results of initial analysis of controlled trials and retrospective reviews in an effort to identify the circumstances under which each treatment is most effective/appropriate as well as review of limitations each treatment and identify barriers to use such as cost, availability, and culture. Our ultimate goal is to contribute suggestions for the use of sugammadex (Bridion) in the clinical setting by developing an understanding of how this agent can be used to produce the greatest benefit to the surgical patient population.

Results

Recovery of Neuromuscular Blockade

An analysis conducted by Herring et al[14] consisting of 26 studies performed during the emergence of sugammadex as part of the sugammadex development program sponsored by Merck & Co., Inc. contrasts its efficacy to that of neostigmine, or a placebo, in reversing deep neuromuscular blockade induced by rocuronium or vecuronium. Data was compiled from these studies in an effort to show the effectiveness of treatment with sugammadex across diverse patient populations, allowing for deep levels of neuromuscular blockade and improved operating conditions during surgical procedures without the risk of residual neuromuscular blockade afterward from inadequate muscle relaxant reversal[14]. The data included in this analysis were pooled from multicenter, randomized, Phase II and Phase III trials that were conducted between December 2002 and August 2010 consisting of a total of 1855 surgical patients equal or greater to 18 years of age, ASA Class 1-3, requiring neuromuscular blockade for the planned procedure[14]. The primary variable examined is time to recovery of train-of-four (TOF) to 0.9 after administration of sugammadex at the recommended dose of 2.0- 4.0 mg/kg at 1-2 post-tetanic counts and 16 mg/kg for reversal 3 minutes after rocuronium administration of 1.2 mg/kg or bolus dose of vecuronium[14].

Results illustrated in Herring et al[14] state the geometric mean time to recovery to TOF ratio of 0.9 to be approximately 1.9 minutes and 2.9 minutes after sugammadex 2.0 mg/kg administration in relation to neuromuscular blockade elicited by rocuronium and vecuronium respectively. When assessed at 5 minutes post sugammadex administration, the investigators found a total of 96% and 86% recovery rate respectively, versus 16% and 9% following use of neostigmine. This analysis also demonstrates that though time to recovery to TOF of 0.9 increases as the depth of neuromuscular blockade present prior to reversal increases, time to recovery with sugammadex treatment is still significantly less[14]. In addition, sugammadex may be used even under circumstances in which a patient presents with no post tetanic twitch count – since neostigmine is not appropriate in this situation, the use of sugammadex reigns superior without comparison. The investigators conclude that the consistency in results across all 26 studies confirm that the use of sugammadex yields more rapid and complete reversal of neuromuscular blockade versus neostigmine, and the role of sugammadex in emergent situations where immediate reversal of paralytic agent is needed (such as in inability to intubate after muscle relaxation has taken place) renders it invaluable in the clinical setting[14].

This analysis presents irrefutable evidence demonstrating the superior efficacy of sugammadex over that of neostigmine in terms of TOF recovery when this variable is isolated as it is in the studies conducted. All 26 studies included in this article were supported by Merck Co., Inc., producers of sugammadex, making it prudent to acknowledge the potential presences of bias in experimentation and results. The likelihood of this is low since the results portrayed in this analysis are congruent with other studies in this same vein of inquiry. This pooled analysis contributes significant support for the use of sugammadex in the clinical setting; however variables such as cost and side effects are not mentioned, making it difficult to claim that sugammadex should be used under all circumstances instead of neostigmine without further investigation of those specifics.

Further investigation of the use of sugammadex administration includes a Cochrane review with meta-analysis and tri-

al sequential analysis conducted by Hristovska, et al.[3] (2018), which compares the efficacy and safety of sugammadex and neostigmine by focusing on recovery time from neuromuscular blockade to TOF > 0.9 but also includes comparison of the incidence of adverse events such as bradycardia and the presence of postoperative residual paralysis. This review includes 41 randomized clinical trials involving surgical patients of >18 years of age, ASA physical status 1-4, requiring neuromuscular blockade for a total of 4206 participants[3]. Outcomes related to recovery time from neuromuscular blockade to TOF of > 0.9 were measured with comparison of administration of sugammadex 2 mg/kg and neostigmine 0.05mg/kg in the presence of the second twitch in a TOF count as well as recovery time from post-tetanic twitch count of 1-5 to recovery of TOF > 0.9 with comparison of administration of sugammadex 4mg/kg and neostigmine 0.07 mg/kg[3]. The incidence of postoperative adverse events was carefully analyzed to only include those associated with medications used for muscle relaxant reversal[3].

The research compiled and analyzed by Hristovska et al[3] is consistent with other investigators' findings as it demonstrates decreased recovery time to TOF > 0.9 after deep neuromuscular blockade with the use of sugammadex compared to recovery time after use of neostigmine, averaging 2.9 min and 48.8 min respectively when sugammadex 4 mg/kg and neostigmine 0.07 mg/kg were administered. Another primary outcome investigated by this review is the presence of postoperative residual paralysis, defined as inability to perform a 5-second head lift, reports of general muscle weakness after extubation and in the PACU, oxygen desaturation < 90% and/or oxygen required during transport, respiratory complication, or reports from the author of residual neuromuscular blockade, which allowed inclusion of 424 participants[3]. The authors found that use of sugammadex significantly lowered the risk of this adverse event compared to incidence of residual muscular paralysis after the use of neostigmine[3]. The investigators of this review were also able to conclude that the incidence of bradycardia after reversal of muscle relaxant is significantly less after use of sugammadex compared to neostigmine due to the mechanism of action of the agent – being a synthetic gamma-cyclodextrin with hydrophilic exterior an and hydrophobic core, rocuronium molecules are encapsulated and thereby inactivated without any influence on acetylcholine or associated muscarinic receptors[3].

Outcomes pertaining to other side effects associated with muscle relaxant reversal such as intra-ocular pressure, hemodynamics, bleeding events, renal function, gastric emptying, thyroid function, cognitive function, and pain were not assessed in this study since the reported data format in the included studies did not meet the requirements for meta-analysis, making this review useful in gleaning insight of a few aspects of the use of sugammadex but inappropriate if trying to obtain a comprehensive understanding and assessment of the agent. The reliability of many of the studies is called into question during the review of this article in that there is an abundance of trials that obtained a low GRADE quality of evidence owing to the presence of a high risk of bias and/or overall imprecision[3]. Furthermore, exclusions based on date of trial, dosages of agents used, or type of patient included were not made during compilation of studies for this review and therefore accuracy of the final results might be decreased. Since the outcomes identified and resulting conclusions remain consistent throughout the studies included in this review as well as others of the same kind, it is reasonable to allow for some variance in method and in fact might even bolster the support for superior efficacy of sugammadex since this is evident despite variability in dose administered and patient population.

As the benefits of using sugammadex for neuromuscular blockade reversal have become increasingly known, investigation of the application of this agent in clinical practice is necessary to understand if these benefits outweigh the cost associated with the drug. For example, a retrospective audit conducted by Kadam and Howell[4] assessing unrestricted and restricted access to sugammadex in a health care facility gives insight to how sugammadex truly impacts the healthcare environment by determining if overall reduced recovery time as a result of unrestricted use of the drug yields more positive outcomes and makes fiscal sense in comparison to the use of neostigmine. This audit consists of surgical cases from January 1st to December 31st, 2014 - during this time period the first six months was designated for unrestricted use of sugammadex and the second six months for restricted use with total of 1347 and 1302 patients included in each category respectively, with the exclusion of 19 patients admitted to the ICU and 275 patients with incomplete recorded data[4]. The dosage of sugammadex studied ranged from 100mg – 400mg with a median of 200mg, with a decrease in total usage as represented by vial consumption from 1830 vials during the first six months to 843 in the second six months equaling a 54% reduction in use[4]. The mean operating time and mean recovery time was then weighed against the cost of sugammadex (approximately 100 times more costly than neostigmine for this facility) for both time periods[4].

Kadam and Howell (2018)[4] found that mean operating time was not affected by the restriction of sugammadex in the second 6-month audit period, however the mean recovery time which was decreased during the period of unrestricted use did increase significantly when the use of sugammadex was restricted as reported by $p < 0.0001$. Side effects caused by sugammadex use were not increased despite unrestricted use allowing the authors to claim that unrestricted use is considered safe[4]. Despite the reduction in time of recovery from neuromuscular blockade with the use of sugammadex, the investigators conclude that the cost differential between sugammadex and neostigmine and the reported expenditure for the duration of the audit do not support even the restricted use of sugammadex since they do not believe the benefits of reduced recovery time offset the overall cost of the drug[4]. The investigators also report that though the study demonstrates increased recovery time during the period of restricted use, they cannot rule out other causes of delay such as patient factors or facility factors such as staffing shortages causing even more doubt as to the practicality of implementing common use of sugammadex in their clinical setting[4].

This analysis is limited in that it only samples one facility and relies on retrospective review of electronic patient charts to gather data; this method contains a marked degree of unreliability compared to conducting original randomized clinical trials where the sample population and measured variables/outcomes are controlled and defined by specific parameters. It is important to recognize that this study does support the claim that sugammadex is more efficient in reversing neuromuscular

blockade than neostigmine which is consistent with the general consensus. Since this study sheds light on the monetary aspect of sugammadex use, it is therefore equally important to recognize that this treatment is more costly when compared to neostigmine and further inquiry as to fiscally prudent use must be made in order to argue for its application in standard clinical practice. This article however does not address the cost of administering an anticholinergic agent with neostigmine during reversal, which is necessary in almost all cases and therefore does not portray a completely accurate view of expenditure associated with neostigmine use. Overall, this study implies that the use of sugammadex may be most appropriate when confined to specific circumstances with refined parameters, and with the understanding that the benefit of complete and efficient neuromuscular blockade in these situations outweighs the associated costs.

Postoperative Nausea and Vomiting

We conducted an analysis of study performed by Paech, et al.[18] (2018) looking at recovery characteristics of patients receiving either sugammadex or neostigmine and glycopyrrolate for reversal of neuromuscular block. They conducted this study using a randomised controlled trial and looked at postoperative complications like nausea and vomiting, double vision, dry mouth, and sedation on 304 women undergoing laparoscopic gynecological surgery[18].

The results of the study showed that incidence of early nausea and vomiting not significantly different between sugammadex and neostigmine (49% vs. 51%; p = 0.731). There was a decreased incidence of double vision (11.5% vs 20%; p = 0.044) and dry mouth (71.6% vs. 85.5%; p=0.003) with sugammadex. Two hour sedation scores were also lower after sugammadex (median (IQR [range] 0 (0-3 [0-10]) vs 2 (0-4.[0-10]); p=0.021. The primary outcome they were assessing was nausea and vomiting during the first six hours while the other outcomes were secondary[18].

The primary outcome they assessed was nausea and vomiting within 6 hours postoperatively. This study has no external funding or competing interest. The study resulted in an almost identical outcome for nausea and vomiting between the groups but is concerning because they grouped in patients randomly and did not address if they high or low risk for nausea and vomiting. Factors such as smoking, history of motion sickness, history of postoperative nausea and vomiting (PONV) and intraoperative and postoperative narcotics were not taken into account. Female is also a modifier for increased risk of PONV which all participants shared. Without assessing patient risk for PONV and prophylaxis treatments given you introduce bias into the study. There is too many factors not assessed that comprise the legitimacy of this study. Though the study has its flaws it still did not find any results that showed sugammadex to be inferior to neostigmine. We concluded that sugammadex if given to this population regardless of PONV risk would be no more beneficial than traditional neostigmine reversal[18].

Koyuncu et al[1] (2015) also conducted a randomized, blinded trial to assess postoperative nausea and vomiting. They looked at 100 American Society of Anesthesiologist (ASA) 1 and 2 patients undergoing extremity surgeries. They randomly assigned patients to receive either neostigmine and atropine or sugammadex for reversal of neuromuscular blockade at the end of surgery when they had 4 twitches with fade present. Their main outcome was PONV but also assessed recovery parameters, antiemetic consumption, and side effects[1].

They concluded with $P < 0.05$ that nausea and vomiting scores were lower in the sugammadex patients upon arrival to the PACU. Antiemetic and analgesic consumption were similar for each group while extubation (median [interquartile range], 3 [1-3.25] vs 4 [1-3.25]; $p < .001$) first eye opening (4 [3-7.25] vs 7 [5-11]; $p < .001$), and head lift (4 [2-7.25] vs 8 [11-25]; $p < .001$) in minutes were all shorter in patients receiving sugammadex. They concluded antagonism of neuromuscular blockade with sugammadex speed recovery of neuromuscular strength only slightly and transiently reduces PONV compared with neostigmine and atropine[1].

This study along with the other study on PONV failed to characterize patients by their PONV risk but did better to assess antiemetic and analgesic consumption which can help or hurt PONV. They concluded that PONV is transiently decreased in sugammadex and recovery is quicker. This study is a better predictor of PONV and can be concluded that it is decreased initially after surgery with sugammadex. We also concluded from this study along with others that recovery from neuromuscular blockade is faster which aligns with the fast onset of suggamadex[1].

Research by Ledowski et al[2]. (2014) demonstrates that residual neuromuscular blockade is a multifactorial cause for postoperative decline and is associated with morbidity in the recovery period. This study contains retrospective analysis of medical records of 1444 surgical patients who received neuromuscular blocking agents during surgery in an effort to determine the effect of sugammadex on endpoints including unwanted events in the PACU (such as PONV or cardiac arrhythmia, SaO_2 less than 96% on 6L of oxygen, bronchospasm, and need for airway intervention including tracheal intubation), pulmonary complication or symptoms within 7 postoperative days, PACU turnover time, and length of hospital stay[2]. Of the total patient population, 722 patients received sugammadex for reversal and 722 were given either neostigmine or no reversal in an effort to duplicate the circumstances of a previous pilot study[2]. Those that received sugammadex or neostigmine were given a mean dose of 2.7 mg/kg and 2.4 mg respectively with neostigmine being combined with glycopyrrolate 0.4 in all but three cases[2].

This study showed that there was no difference in the groups' use of intraoperative fentanyl and postoperative pain scores and fentanyl administration were not significantly different between the groups[2]. Surgeries that used sugammadex were significantly shorter than not administered sugammadex (NON-SUG) group, but airway-associated complications were not significantly different and neither group required a reintubation[2]. There was a significant increase consumption of antiemetic drugs in PACU in the NON-SUG group (18.2% vs. 13.6%)[2]. They related this to the higher incidence in PONV in the neostigmine part of the group (21.5% vs 16.9%) in the non reversal group. What makes these results more significant is that the group that was reversed with neostigmine they all received prophylactic antiemetic drugs more often (SUG 67.3% vs. NEO 74% vs. NONE 60.8%; $p < 0.05$)[2]. All patients from ASA 1-4 showed increased pulmonary outcome scores as age increased

but in the ASA 3 & 4 group the use of sugammadex decreased the slope of increase drastically[2]. The pulmonary outcome score correlated with length of hospital stay but no difference was found between the groups[2].

This study pulled together multiple factors including types of surgeries, sex, age, BMI, smoking, alcohol, pulmonary disease, ASA, anesthetic, and urgency of operation[2]. They compiled these and their significance. After this they found that PONV and antiemetic consumption was decreased in the sugammadex group. They looked at all factors that can increase the risk of PONV and found the correlation in decreased PONV. This study was more extensive than other PONV studies we found and confirmed the decrease in PONV from a previous study and draws into question the study that found no significant difference in PONV scores. They also found that pulmonary outcome scores were decreased more in elderly ASA 3 and 4 patients. This could be due to the decrease in reserve seen with older adults and increased issues with lingering muscle relaxant, where sugammadex fully reverses relaxant. With the other studies combined with this study shows that sugammadex is better for use if PONV is a concern and attempted to be avoided. It could also be concluded that if a patient is elderly or at increased risk of pulmonary issues sugammadex is the superior drug for reversal to optimize patient pulmonary outcomes. If the patient is a low risk of PONV and younger with low risk of pulmonary complications than neostigmine would be an adequate medication for reversal of muscle relaxant[2].

PACU Discharge Times

Carron, et al. (2017)[5] conducted a study looking at sugammadex and it's time to postoperative discharge. Bias was assessed and Michelle Carron and Carlo Ori received payments for lectures from Merck Sharp & Dohme. The study compared reversal of muscle paralysis with sugammadex to neostigmine and conducted a systematic review and a meta-analysis to interpret the results. A total of 518 participants were included across 6 studies. The study wanted to compare results from other articles to see if the conflicting data on discharge times were revealed when all were compiled. The study looked at multiple discharge times such as discharge from OR to PACU, PACU to surgical ward and readiness of discharge to each of those[5].

The results of this study concluded that discharge from OR to PACU was significantly faster with a mean difference of 22.14 minutes. Discharge to the surgical ward from the PACU was also faster with a mean difference time of 16.95 minutes. Discharge readiness from the OR to the PACU was also shorter with mean difference being 5.58 minutes. All three categories were significant with p values less than 0.05. The last category was discharge readiness from the PACU to the surgical ward which showed a mean difference of 1.10 minutes and was not significant yielding a p value of 0.6394[5].

The study yielded significant results and were more evident for discharge time from the OR to the PACU. Times decreased in the following categories supposedly showing the quick onset associated with sugammadex use for reversal, which is reached slower with neostigmine.

Once reversal of neuromuscular blockade is reached and it would be expected that readiness to discharge to the surgical ward would be around the same. After looking at the study and bias within it we concluded it was still significant and showed greater efficacy in the reversal time compared to neostigmine[5].

Postoperative Respiratory Events

Shah et al.[7] (2018) conducted a study regarding the effects of Sugammadex vs Neostigmine and their effect of postoperative mechanical ventilation in the recovery period. These authors hypothesized that the use of Neostigmine when compared to sugammadex would demonstrate increased chances of residual neuromuscular blockade and would lead to morbidity from pulmonary issues, such as: obstruction, pneumonia, and hypoxemia. The hypothesis was tested with IRB approval, through a study put into action at Emory University Hospital between October 1, 2015 and October 1, 2016. The research design was divided into two periods: six and a half months before the introduction of sugammadex and five and a half months after sugammadex was made available in the operating room. The choice of neostigmine *vs* sugammadex was solely up to the provider caring for the patient; inclusion criteria for this study were patients undergoing general endotracheal anesthesia, with electronic anesthesia record during the study period, and had recovered in the PACU. The study compared the categorized rates of PACU mechanical ventilation to examine the effects of the newly introduced drug, sugammadex, following a post-hoc chart review to figure out the reason for postoperative mechanical ventilation. After sorting through exclusion criteria, there were 3,789 patients in the pre-sugammadex introduction, and 3,419 in the second period of the introduction of sugammadex[7].

Interestingly, following the introduction of sugammadex, the use of neostigmine dropped from 90.6% to 30.7%, sugammadex became the antagonist of choice, and a small number of cases (14) used both neostigmine and sugammadex, suggesting sugammadex acted as a rescue agent. The study revealed that the overall incidence of PACU mechanical ventilation was 86 out of 3,798 cases (2.3%) in the pre-sugammadex period, and 60 of the 3,419 cases (1.8%) in the post-sugammadex introduction[8]. More statistics revealed that the introduction of sugammadex into the OR did not decrease the rate of PACU mechanical ventilation, but mechanical ventilation related to residual neuromuscular blocking did decreased significantly with the introduction of sugammadex (from 0.63% to 0.20%)[7].

As found in many articles in this literature review, there are many positive effects that have occurred since the introduction of sugammadex. When studying not only mechanical ventilation in the recovery room, but also nausea, vomiting, and recovery rates from paralysis, one could infer that there are numerous benefits to the introduction of sugammadex into american operating rooms. With the statistics found in this article, it allows the provider to practice more confidently in knowing that using sugammadex over neostigmine will overall improve their patients' outcome in not needing further mechanical ventilation within the PACU.

In an article written by Unal et al[8] (2015), the effects of sugammadex and neostigmine were studied in regards to postoperative respiratory complications. The purpose of this study was to compare the postoperative respiratory complications of neostigmine vs sugammadex in patients undergoing surgery for obstructive sleep apnea. The prospective randomized study was

conducted in a research hospital after receiving ethical approval and included patients who were needing operation for obstructive sleep apnea, were ASA classes I and II, and in the age group of 19-65 years old. Exclusion criteria were patients who were on medications that would interact with muscle relaxants, patients with morbid obesity, pregnant patients, liver and kidney disease, and patients with neuromuscular and respiratory disease. Patients in this study were divided into groups by randomized selection using numbered envelopes. According to the envelope given to the anesthetist, some would receive sugammadex, 2 mg/kg, while others received 0.04 mg/kg of neostigmine and 0.5 mg of atropine. Monitoring of neuromuscular activity was performed from the adductor pollicis muscle via an acceleromyography technique. Postoperative pulmonary complications were recorded and included the following: cough, breath holding, increased secretions, desaturation (SPO_2 < 90), laryngospasm, bronchospasm, hypoxemia (PaO_2 < 60, apnea, and pulmonary disorders[8].

The study was completed with a total of 74 patients that fell into the inclusion criteria. The results revealed that post-extubation, desaturation occured 12 patients (32.4%) in the neostigmine + atropine group and 4 patients (10.8%) in the sugammadex group[8]. There also were other major differences in the two, as three patients in the neostigmine group also suffered from hypoxemia (PaO_2 < 60) and did not improve with airway maneuvers/supplemental oxygen and required re-intubation postoperatively[8]. In total, eight patients in the neostigmine group, and one patient in the sugammadex group required unplanned admission to the intensive care unit[8]. Comparing this article to the Korean Journal of Anesthesiology, both are showing results that sugammadex has a less chance of pulmonary complications in the postoperative period. Both studies are showing results of better pulmonary outcomes in the sugammadex group, however; the anesthetist can't be naive in thinking that there are no pulmonary risks involved with sugammadex, as the studies prove otherwise.

In the journal, Anaesthesia and Intensive Care, an observational, non-interventional, and non-randomized study occurred to compare postoperative residual curarisation and early adverse respiratory events in patients receiving either neostigmine or sugammadex[6]. The primary objective was to evaluate the incidence of postoperative residual curarisation which was defined by a train of four < 90% upon arrival into the postoperative care unit. Other variables evaluated in the study consisted of oxygen saturation (SPO_2) upon PACU arrival, episodes of SPO_2 < 90% in the PACU, airway maneuvers and/or stimulation to maintain SPO_2 > 90% in the PACU, and the need for reintubation. In total, 624 patients were included in the study, all undergoing different types of elective surgical procedures that required general anesthesia with neuromuscular blocking agents. Criteria also included the patient being 18 years of ago or older, non-emergency surgery, and all patients were required to sign informed consent for neuromuscular blocking drugs and tracheal intubation[6].

The results of the study revealed that 14% of the patients studied (88/624) had postoperative residual curarisation. Of the patients who had residual curarisation, fifteen percent spontaneously recovering from neuromuscular blockade without any form of reversal. Another 15% (21/139) reversed with neostigmine had postoperative residual curarisation, while only 2% (1/44) of patients who received sugammadex had residual curarisation. Of all the patients participating in the study, none required re-intubation during their PACU stay[6].

As mentioned above, numerous studies are revealing that the use of sugammadex over neostigmine is revealing better outcomes. In this study, the differences were 15% to 2% (neostigmine to sugammadex) in having residual curarisation when entering into the recovery period[6]. As providers in anesthesia, it is our duty to provide our patients with the best possible chance at thriving after any surgical procedure. Whether the patients are young or healthy, or older with much comorbidity, we must give them the best chance in the postoperative period, and as this study and many others are showing, the use of sugammadex decreases pulmonary complications in the postoperative period.

Sugammadex was critiqued over multiple postoperative outcomes and the results from the studies listed showed that sugammadex resulted in improved outcomes in most studies when compared to neostigmine. In all of the studies assessed and the multiple outcomes assessed within each, there was no outcome that showed neostigmine to be superior to sugammadex with statistical significance. The results on PONV showed in multiple studies that sugammadex decreases PONV in the first hours postoperatively[1,2]. Multiple studies looked at the reversal time from neuromuscular blockade and showed substantial decrease in recovery time from neostigmine groups[3,4]. These same results ultimately led to other studies on discharge times. The results on discharge times showed improved discharge and discharge readiness times compared to neostigmine[5]. Results on postoperative pulmonary complications showed that residual curarisation was the greatest outcome decreased[6]. With the decrease in residual curarisation this led to results of decreased complications associated with residual curarisation such as postoperative desaturations and mechanical ventilation[7,8]. The conclusion of this study resulted in an understanding that sugammadex has a greater efficacy with more rapid and complete reversal of neuromuscular blockade and decrease in side effects and complications related to the side effects predominantly seen with the use of neostigmine.

Discussion

The compilation of data presented in this review showing the inherent efficacy of sugammadex in reversal of neuromuscular blockade was acquired from randomized trials while majority of data reporting the incidence of adverse postoperative events was acquired from retrospective study. Common goals of majority of investigation regarding use of muscle relaxant reversal agents are associated with identifying factors that cause complications and making efforts to prevent or decrease these by the use of more efficacious treatment. Most research reflects high concern with postoperative events caused by pulmonary status as these are arguably the most detrimental to patient recovery and can carry the most severe consequences.

The original inquiry of this review aimed to understand the differing roles of sugammadex versus anticholinesterase agents in muscle relaxant reversal and their impact on postoperative events. Efficacy of sugammadex has been proven greater

than anticholinesterase/anticholinergic as evidenced by rapid return of TOF, which is consistent throughout the literature and studies most of which report significantly better results regarding achievement of complete reversal of neuromuscular blockade. Postoperative outcomes are better specifically in terms of respiratory events in high risk patients due to lack of residual muscular blockade after sugammadex use - this effect is more pronounced in elderly as age is an independent predictor of postoperative pulmonary outcomes[2]. Despite the overwhelming support of sugammadex as ideal for reversal of muscle relaxation, Sugammadex costs are greater than that of neostigmine (the most commonly used anticholinesterase agent), limiting availability and use. However costs may be outweighed by reduced OR time, reduced resources in PACU to support ventilation, more rapid postoperative discharge, and decreased hospital admission in relation to pulmonary complication, which reduce total patient cost despite increase in drug-related cost[8].

Research Hypotheses and Conclusions

Majority of studies produce consistent results in examining the mechanism of action of and role of sugammadex in relation to that of neostigmine, however many do not discuss cost/benefit of the use of sugammadex - of the ones that do, several have shown that neostigmine/anticholinergic use can produce results similar to that of sugammadex in healthy patients so the unrestricted use of sugammadex is not recommended or warranted. We have concluded that though ASA 1-3 patients were mostly studied, these patients may not glean the most benefit from use of sugammadex since adequate neuromuscular strength to support oxygenation/ventilation can be achieved with neostigmine/anticholinergic in a majority of this population. These patients are not at high risk for other postoperative events especially if neostigmine/anticholinergic is dosed appropriately. Almost all studies supported their hypothesese that sugammadex use proved to be more beneficial in improving patient outcomes on many endpoints; however those that venture to make recommendations for practical use consistently report that standardized use of this agent on all populations is not necessary and fiscally detrimental.

Validity Issues

Many studies published regarding the efficacy and use of sugammadex report a high degree of bias and imprecision. One such publication admits that, according to the GRADE system, the quality of their findings ranked low to moderate across different out-comes[3]. It is also of concern that the initial studies regarding sugammadex use and efficacy were conducted by the corporation that produced sugammadex. Many trials did not have narrow parameters for inclusion of patients studied (only few exclusion criteria) so they were unable to identify/isolate variables that contribute to postoperative decline unrelated to residual neuromuscular blockade and might be caused by other factors such as lingering effects of opioids, age, emergency surgery, long surgery duration, abdominal surgery, vascular surgery, and obesity[3]. In addition, the investigators who conducted many of the trials were unable to standardize anesthetic in all patients to rule out these other variables forcing them to draw conclusions from trends in data rather than true quantifications which is arguably less accurate. In review the research of postoperative outcomes in patients, most data collection is retrospective, relying on chart audit and provider report. This creates the possibility of unreported or misreported case details or postoperative events. Finally, some results regarding the incidence of postoperative events such as PONV were conflicting and yielded inconsistent and irreproducible results questioning the legitimacy of any conclusions drawn from these trials.

Gaps in Research and Prospects for Future Research

As with almost all research conducted, there will always be gaps in the populations studied. Many of the literature reviews focused on healthy patients that were ASA status 1-3. As an anesthetist, the goal is to figure out what will work best for even those “unhealthy” patients. Patients that were often excluded were those with pre-existing pulmonary disease at high risk for postoperative complications, the elderly, those with neuromuscular disease i.e. myasthenia gravis, and other populations that require full neuromuscular blockade reversal to prevent postoperative decline. These patients with increased comorbidities that place them at high risk for complication are generally excluded from studies as the researchers felt that including these patients would contaminate their results or skew potential trends in data. Another gap in research is that many studies focused on the general use and efficacy of sugammadex, but the best use of the agent was not studied. A more tailored approach to research is required to identify the role of sugammadex in the clinical setting.

In future studies of sugammadex, researchers should explore the possibility of creating parameters for the use of sugammadex based on criteria that place the patient at a high risk for postoperative events after receiving neuromuscular blockade. Implementation of a scale that restricts the use of sugammadex to these circumstances or more prudently a combination of these circumstances would allow for targeted use of sugammadex to situations that present with the highest risk of postoperative decline. In addition to the parameters and dosage for use as recommended by manufacturer based on TOF (ie. no pre-tetanic twitches/post-tetanic twitches, Rocuronium dose given less than 3 min ago, etc.) a combination of certain patient demographics or occurrence of events during an anesthetic and emergence such as one pre tetanic twitch as measured by TOF, paralytic use within 10 min of culmination of operation, long duration of surgery and paralytic use at large doses for example >100mg Rocuoronium or > 50 mg Vecuronium, etc., elderly with age greater than 75 years, obesity with BMI greater than 35, concomitant pulmonary disease or abnormality in PFTs, conditions such as obstructive sleep apnea, or neuromuscular disease should warrant the use of sugammadex in the clinical setting.

The true value of sugammadex use in relation to cost might be very difficult to quantitatively prove without true isolation of variables and highly selective population studies with strict parameters for inclusion or exclusion. With the given data, utilizing sugammadex in the manner described above makes most fiscal sense while optimizing patients for postoperative recovery, especially those at high risk for postoperative decline.

Conflicts of Interest: There was no financial funding or conflict of interest for any author within this study.

Appendix
Evidence Table

CITATION	PARTICIPANT	RESEARCH DESIGN/ FRAMEWORK/ OBJECTIVE	METHODS/MEASURES (SELF-REPORTED)	RESULTS	NOTES
Paech, M. J., Kaye, R., Baber, C., & Nathan, E. A. (2018). Recovery characteristics of patients receiving either sugammadex or neostigmine and glycopyrrolate for reversal of neuromuscular block: A randomised controlled trial. Anaesthesia Supplement, 73(3), 340-347. doi:10.1111/anae.14174	307 women scheduled for day-surgical laparoscopic gynecological procedure <1 hour under general anesthesia	A randomized controlled trial	In recovery, PONV was assessed by observation of the number of episdoses of vomiting or retching and a 0-10 numerical rating score. Post op nausea and vomiting was re-assessed at 2, 6, and 24 hours postoperatively.	The cumulative incidence of PONV from waking until 6 hours after surgery did not significant differ between the groups (49% forsugammadex and 51% for neostigmine).	
Koyuncu, O., Turhanoglu, S., Akkurt, C.O., Karcioglu, M., Ozkan, M.,Ozer, C....Turan, A. (2015). Comparison of sugammadex and conventional reversal on postoperative nausea and vomiting: a randomized, blinded trial. Journal of Clinical Anesthesia, 27(1), 51-56. doi: 10.1016/j.jclinane.2014.08.010	100 ASA 1 and 2 patients scheduled for extremity surgery (tendon repair and skin graft) during general anesthesia	prospective, randomized, double-blinded study // objective: to determine whether sugammadex causes less PONV than neostigmine	Baseline PONV was assessed using Apfel score. Times recorded: duration of anesthesia, neuromuscular antagonism, extubation, first eye openening, head lift started with admin of reversal agent. TOF of adductor pollicis recorded. PONV evaluated on 0-3 scale ranging from no nausea to retching or vomiting.	According to PONV scale, nausea and vomiting scores were significantly lower with sugammadex than neostigmine upon arrival to PACU but no significant differences in remaining initial 24 postoperative hours.	Hypothesized causes of for results: Decreased PONV with administration of sugammadex - 1. speedy recovery of neuromscular strength alleviates muscle weakness that may lead to hypoventilation and hypoxia contributing to PONV
Unal, D.Y., Baran, I., Mutlu, M., Ural, G., Akkaya, T., &Ozlu, O. (2015) Comparison of sugammadex versus neostigmine costs and respiratory complications in patients with obstructive sleep apnoea, TürkAnesteziVeReanimsyunDernegi, 43(6), 387-395. doi:http://dx.doi.org.proxy.lib.utc.edu/10.5152/TJAR.2015.35682	74 ASA I or II ranging from 19 to 65 years; age, gender, BMI, and apneoa-hypopnoea index (AHI) were recorded	Randomized trial // objective: compare efficacy of sugammadex versus neostigmine in reversing rocuronium induced musclar blockade, incidence of post-operative respiratory complications, and costs for patients undergoing OSA surgery	74 patients radomized into 2 groups, 1 given 2mg/kg sugammadex (Grp S), other given 0.04 mg/kg neostigmine and 0.5 atropine (Grp N). Groups were copared regarding time to TOF 0.9, operating room time, PACU stay, post op respiratory complications, costs related to block reversal, anesthesia care and complication treatment.	Study verified the efficacy of sugammadex over neostigmine for reversal of rocuronium induced neuromuscular blockade - sugammadex reversal decreased incidence of respiratory and circulatory complications after OSA operations and despite higher reversal cost, complication and treatment cost / total cost were lower in sugammadex group.	Time to TOF, operating time, and PACU stay shorter in patients treated with sugammadex. GROUP N: O2 desaturation after extubation: 32.4%; 3 pts reintubated; 8 unplanned ICU admissions; NPPE in 1pt // GROUP S: O2 desaturation after extubation: 8%; 1 unplanned ICU admission // Reversal cost higer in GROUP S, however complication treatment cost and total cost lower in GROUP S
Carron, M., Zarantonello, F., Lazzarotton, N., Tellaroli, P., Ori, C., (2017). Role of sugammadex in accelerating postoperative discharge: A meta-analysis. Journal of Clincal Anesthesia. doi: https://doi.org/10.1016/j.jclinane.2017.03.004	518 people across 6 studies	A systematic review and meta-analysis	A comprehensive search was conducted using PubMed, Web of Science, Google Scholar, and Cochrane Library electronic databases to identify randomized controlled trials written in English. Two reviewers independently selected the studies, extracted data regarding postoperative discharge, and assessed the trials' methodological quality and evidence level. Postoperative discharge time was determined from the operating room (OR) to the postanesthesia care unit (PACU) and from the PACU to the surgical ward. This study was conducted using PRISMA methodology.	Compared with neostigmine, sugammadex was associated with a significantly faster discharge from the OR to the PACU Similarly, discharge-readiness was shorter for sugammadex than for neostigmine from the OR to the PACU However, discharge-readiness was similar in both groups for patients moving from the PACU to the surgical ward	Sugammadex leads to faster discharge from the OR to PACU, which decreases OR time and resources. Sugammadex also decreases discharge from the PACU to the surgical ward. This decreases PACU crowds and relieves nurses to decrease patient to nurse ratios.

Herring WJ, Woo T, Assaid CA, et al. Sugammadex efficacy for reversal of rocuronium- and vecuronium-induced neuromuscular blockade: A pooled analysis of 26 studies. Journal of Clinical Anesthesia. 2017;41:84-91. doi:10.1016/j.jclinane.2017.06.006.	1855 patients across 26 studies that were >18 years of age, ASA Class 1-3, and scheduled to undergo general anesthesia requring neuromuscular blockade	Multicenter, randomized studies performed between December 2002 to 2010// Objective: to compare the efficacy of sugammadex with neostigmine or placebo for reversal of the effects of rocuronium or vecuronium when administered at different depths of blockade.	The anesthesia regiment in these studies was propofol for induction of anesthesia with propofol or sevofloraine for maintenance of anesthesia. Patientesrecevied Rocuronium (0.6-1.2mg/kg) or vecuronium (0.1mg/kg) for NMB. Neuromuscular monitoring was performed using the TOF-Watch SX. An analysis of recovery time to ROF ratio of 0.9 was performed for the population. Analysis was performed using ANOVA on long-transformed recovery times.	In total, 96% and 86% of sugammadex treated subjects recovered to a TOF rato of 0.9 wihin 5 minutes of sugammadex administration at reapearance of second twitch ,follwing rocuronium and vecuronium induced neuromuscular blockade. IN contrast, 16% and 9% of neostigmine-treated subjects recovered within 5 minutes, while no subjects receiving placebo recovered within 5 minutes, for eithe rocuronium or vecuronium induced NMB.	This study shows that using sugamamadex for reversal of neuromuscular blockade has faster recovery times within 5 minutes of administration when compared to Neostigmine and placebo. This will lead to decreased cost of in operating room time, and can assure that your patients musculature is stronger after administration of sugammadex.
Hristovska, A., Duch, P., Allingstrup, M., Afshari, A. (2017). The comparative efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade in adults. The Association of Anaesthesia of Great Britian and Ireland. 73: 631-641.	4206 participants from 41 studies. Adults >18 years of age. ASA status 1-4, who received non-depolarizing neuromuscular blocking agents for an elective in-patient or day-surgery procedure.	A Cochrane systematic review with a meta-analysis and trial sequential analysis	After administration of neuromuscular blockade reversal outcomes were recovery time from moderate neuromuscular blockade from reappearance of second twitch to train-of-four >0.9; recovery time from deep neuromuscular blockade from reappearance of post-tetanic count 1-5 to train-of-four >0.9; and risk of adverse and serious adverse effects.	Recovery from moderate neuromuscular blockade was 2.0 minutes with sugammadex compared to 12.9 for neostigmine. Recovery from deep neuromuscular blockade was 2.9 for sugammadex compared to 48.8 for neostigmine.	Sugammadex proved to provide faster recovery no matter the depth of neuromuscular blockade and postoperative complications were decreased with sugammadex. Though postoperative complications were decreased serious adverse effects remained the same.
Ledowski, T., Falke, L., Johnston, F., Gillies, E., Greenaway, M., De Mel, A., Tiong, W., Phillips, M. (2014). Retrospective investigation of postoperative outcome after reversal of residual neuromuscular blockade. European Society of Anaesthesiology. 31:423-429. DOI: 10.1097/EJA.0000000000000010	1444 patients who received at least one dose of nondepolarizing muscle relaxant intraoperatively during 2011 (722 sugammadex, 212 neostigmine, and 510 no reversal)	Retrospective data anaylsis	Endpoints included unwanted events in the postanaesthesia care unit (PACU); symptoms of pulmonary complications within 7 postoperative days (0 to 100 outcome score based on temperature >38 degrees C, leucocyte count >11 x10^9 1^-1; physical examination consistent with pneumonia and shortness of breath); PACU turnover time, and length of hospital stay.	The incidence of postoperative nausea and vomiting (PONV) in PACU was higher in neostigmine-reversed than sugammadex-reversed patients (21.5 vs. 13.6%; P <0.05). No differences were found regarding other PACU incidents, length of PACU stay or hospital stay. Pulmonary outcome deteriorated significantly	Sugammadex leads to better outcomes when looking at postoperative nausea and vomitting, and better pulmonary outcome when compared to neostigmine reversal and nonreversal of neuromuscular blockade.
Yoo, J.B., Lee, E., Ahn, J., Jang, H. (2017). Clinical factors and non-clinical factors associated with delayed stay in post-anesthetic care units for common types of surgery. International Information Institute, 20(1A), 355-362. Retrieved from https://proxy.lib.utc.edu/login?url=https://search-proquest-com.proxy.lib.utc.edu/docview/1901705635?accountid =14767.	119 patients (ages older than 19) between April and August of 2013	Randomized study that used SPSS 21.0 for windows	Study tools used were used to assess clinical factors, such asoxyugen saturation at time of PACU entraces, degree of recovery of consciousness, hypothermia during PACU stay, nausea, additional adminstration of narcotics and transfusions, glycemic control, and delayed removal of endotracheal tube. Patients also were not allowed to leave hte PACU until they were ranked a score 8 out of 10.	Results: of the 119 participants, 37 (31.1%) had longer than average stays in the PACU. The clinical factors that affected the duration of stay in the PACU, included the following: delayed recover of consciousness from anesthesia (73%)	
Monk, T., Rietbergen, H., Woo, T., Fennema, H. (2017). Use of Sugammadex in Patients With Obesity: A Pooled Analysis. American Journal of Therapeutics. 24:507-514.	1418 patients across 27 studies	A pooled analysis	Patients included in the pooled analysis were selected from all available studies where sugammadex was administered after a neuromuscular block induced by rocuronium or vecuronium, with sugammadex dose based on the routine dose recommendations of 4 mg/kg in cases using deep block [1-2 post-tetanic counts (PTC) or 15 minutes after last rocuronium dose] or 2 mg/kg in case of a moderate block [reappearance of the second twitch (T2)	Reversal after rocuronium administration was 1.9 for nonobese patients and 1.8 for obese patients. There was no correlation between BMI and recovery time. Reversal after vecuronium administration was within 3 minutes on average and also showed no correlation between obese and nonobese patients.	Obese patients (>30BMI) will have recovery times similiar to nonobese patients (<30BMI) when administered sugammadex for reversal.

Kadam, V., Howell, S., (2018). Unrestricted and Restricted Access to Sugammadex and Side Effect Profile in a Teaching Hospital Centre for Year 2014. Anesthesiology and Pain Medicine. 8:1. DOI: 10.5812/aapm.63066.	1347 and 1302 patients were included for the unrestricted and restricted periods, respectively.	A retrospective audit	A retrospective audit was conducted for the period January 1st to December 31st 2014. Sugammadex use was unrestricted during the first 6 months of this period and restricted over the following period. Patients who had endotracheal intubation for any surgery were included in the audit. Non- intubated patients, patients with incomplete data and patients who were intubated and transferred to the intensive care unit were excluded.	1347 and 1302 patients were included for the unrestricted and restricted periods, respectively. There were no significant dif- ferences between the time periods with respect to patient characteristics (Age, ASA) or side effects (oxygen de-saturation, nausea). While mean time in theatre was similar across the time periods, mean recovery time was significantly longer during the restricted period	Though unrestricting Sugammadex reduced recovery time but has had minimal impact on other clinical outcomes. Neostigmine represents a cheaper alternative and its use remains standard practice in this facility.
O'Reilly-Shah, V.N., Lynde, G.C., Mitchell, M.L., Maffeo, C.L., Jabaley, C.S., & Wolf, F.A. (2018). Initial experience with the unrestricted introduction of sugammadex at a large academic medical center: a retrospective observational study examining postoperative mechanical ventialtion and efficiency outcomes. Korean Journal of Anesthesiology, 2-10. doi. org/10.4097/kja.d.18.00063	Patients undergoing general anesthesia over 12 month period	Retrospective observational study including post-hoc chart review and multiple variable linear regression // hypothesis that unrestricted introduction of sugammadex at Emory University Hospital	Retrospective observation - data recorded between 10/1/2015-10/1/2016: First 6.5 months reviewed before sugammadex introduction (P1), next 5.5 months reviewed after sugammadex introduction (P2). Sugammadex was supplied as part of a standard med tray for every surgical case without restrictions on provider use. Education about its use taken place prior to introduction, Neostigmine and glycopyrrolate were in cluded, choice of NMBA was at discretion of care team. After exclusions, 7217 cases were included in the final analytic dataset.	Associated with significant reduction in PACU MV due to rNMB, but no change was observed in the studied efficiency outcomes or overall utilization of MV in the pACU. Rates of PACU MV decreased from 0.63% to 0.20% following intro of sugammadex. Use of sugammadexliekly enabled the reversal and extubation- of patients who previously would have otherwise requried post op MV.	rNMB accounted for 27.9% of PACU MV in P1 and 11.7% in P2.
G. V., Smet, V., … Vandeput, D. (2012). A prospective, observational study comparing postoperative residual curarisation and early adverse respiratory events in patients reversed with neostigmine or sugammadex or after apparent spontaneous recovery. Anaesthesia& Intensive Care, 40(6), 999–1006. Retrieved from https://proxy.lib.utc.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=ccm&AN=108079434&site=ehost-live	624 patients where studied, that were undergoing different types of elective surgical procedures that required general anestehsia with NMBD;s.	A prospective, obsersavtional, non-interventional, and non-randomized study	Immediatley after arival to PACU the nurse recorded tympanic temperature and acceleromyographic responses of the adductor policcis muscle (as the TOF%) upon TOF-Watch stimulation of the ulnar nerve. Two consecutive TOF measurements were obtained and the closest two rations were averaged. a TOF of 90% was used as the cut off value to exclude postoperative residual curarisations (PORC). Lastly, the PACU nurses documentsed the following evenets during the first 30 minutes of PACU time: episodes of hypoxemia (SPO2 > 90%), the lowest SPO2 observed, the requiremnte for either verble or tactile simulation to maintain an SPO2 >90%, and evidence of airway obstruction that required an airway maneuver	The incidence of postoperative residual curarisation (PORC) after neuromuscular blocking drugs strongly decreased wihtin this institution from 59% in 2005 to 14% in 2011. The study showed that 15% of those who apparently spontaneously recovered from their neuromuscular block and 15% of those antagnoised with neostigmine exhibited PORC in the PACU, as opposed to only 2% of the patients who received sugammadex for reversal.	

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