Comparative study between sugammadex and neostigmine as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anaesthesia

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Abstract

Aim. The neuromuscular blocker has long been used during surgical procedures. The neuromuscular blockade produced by rocuronium can be reversed with sugammadex and neostigmine as reversal agents. This systematic review aims to determine the impact of sugammadex and neostigmine comparison as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anaesthesia.

Materials and Methods. This review examined recent studies assessing the impact of sugammadex and neostigmine comparison as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anaesthesia. Data were searched from Google Scholar, PubMed, Hindawi, Anesthesiology, MEDLINE, and CENTRAL using keywords ‘General Anesthesia,’ ‘Reversal Agent,’ ‘Rocuronium for Pediatric Patients,’ ‘Neuromuscular Blockers,’ ‘Sugammadex and Neostigmine,’ ‘Role of Analgesics.’ The review followed PRISMA guidelines.

Results. The initial search for publications comparing sugammadex and neostigmine as a reversal agent of rocuronium for pediatric patients yielded 9000 papers, from which 600 were selected. The reviews' articles were further analyzed to ensure they were pertinent to the Comparative Impact of Reversal Agents (Sugammadex And Neostigmine) of Rocuronium for Pediatric Patients. Around 319 references were examined for their potential applicability to the medical field of anesthesia. A total of 15 articles were included, with preference given to those published from 2014 to 2023 during the last ten years.

Conclusion. The particular relaxant-binding medication promptly and successfully alleviates rocuronium-induced neuromuscular blockade in pediatric surgery patients. Considering the study’s outcomes, it can be concluded that sugammadex may restore any level of steroidal muscle relaxant-induced neuromuscular block faster than neostigmine.

Keywords

Analgesics, Central Nervous System, Muscle Relaxants, Neuromuscular Blockers, Neostigmine, Pediatric Patients, Pain, Reversal Agents, Surgery, Sugammadex

Imprint

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Introduction

Surgical trauma may be followed by discomfort, ileus, stress-induced catabolism, nausea, vomiting, higher cardiac demands, risk of thrombosis, and reduced pulmonary function (1). These issues may result in complications, the need for hospitalization, postoperative tiredness, and a protracted recovery period (1). Significant possibilities for improved recovery have been made possible by developing safe and fast-acting anesthetics, enhanced pain management by effective multimodal analgesia, and stress reduction through localized anesthetic techniques, β-blockade, or glucocorticoids (1). It is possible to significantly improve recovery and minimize hospital stays, even after major procedures, when these techniques are used in conjunction with a change in postoperative care (1). The anesthesiologist is critical in promoting early postoperative recovery by providing minimally invasive anesthesia and pain relief, coordinating with surgeons, surgical nurses, and physiotherapists to reduce risk and discomfort, and providing minimally invasive anesthesia and pain relief (1).
The word anesthesia means “insensibility” (2) and describes the loss of sensation in all or any body parts. Drugs that suppress the activity of nerve tissue locally, regionally, or within the Central Nervous System (CNS) (3) are used to produce anesthesia (2). The term “general anesthesia” has evolved a considerable pharmacological modification. General anesthetics include central nervous system stimulants and depressants (2, 3). Anesthesia operates by suppressing nervous system signals. The brain, spinal cord, and nerves make up the nervous system. The spinal cord and nerves carry signals from the body to the brain (4). Anesthesia prevents the brain from receiving pain signals. Analgesic drugs are employed to alleviate patients’ pain. For safe and empathetic patient care, anesthetics, sedatives, and analgesics can reduce pain, induce amnesia, and cause muscular relaxation (2, 3).

General anesthesia, regional anesthesia, sedation (sometimes known as “monitored anesthesia care”), and local anesthesia are the four basic types of anesthetic used during surgery and other operations (5, 6).

Table 1. indicates four primary types of anesthesia employed during surgeries and medical patient care. The varied applications of anesthesia (including immobilization, muscular relaxation, and antinociception) and the needs specific to each species, age group, and illness condition are required for using a range of medicines, pharmacological combinations, and techniques. Table 2. describes the type of drug or the method of drug delivery is frequently used to categorize anesthetic techniques (2):

The surgical and anesthesiological fields have undertaken several endeavors in subsequent years to enhance postoperative results and reduce morbidity and discomfort (1). During surgical procedures, the neuromuscular blocker has long been employed (7). Neuromuscular blockers, analgesics, and sedatives are significant among all the medications used for general anesthesia (7, 8) and facilitate anesthetics in the perioperative period (9). However, neuromuscular block-

Table 1

<table>
<thead>
<tr>
<th>Anaesthesia</th>
<th>Types</th>
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</thead>
<tbody>
<tr>
<td>General Anaesthesia</td>
<td></td>
</tr>
<tr>
<td>Regional Anaesthesia</td>
<td></td>
</tr>
<tr>
<td>Sedation Anaesthesia</td>
<td></td>
</tr>
<tr>
<td>Local Anaesthesia</td>
<td></td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>S.No</th>
<th>Categories</th>
<th>Characterizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Inhalation</td>
<td>Combining oxygen inhalation with anesthetic gases or vapors</td>
</tr>
<tr>
<td>02</td>
<td>Injectable</td>
<td>Subcutaneous, intramuscular, and intravenously administered anesthetic injections</td>
</tr>
<tr>
<td>03</td>
<td>Total Intravenous Anesthesia (TIVA), Partial Intravenous Anesthesia (PIVA), and Targeted Controlled Infusion (TCI)</td>
<td>A method of anesthesia that creates an appropriate anesthetic state through the intravenous infusion of one or more drugs.</td>
</tr>
<tr>
<td>04</td>
<td>Oral or Rectal</td>
<td>Usually, liquid anesthetics, analgesics, or suppositories are administered via these channels.</td>
</tr>
<tr>
<td>05</td>
<td>Local and Conduction</td>
<td>Anesthetic medication can be given topically, locally, or around a nerve trunk.</td>
</tr>
<tr>
<td>06</td>
<td>Electronarcosis, Electroanesthesia, or Electrosleep</td>
<td>Deep narcosis is induced by transmitting electrical currents through the brain.</td>
</tr>
<tr>
<td>07</td>
<td>Transcutaneous Electrical Nerve Stimulation (TENS, TNS, or TES)</td>
<td>Low-intensity, high-frequency electric skin stimulation through surface electrodes results in local analgesia.</td>
</tr>
<tr>
<td>08</td>
<td>Hypnosis</td>
<td>Sometimes a non-drug-induced trance state is used</td>
</tr>
<tr>
<td>09</td>
<td>Twilight anesthesia</td>
<td>A severe sedation state is characterized by the patient’s cooperativeness, limited or no recall, and consciousness (amnesia).</td>
</tr>
<tr>
<td>10</td>
<td>Acupuncture</td>
<td>An approach of therapy that uses long, thin needles to relieve pain</td>
</tr>
<tr>
<td>11</td>
<td>Hypothermia</td>
<td>Low body temperature reduces insensitivity, the need for anesthetic drugs, and lower metabolic demands.</td>
</tr>
</tbody>
</table>
ers are intended to specifically block nicotinic cholinergic receptors at the neuromuscular junction (8). The administration of the neuromuscular blockers provided to ensure favorable surgical conditions may be complicated by medications given to patients undergoing anesthesia (10). Local anesthetics impede nerve transmission due to their impact on voltage-dependent sodium channels, which reduce neuromuscular conduction. They can also lower receptor sensitivity to ACh, inhibit calmodulin-dependent processes, and impede presynaptic feedback, inhibiting ACh synthesis, mobilization, and release (10).

In the modern idea of balanced anesthesia, muscle relaxants are widespread. They can be classified into depolarizing (like succinylcholine) and non-depolarizing (like benzylisoquinoline and steroid-based) muscle relaxants (11). Although Neuromuscular Blocking (NMB) offer better intubating circumstances, care should be taken when using them in challenging airway conditions because even fast-acting rocuronium or succinylcholine with sugammadex reversal (12) has an unacceptable ventilatory depression risk that is particularly high in obese and severely obese people (7). Postoperative residual neuromuscular blockade issues, which may be associated with airway obstruction, hypoxia, increased mortality, and pulmonary complications, have been emphasized (13) despite the widespread use of Neuromuscular Blocking Drugs (NMBDs) or Neuromuscular blocking agents (NMBA) to facilitate surgical procedures and tracheal intubation during anesthesia. After surgery, the neuromuscular blockade must be quickly and completely reversed (13).

Sugammadex is the inaugural clinical drug in a new class of medication known as selective relaxant binding agents (12, 14). Sugammadex is a ring-shaped modified gamma-cyclodextrin reversal agent that binds to steroidal NMBs in a 1:1 ratio (15), with rocuronium having a 2.5 times stronger affinity (14, 16, 17). Sugammadex may potentially replace succinylcholine as the “gold standard” muscle relaxant (14) for rapid sequence induction because of its pharmacodynamic profile when combined with rocuronium (14, 17). In patients with reduced neuromuscular transmission, i.e., neuromuscular disorders such as myasthenia gravis, the administration of rocuronium or vecuronium (17), with the possibility of their actions being reversed with sugammadex appears to be safe (14). According to studies done on surgical patients, sugammadex quickly and effectively reverses the neuromuscular blockade caused by rocuronium (13). Sugammadex can also counteract the effects of vecuronium, which is similar to rocuronium (13). Sugammadex has been contrasted with acetylcholinesterase inhibitors, particularly neostigmine (18, 19). Neostigmine is slower to work than sugammadex in reversing NMBs. Sugammadex starts working between 3 and 18 times more quickly than neostigmine (7, 16, 20). Neostigmine and edrophonium are acetylcholinesterase inhibitors that reverse non-depolarizing neuromuscular inhibition (13). Furthermore, no widely utilized reversal medications, including neostigmine and edrophonium, can reverse substantial blockade. Sugammadex only or along with these is used for treating severe neuromuscular blockade (NMB) in children undergoing surgery (21).

Sugammadex promptly binds free intravascular rocuronium after being given intravenously (central compartment) (12). This causes a concentration gradient that moves rocuronium from the peripheral compartments, such as the effect compartment or the neuromuscular junction, to the central compartment, similarly enclosed in sugammadex (22). As a result, muscle activity and neuromuscular transmission are quickly recovered. Hence, a greater sugammadex dose is preferable to a smaller one to reduce the plasma level of free rocuronium (14). The pharmacokinetics of sugammadex exhibit a linear, dose-dependent relationship in the dosing range of 0.1 to 16 mg/kg (14). Pediatric patients’ responses to muscle relaxants and how quickly they recover from neuromuscular block depend greatly on their age (23). The doses advised for adults appear to be just as effective but have a quicker onset time and a relatively constrained range of individual responses. Sugammadex has been authorized for usage in children above the age of two (24-26) at a dose of 2 mg/kg to reverse a moderate (TOF count > 2) neuromuscular block (23, 27). Sugammadex and neostigmine are reversal agents or used as drugs to combat the effect of anesthesia after surgery, and their efficacy and safety were also estimated in pediatric patients (28, 29). Compared to Neostigmine, Sugammadex significantly assists pediatric patients in recovering from rocuronium-induced neuromuscular blockade (25, 30, 31). In pediatric patients, rocuronium-induced NMB can be quickly and effectively reversed by sugammadex (30). There are three methods for administering the neuromuscular block if a patient...
needs a second procedure after taking sugammadex: succinylcholine, atracurium, cisatracurium, or mivacurium, benzylisoquinoline muscle relaxants, or rocuronium’s second usage (32, 33).

This systematic review aims to determine the impact of sugammadex and neostigmine comparison as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anesthesia.

**Abbreviations:** Central Nervous System (CNS); Neuromuscular Blocking (NMB); Neuromuscular Blocking Drugs (NMBDs); Neuromuscular blocking agents (N MBA); Train-of-Four (TOF); General Anesthesia (GA).

**Material and Method**

**Search Strategy**

In order to execute this review, recent research and review articles/publications based on the comparative study between sugammadex and neostigmine as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anesthesia were considered. Data was gathered from Google Scholar, PubMed, Web of Science, NCBI, Hindawi, Critical Care Medicine, PLoS ONE, National Library of Medicine, ResearchGate, Internal Medicine Journal, Journal of Medical Internet Research, MEDLINE, EMBASE database, ScienceDirect, Scopus, Anesthesiology, European Journal of Anaesthesiology, Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI), and BioMed.

For this study, we searched through the literature to find articles that addressed the role of sugammadex and neostigmine as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anesthesia. Studies were selected from different years ranging between 2014 to 2023 using keywords 'General Anesthesia,' 'Anesthesia,' 'Anesthesia in Neuromuscular Disorders,' 'Sugammadex,' 'Neostigmine,' 'Reversal Agent,' 'Rocuronium for Pediatric Patients,' 'Surgery under General Anaesthesia,' 'Comparison between Sugammadex and Neostigmine as a Reversal Agent,' 'Neuromuscular Blockers,' 'Sugammadex and Neostigmine Neuromuscular Blockers,' 'Role of Analgesics,' 'Rocuronium for Surgery under General Anaesthesia.' Access was made to the whole texts of the articles that were found. PRISMA guidelines were followed for this review.

At first, 13,000 results were given, upon which search filters such as year of publication, field of expertise, and article type were applied. The custom range of years was set within the last ten years, from 2014 to 2023, so the results were shortened by 9000. Furthermore, 8400 results were extracted for various reasons, as discussed in figure 01 below. However, two relevant articles were separated for future reference. Specific terms were employed, as discussed above, for the literature search purposes. The final results from which we collected our research were 600. The final 15 articles were selected for the investigation and examination that is utilized and based on this systematic review.

The SPIDER framework was employed to determine which studies to include in this systematic review, as shown in Table 3. The PICO model was also used to evaluate databases, as shown in Table 5.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>SPIDER Framework</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample</strong></td>
<td>Adults, Pediatrics, Global</td>
</tr>
<tr>
<td><strong>Phenomenon of Interest</strong></td>
<td>Impact of Sugammadex and Neostigmine as reversal agents during surgery under general Anesthesia.</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Review of already published articles using search engines.</td>
</tr>
<tr>
<td><strong>Evaluation</strong></td>
<td>Reversal Agents Efficacy.</td>
</tr>
<tr>
<td><strong>Research Type</strong></td>
<td>Case reports, controlled studies, cohort, randomized controlled clinical trials, double-blinded trials, retrospective and prospective randomized studies and analyses, systematic reviews, meta-analyses, randomized control trials, multicenter controlled trials, and qualitative analysis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Data selection strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Years</strong></td>
<td>2014-2023</td>
</tr>
</tbody>
</table>
| **Search Engines** | • Google Scholar  
• PubMed  
• NCBI  
• Hindawi  
• BioMed  
• PLoS ONE  
• Web of Science  
• Journal of Medical Internet Research  
• MEDLINE  
• EMBASE  
• ScienceDirect  
• Scopus  
• Anesthesiology  
• European Journal of Anaesthesiology |
| **Keywords** | • General Anesthesia  
• Anesthesia  
• Anesthesia in Neuromuscular Disorders  
• Sugammadex  
• Neostigmine  
• Reversal Agent  
• Rocuronium for Pediatric Patients  
• Comparison between Sugammadex and Neostigmine as a Reversal Agent  
• Neuromuscular Blockers |
### Table 5

<table>
<thead>
<tr>
<th>PICO Model</th>
<th>Search strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Adults, Pediatrics.</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>To reverse a moderate (TOF count &gt; 2) neuromuscular block, sugammadex is approved for usage in children older than 2 years old at a 2 mg/kg dose.</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>Neostigmine, Succinylcholine, Atracurium, Cisatracurium, Or Mivacurium, Benzylisoquinolone.</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>To counteract the effects of analgesics, anesthetics, or potentially dangerous drugs.</td>
</tr>
</tbody>
</table>

### Inclusion Criteria

The following addition and omission criteria were used to filter the titles rather than study relevance. We only selected those studies submitted to peer-reviewed journals for approval that were already published. These studies were taken into consideration to understand the research criteria better.

- All English-language research published in peer-reviewed publications was included for review.
- Studies describing anesthesia practices were included.
- Studies related to anesthesia during surgery and operations were included.
- Studies on assessing neuromuscular blockers’ impact were also considered.
- Reviews of recent developments in anesthesia.
- Studies between the comparison of sugammadex and neostigmine as a reversal agent were included in the review.
- Studies related to Surgeries under General Anaesthesia were also considered.
- Impact of reversal agents of Rocuronium for Pediatric Patients 2-12 Years Old was reviewed.
- Studies based on adults and pediatrics were included.
- This study includes randomized controlled trials of sugammadex vs. neostigmine for reversing neuromuscular blockade.
- The study included randomized controlled clinical trials, double-blinded trials, retrospective and prospective randomized studies and analyses, systematic reviews, meta-analyses, case reports, randomized control trials, and multicenter controlled trials.

### Exclusion Criteria

The exclusion criteria involve:

- Papers written in languages other than English were excluded.
- Studies focusing solely on the negative impact of anesthesia were excluded.
- Papers not aimed at anesthesia and the advancement of its treatment were excluded from the review.
- The objective was unrelated to anesthesia and its positive impact on reducing pain.
- Papers related to anesthesia and neuromuscular blockers but whose main objective was unrelated to assessing the comparison between sugammadex and neostigmine as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anesthesia were excluded from the review.
- Duplicate studies were excluded.
- Studies lacking predefined findings’ supporting data.
- Studies whose titles were related to the study but whose text was not relatable were excluded from the review.

The outcomes of this systematic review have been summarized and made explicit by exclusion and inclusion criteria. Articles that did not meet the inclusion requirements were excluded, duplicate records were eliminated, records with irrelevant titles, abstracts, and keywords were removed, and articles for which no full text was available were also excluded. Among the 9000 research, 600 were retrieved, and 8400 papers were eliminated due to their no direct relevance to the study’s main goal and were written primarily in languages other than English, most commonly Arabic, French, Spanish, and Dutch.

### Data Extraction

Using Microsoft Excel, the researcher extracted and sorted the sample size, study type, duplicates, full-text articles, and empirical studies, making the systematic review approach practicable. The reason for the exclusion and reduction of data is depicted in the flowchart, as seen in figure 1.

### Results

The initial search for publications concerning the comparison between sugammadex and neostigmine as a reversal agent of rocuronium for pediatric pa-
tients 2-12 years old going for surgery under general anesthesia yielded 9000 papers, from which 600 were selected. The reviews’ articles were further analyzed to ensure they were pertinent to assessing the impact of sugammadex and neostigmine as a reversal agent. Around 319 references were examined for their potential applicability to the medical field of anesthesia. A total of 15 articles were included, with preference given to those published during the last ten years, from 2014 to 2023. Figure 01 illustrates the PRISMA 2023 article identification flowchart, displaying the systematic review’s many stages in identifying studies.

Figure 1 comprises the flowchart for the studies that have been reviewed. A search of the reviewed literature resulted in 9000 articles, of which 4300 duplicates were removed. Records identified after automation tools were 600, from which 281 articles were excluded after screening the titles and abstract. Reports accessed for eligibility were 319. Based on languages other than English, 85 studies were excluded. Moreover, 219 studies were removed for other reasons leaving 15 eligible studies for inclusion.

Systematic Overview

Figure 2 indicates the strategies involved in systematic review writing. Research study types include systematic reviews. Integrating the findings from all previous scientific studies, it aims to respond to a particular research question. This offers evidence that is more convincing and reliable than the findings of individual investigations. When performing systematic reviews, the objective is to analyze the thorough,

![Identification of studies via databases and registers diagram]

Figure 1. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses
systematic, exacting, and clear literature. Additionally, a method based on and modified from Cochrane's method was employed, as shown in figure 02. These 15 steps are essential for effectively determining the concept and objective of the research topic.

**Discussion**

In the modern interpretation of balanced anesthesia, neuromuscular blockade (NMB) is frequently utilized worldwide to aid in endotracheal intubation and maintain patient immobility throughout the surgery (21). Muscle relaxation is necessary during surgery to facilitate the surgical operation with a sufficient anesthetic intensity; nevertheless, this muscle relaxation must be entirely reversed following the surgery (30). If the complete reversal is not accomplished properly, postoperative residual neuromuscular blockade (NMB) can induce atelectasis, desaturation in the lungs, problems with vision, and delayed recovery (30). Any medicine used to reverse the effects of anesthetic agents, narcotics, or potentially toxic drugs is called a reversal agent (34).

A Study (30) observed that pediatric patients demonstrated considerable age-dependent variability in their response to muscle relaxants and NMB reversal medications, in contrast to adult patients (30). Variations in the pharmacokinetic and pharmacodynamic characteristics of the medications in patients of various age groups are responsible for this variability (30). This meta-analysis demonstrated that sugammadex significantly reduces the rocuronium-induced NMB reversal time and extubation time in pediatric patients undergoing general anesthesia surgery, with similar postanesthetic side effects, compared to neostigmine or a placebo (30).

According to (21), sugammadex is a selective relaxant-binding agent that encases the muscle relaxant and makes it inactive, quickly and fully reverses the effects of the neuromuscular blocking drug rocuronium. Since 2008, the European Union has licensed it to treat moderate and severe NMB caused by rocuronium (21). In contrast to neostigmine, this study found that sugammadex at a 4 mg/kg dose was associated with a prompt and full recovery from a deep rocuronium-induced neuromuscular block in pediatric patients undergoing surgical procedures under general anesthesia (21). Sugammadex usage also eliminated the requirement for atropine, an anticholinergic medication. When used to reverse a significant neuromuscular block, Neostigmine produces a slower recovery (21).
Furthermore, (35) evaluated that sugammadex helps reduce the time needed for extubation and the risk of postoperative atelectasis in children having heart surgery, causing fewer negative side effects. Sugammadex for expedited surgery may be effective for kids having cardiac operations (35). Children receiving fast-track cardiac surgery (aged 1-6 years; N=60) were participants in a prospective, randomized, controlled study, the findings revealed by (35). When comparing the sugammadex 4-mg/kg group to the neostigmine plus atropine group, the extubation time and the time to recovery of the train-of-four (TOF) ratio 0.9 were substantially shorter in the sugammadex 4-mg/kg group (P<0.01 for both) in order to reverse the neuromuscular block (NMB) induced on by rocuronium (35).

Moreover, a study conducted by (36) determined that compared to neostigmine, sugammadex 2 mg/kg significantly accelerated the recovery of children and adolescents from mild neuromuscular blockade induced by rocuronium or vecuronium (36). Sugammadex 4 mg/kg reversed profound neuromuscular blockade at about the same time as mild neuromuscular blocking. Sugammadex vs. neostigmine showed no appreciable differences in clinically relevant hypersensitivity, bradycardia, or anaphylaxis (36). These findings support the use of sugammadex in patients 2 to 17 years old to reverse mild and severe neuromuscular blockade carried on by rocuronium and vecuronium (36).

Additionally, (37) examined the effect of reversal agents. It determined that when used as directed, rocuronium is immediately reversed by sugammadex, while vecuronium causes significant and profound NMB to take effect within three minutes of rocuronium 1.2 mg/kg. The substantial recovery observed across several patient factors further reinforced the recommendations for dose (37).

Another study (38) described a prospective, randomized, controlled study with 60 healthy pediatric patients receiving elective entropion surgery (aged 1 to 11 years). Compared to the pyridostigmine and glycopyrrolate combination group, the mean time from administration of the reversal agent to achieving TOF ratio >0.9 was substantially shorter in the sugammadex 2 mg/kg group compared to the neostigmine plus atropine group (P=0.002) (24). In addition, another study (41) demonstrated that dexamethasone inhibits sugammadex reversal in human muscle cells with functioning innervation. The findings of a prospective, randomized, double-blind, controlled study examining the effect of dexamethasone administered after induction of General Anesthesia (GA) revealed no effect on the time it took for children undergoing tonsillectomy and adenoidectomy to experience NMB reversal by sugammadex. Adenoidectomy and tonsillectomy in pediatric patients do not significantly impact the reversal time of sugammadex when IV dexamethasone is administered at a dose of 0.5 mg/kg after induction of anesthesia (41).

Furthermore, (42) a prospective observational study (age: 18 years; N=99) on 99 pediatric patients with concomitant cardiac, circulatory, and congenital heart illnesses was conducted. Twenty (20%) patients in all developed bradycardia after receiving sugammadex (six of these patients had bradycardia before re-
ceiving sugammadex), but none of the patients needed to be treated for bradycardia (42). A study by (43) examined the efficacy and safety of sugammadex in pediatric patients undergoing surgery.

Sugammadex accomplishes surgeries more quickly than neostigmine across age categories, with the neonatal population exhibiting a significant variation (43). The findings of an early abstract estimated by (44) outlined the effectiveness and safety of using sugammadex 4 mg/kg in newborns (aged 1 day [n=8] and 1-7 days [n=15]; N=23). Sugammadex showed a rapid reversal of significant rocuronium-induced NMB in both age groups (44). Rocuronium is a neuromuscular-blocking drug frequently used in clinical anesthesia and given to patients of all ages, including infants.

The first selective relaxant binding agent, Sugammadex, was developed to reverse a neuromuscular block imposed by either rocuronium or vecuronium. Sugammadex showed significance as a reversal agent (44).

Moreover, a prospective study (45) showed the significance of sugammadex as a reversal agent in pediatric patients. Sugammadex, a specific antagonist of steroidal non-depolarizing neuromuscular blocking drugs, is occasionally administered to children. Sugammadex or neostigmine was given erratically after it was confirmed that there was no post-tetanic count in the 40 children who had surgery. Plasma concentrations were assessed two minutes after the rocuronium injection, and the response to train-of-four stimulation was continually monitored. A three-compartment PK model was created, and it took an average of 1.1 (IQR: 0.88–1.8) min from the administration of 8 mg/kg to the recovery of T4/T1 greater than or equal to 0.9. No unfavorable incidents were noticed (45).

At last, this study can be summarized by describing the efficacy and safety of reversal agents used in clinical practices. A study (46) evaluated the pharmacokinetics and metabolism of reversal agents. The study's literature determined the efficiency of sugammadex and described that the rocuronium/vecuronium-sugammadex combination that was recently synthesized is extremely stable and unaffected by temperature or pH. Sugammadex has a half-life of elimination of around 100–150 min. It is not absorbed by the body and is eliminated by the kidneys at roughly 75 to 120 ml per minute, equivalent to the average glomerular filtration rate. The body quickly excretes sugammadex (46). Different sugammadex doses are advised depending on the muscle relaxant employed and the intensity of the neuromuscular block at the time of reversal.

The doses should quicken the recovery from the neuromuscular block in an average of 3 minutes to a TOF ratio of 0.9 (46). Children's responses to muscle relaxants and recovery rates from neuromuscular block vary greatly depending on age. Sugammadex was approved for use in children older than 2 years old and exclusively for reversal, with a dose of 2 mg/kg of a moderate (TOF count of >2) neuromuscular block. Sugammadex should be administered “off-label” to pediatric patients in an emergency as long as quantitative neuromuscular monitoring is deployed (46).

According to this in-depth study and screening process, the articles selected for the systematic review are associated with the impact of sugammadex and neostigmine comparison as a reversal agent of rocuronium for pediatric patients 2-12 years old going for surgery under general anesthesia as seen in Table 6.

Table 6
Showing the List of Studies Included in this Systematic Review

<table>
<thead>
<tr>
<th>S.No</th>
<th>Title</th>
<th>Author</th>
<th>Year</th>
<th>Conclusion</th>
<th>Reference No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Comparative study between sugammadex and neostigmine in neurosurgical anesthesia in pediatric patients.</td>
<td>Ghoneim, A. A., &amp; El Beltagy, M. A.</td>
<td>2015</td>
<td>When given at the recurrence of T2 of TOF at a dose of 4 mg/kg, sugammadex quickly and successfully reverses rocuronium-induced NMB in pediatric patients undergoing neurosurgery.</td>
<td>21</td>
</tr>
<tr>
<td>02</td>
<td>Sugammadex for reversal of rocuronium-induced neuromuscular blockade in pediatric patients: a systematic review and meta-analysis</td>
<td>Won, Y. J., Lim, B. G., Lee, D. K., Kim, H., Kong, M. H., &amp; Lee, I. O.</td>
<td>2016</td>
<td>We propose sugammadex as a quick and efficient treatment for pediatric patients with rocuronium-induced NMB. Although there was no evidence that sugammadex had a greater frequency of adverse events than neostigmine or a placebo, there may still be a need for more information about the medication's safety in pediatric patients.</td>
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<td>S.No</td>
<td>Title</td>
<td>Author</td>
<td>Year</td>
<td>Conclusion</td>
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<td>03</td>
<td>Sugammadex for fast-track surgery in children undergoing cardiac surgery: a randomized controlled study.</td>
<td>Li, L., Jiang, Y., &amp; Zhang, W.</td>
<td>2021</td>
<td>Sugammadex can minimize postoperative atelectasis incidence and extubation duration with fewer negative outcomes in pediatric heart surgery patients. Sugammadex for accelerated surgery may be advantageous for kids having heart surgery.</td>
<td>35</td>
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<td>04</td>
<td>Sugammadex for reversal of neuromuscular blockade in pediatric patients: Results from a phase IV randomized study.</td>
<td>Voss, T. Wang, A., DeAngelis, M., Speek, M., Saldien, V., Hammer, G. B., &amp; Herring, W. J.</td>
<td>2022</td>
<td>Sugammadex 2 mg/kg significantly accelerated the recovery of pediatric participants from moderate neuromuscular blockade brought on by rocuronium or vecuronium compared to neostigmine. Sugammadex 4 mg/kg took about the same time to reverse deep neuromuscular blockade.</td>
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<td>05</td>
<td>Sugammadex efficacy for reversal of rocuronium- and vecuronium-induced neuromuscular blockade: a pooled analysis of 26 studies.</td>
<td>Herring, W. J., Woo, T., Assaid, C. A., Lupinacci, R. J., Lemmens, H. J., Bloibner, M., &amp; Khuenl-Brady, K. S.</td>
<td>2017</td>
<td>When rocuronium and vecuronium are used as directed, sugammadex quickly and predictably reverses moderate and profound NMB, with an effective reversal occurring 3 minutes after rocuronium 1.2 mg/kg. Multiple patient characteristics showed robust recovery, supporting the stated dose recommendations.</td>
<td>37</td>
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<td>06</td>
<td>Comparison of sugammadex and pyridostigmine bromide for reversal of rocuronium-induced neuromuscular blockade in short-term pediatric surgery: A prospective randomized study.</td>
<td>An, J., Lee, J. H., Kim, E., Woo, K., Kim, H., &amp; Lee, D.</td>
<td>2020</td>
<td>Sugammadex reversed rocuronium-induced neuromuscular blockade more quickly than pyridostigmine with glycopyrrolate did in pediatric patients having surgery lasting 30 to 60 minutes, with no difference in the frequency of adverse events between the two groups.</td>
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<td>07</td>
<td>Effects of sugammadex on postoperative respiratory management in children with congenital heart disease: a randomized controlled study.</td>
<td>Xiaobing L, Yan J, Wangping Z, Rufang Z, Jia L, Rong W.</td>
<td>2020</td>
<td>Sugammadex considerably shortens the time needed to extubate children with congenital heart problems, reverses rocuronium-induced neuromuscular block, and releases postoperative CRP and PCT.</td>
<td>39</td>
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<td>08</td>
<td>Reversibility of Rocuronium-Induced Deep Neuromuscular Block with Sugammadex in Infants and Children-A Randomized Study.</td>
<td>Matsui M, Konishi J, Suzuki T, Sekijima C, Miyazawa N, Yamamoto S.</td>
<td>2019</td>
<td>The findings suggested that even in infants and children, a sugammadex dose of 4 mg kg⁻¹ is advised for recovery from rocuronium-induced profound neuromuscular block.</td>
<td>40</td>
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<td>09</td>
<td>A comparison of sugammadex and neostigmine for reversal of rocuronium-induced neuromuscular blockade in children.</td>
<td>Ammar, A. S., Mahmoud, K. M., &amp; Kasemy, Z. A.</td>
<td>2017</td>
<td>Compared to neostigmine, the administration of sugammadex to children led to quicker extubation and recovery times and a lower frequency of side events.</td>
<td>24</td>
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<td>10</td>
<td>The effect of intravenous dexamethasone on sugammadex reversal time in children undergoing adenotonsillectomy.</td>
<td>Gulec, E., Biricik, E., Turkten, M., Hatipoglu, Z., &amp; Unlugenc, H.</td>
<td>2016</td>
<td>Adenoidectomy and tonsillectomy in pediatric patients do not significantly impact the reversal time of sugammadex when IV dexamethasone is administered at a dose of 0.5 mg/kg after induction of anesthesia.</td>
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<td>11</td>
<td>Heart Rate Changes Following the Administration of Sugammadex to Infants and Children With Comorbid Cardiac, Cardiovascular, and Congenital Heart Diseases.</td>
<td>Arends J, Hubbard R, Shafy SZ, Hakim M, Kim SS, Tumin D, Tobias JD.</td>
<td>2020</td>
<td>Sugammadex was rarely associated with bradycardia after treatment, even in patients with congenital heart disease. There was no need for treatment because bradycardia was not linked to clinically significant hemodynamic abnormalities.</td>
<td>42</td>
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<td>12</td>
<td>Retrospective Analysis of the Safety and Efficacy of Sugammadex Versus Neostigmine for the Reversal of Neuromuscular Blockade in Children.</td>
<td>Gaver RS, Brenn BR, Gartley A, Donahue BS.</td>
<td>2019</td>
<td>The results of this study suggest the safe and effective use of sugammadex for treating neuromuscular blockade in pediatric patients of all ages. Sugammadex completes operations more quickly than neostigmine across age categories, with the neonatal population showing the biggest difference.</td>
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Limitations
- Most of the screened articles were not in English and were unreachable.
- Sugammadex acts faster than neostigmine, which is effective for pediatric patients to reverse the effect of anesthesia and bring consciousness timely.
- In patients, sugammadex provides a substantially faster, more predictable, and safer recovery profile from neuromuscular blockade than neostigmine.

The limitations of the study were these considerations.

Recommendations
- Sugammadex is approved for use in children above two at a 2 mg/kg dose to reverse rocuronium-induced neuromuscular blockade (NMB).
- There are three methods for administering the block: succinylcholine, atracurium, and benzylisoquinoline muscle relaxants.

Conclusion
In pediatric surgical patients, rocuronium-induced neuromuscular blockade is quickly and effectively reversed by the specific relaxant-binding drug sugammadex. Further pediatric studies will be required to assess sugammadex’s effectiveness and safety in this group of patients, especially infants under 2 years, particularly when higher amounts of neuromuscular blockers are required. Considering the study’s outcomes, it can be concluded that the steroidal muscle relaxant encapsulator Sugammadex is the first medication in this class to show effectiveness in clinical studies. Compared to Neostigmine, it may quickly reverse any degree of neuromuscular block caused by steroidal muscle relaxants. Sugammadex has transformed how anesthetists view medication reversal and dose-response management in pharmaceuticals. Its intravascular and receptor-distant mechanisms offer significant benefits over the cholinesterase inhibitors, the traditional antagonists of muscle relaxants. With only a few contraindications, it is safe for usage in a massive patient group.

Competing Interest
The review authors declare no competing interest.

References


