



Research article

Safety and efficacy of sugammadex in management of patients with myasthenia gravis undergoing general anesthesia: A systematic review

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ABSTRACT

Objective: The objective of this study was to analyze available evidence on efficacy and safety of sugammadex in reversing neuromuscular blockades in patients with Myasthenia Gravis (MG), thereby providing a comprehensive understanding of its potential benefits and risks in this specific patient population.

Methods: We performed a systematic search for studies from PubMed, Embase, Web of Science, and Google Scholar. Sources were screened using Rayyan, following predefined inclusion and exclusion criteria focusing on English articles published from 2010 to 2024 on MG patients under general anesthesia. Data on patient characteristics and outcomes were extracted, and quality was appraised using the JBI Critical Appraisal Checklist.

Results: Out of 361 initial citations, 24 studies met inclusion criteria. Sugammadex demonstrated rapid and effective reversal of neuromuscular blockades, with ToF recovery times ranging from 79.7 s to 10 min, and short extubation times. The incidence of postoperative myasthenic crisis was low, and no mortalities were reported.

Conclusion: Sugammadex may serve as a reasonable option for the reversal of neuromuscular blockades in MG patients, indicating potential for rapid recovery and a relatively low incidence of serious complications. However, due to the limited number of studies and the nature of the evidence available, further large-scale and rigorous investigations are warranted to better establish its superiority over traditional reversal agents.

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1. Introduction

Myasthenia Gravis (MG) is a common autoimmune disease affecting the neuromuscular junction, characterized by generalized muscle weakness that worsens with activity. It occurs when autoantibodies attack the neuromuscular junction, most commonly targeting acetylcholine receptors (AChR), but also muscle-specific kinase (MuSK) and lipoprotein receptor-related protein 4 (LRP4). These attacks result in muscle weakness that can be either localized or throughout the body. Common presentations include extraocular muscle weakness, bulbar muscle weakness, and limb weakness. Myasthenic crisis is a life-threatening complication of MG that can lead to respiratory failure in about 15 % of patients. Though it can affect anyone with MG, patients with bulbar and respiratory muscle involvement face a higher risk [1]. Treatment options for MG include medications (acetylcholinesterase [AChE] inhibitors, immunosuppressants, and monoclonal antibody therapies), intravenous therapies, and thymectomy for patients with AChR MG [2].

Managing general anesthesia in patients with MG presents unique challenges related to reduced availability of acetylcholine (ACh). These patients are often resistant to depolarizing neuromuscular blocking agents (NMBAs), such as succinylcholine, and highly sensitive to non-depolarizing agents, such as rocuronium or vecuronium. Consequently, meticulous care is required during the induction and maintenance of general anesthesia involving paralytics [3]. Traditional reversal agents for NMBAs include AChE inhibitors, such as neostigmine. These drugs can predispose to complications like postoperative residual neuromuscular block and cholinergic crisis, which results from overstimulation at the neuromuscular junction, leading to bronchospasm, miosis, increased peristalsis, and secretions [4].

Alternatively, Sugammadex, a modified gamma-cyclodextrin, can selectively reverse the effects of steroidal NMBAs like rocuronium without interacting with ACh-R or AChE. This novel reversal agent has shown promise in providing rapid and effective reversal of

Table 1
Literature search instructions.

	Databases (total 3)	Search Terms	Results (total = n)
PubMed	("sugammadex "[MeSH Terms] OR "sugammadex "[All Fields] OR ("sugammadex "[MeSH Terms] OR "sugammadex "[All Fields] OR "bridion"[All Fields]) OR "Org 25969"[All Fields] OR ("modifiable"[All Fields] OR "modified"[All Fields] OR "modifier"[All Fields] OR "modifiers"[All Fields] OR "modifies"[All Fields] OR "modify"[All Fields] OR "modifying"[All Fields]) AND ("gamma cyclodextrin"[Supplementary Concept] OR "gamma cyclodextrin"[All Fields] OR "gamma cyclodextrin"[All Fields])) AND ("myasthenia gravis"[MeSH Terms] OR ("myasthenia"[All Fields] AND "gravis"[All Fields]) OR "myasthenia gravis"[All Fields] OR ("myasthenia"[All Fields] OR "myasthenias"[All Fields]) OR ("myasthenia"[All Fields] OR "myasthenias"[All Fields]) OR ("thymoma"[MeSH Terms] OR "thymoma"[All Fields] OR "thymomas"[All Fields]) OR ("musk"[Supplementary Concept] OR "musk"[All Fields] OR "LRP4"[All Fields]) OR "myasthenia gravis"[MeSH Terms] OR ("myasthenia"[All Fields] AND "gravis"[All Fields]) OR "myasthenia gravis"[All Fields] OR "myasthenias"[All Fields] OR "myasthenias"[All Fields]) OR ("thymoma"[MeSH Terms] OR "thymoma"[All Fields] OR "thymomas"[All Fields]) OR ("musk"[Supplementary Concept] OR "musk"[All Fields] OR "LRP4"[All Fields]) OR "sugammadex "[MeSH Terms] OR "sugammadex "[All Fields] OR ("sugammadex "[MeSH Terms] OR "sugammadex "[All Fields] OR "bridion"[All Fields]) OR "Org 25969"[All Fields] OR ("modifiable"[All Fields] OR "modified"[All Fields] OR "modifier"[All Fields] OR "modifiers"[All Fields] OR "modifies"[All Fields] OR "modify"[All Fields] OR "modifying"[All Fields]) AND ("gamma cyclodextrin"[Supplementary Concept] OR "gamma cyclodextrin"[All Fields] OR "gamma cyclodextrin"[All Fields]))	60	60
Embase	('sugammadex '/exp OR 'sugammadex ' OR 'bridion'/exp OR 'bridion' OR 'org 25969'/exp OR 'org 25969' OR ('modifiable' OR 'modified' OR 'modifier'/exp OR 'modifier' OR 'modifiers' OR 'modifies' OR 'modify' OR 'modifying')) AND ('gamma cyclodextrin'/exp OR 'gamma cyclodextrin')) AND (('myasthenia'/exp OR 'myasthenia') AND 'gravis' OR 'myasthenia gravis'/exp OR 'myasthenia gravis' OR 'myasthenia'/exp OR 'myasthenias' OR 'myasthenias' OR 'thymoma'/exp OR 'thymoma' OR 'thymomas'/exp OR 'thymomas' OR 'musk'/exp OR 'musk' OR 'lrp4') AND ('myasthenia'/exp OR 'myasthenia') AND 'gravis' OR 'myasthenia gravis'/exp OR 'myasthenia gravis' OR 'myasthenia'/exp OR 'myasthenia' OR 'myasthenias' OR 'thymoma'/exp OR 'thymoma' OR 'thymomas'/exp OR 'thymomas' OR 'musk'/exp OR 'musk' OR 'lrp4' OR 'sugammadex '/exp OR 'sugammadex ' OR 'bridion'/exp OR 'bridion' OR 'org 25969'/exp OR 'org 25969' OR ('modifiable' OR 'modified' OR 'modifier'/exp OR 'modifier' OR 'modifiers' OR 'modifies' OR 'modify' OR 'modifying')) AND ('gamma cyclodextrin'/exp OR 'gamma cyclodextrin'))	106	106
Web of Science	(ALL=((sugammadex OR sugammadex OR (sugammadex OR sugammadex OR bridion) OR "Org 25969" OR (modifiable OR modified OR modifier OR modifiers OR modifies OR modify OR modifying) AND ("gamma cyclodextrin" OR "gamma cyclodextrin" OR "gamma cyclodextrin")))) AND ALL=((("myasthenia gravis" OR (myasthenia AND gravis) OR "myasthenia gravis" OR (myasthenia OR myasthenias) OR (myasthenia OR myasthenias) OR (thymoma OR thymoma OR thymomas) OR (musk OR musk) OR LRP4)) ALL=((("myasthenia gravis" OR (myasthenia AND gravis) OR "myasthenia gravis" OR (myasthenia OR myasthenias) OR (myasthenia OR myasthenias) OR (thymoma OR thymoma OR thymomas) OR (musk OR musk) OR LRP4))	47	47
Google Scholar	(sugammadex OR bridion OR "Org 25969" OR "modified gamma cyclodextrin") AND ("myasthenia gravis" OR thymoma OR thymomas OR musk OR LRP4 OR myasthenia OR myasthenias)	148	148

neuromuscular blockades in MG patients without triggering a cholinergic crisis [5]. However, most of the existing literature on sugammadex in MG patients consists of case studies or series, limiting the generalizability of the findings. The present investigation, therefore, aims to fill the gap by systematically analyzing available evidence on efficacy and safety of sugammadex in reversing neuromuscular blockades in patients with MG.

2. Methods

A comprehensive search was written for each of the databases searched. Search strings for the terms “sugammadex,” “gamma cyclodextrin,” and “myasthenia gravis” and synonyms were combined (See Table 1.). Due to the low number of citations located on this topic, a string for safety and efficacy was not included in order to prevent unintentionally losing any relevant citations. PubMed (NIH, NLM), Embase.com (Elsevier), Web of Science (Science Citation Index Expanded, Clarivate) were searched. Additionally, a search of Google Scholar was conducted using “Publish or Perish” Version 8 (Harzing). All resulting citations were downloaded on March 27, 2024. The total number of citations before duplicates were removed was 361. After removing duplicates using Systematic Review Accelerator’s “Deduplicator” (RRID:SCR_023365), 255 novel citations remained. These citations were uploaded into Rayyan.ai (RRID:SCR_017584) for screening.

In this systematic review, we performed a systematic search using the following inclusion criteria: (i) articles published from 2010 to present (2024); (ii) eligible patients diagnosed with MG undergoing general anesthesia, regardless of patient age, country, race, and gender; (iii) investigated interventions including neuromuscular blockade reversal with Sugammadex alone or in comparison to Neostigmine. Exclusion criteria are as follows: (i) articles written in a Non-English language; (ii) articles without full-text access, or abstract-only papers; (iii) studies focused on non-human subjects.

Rayyan was used to screen potential studies and utilized two separate reviewers for a first pass screen of the title and abstract of the studies identified by our comprehensive search according to our inclusion and exclusion criteria. Following this, a second pass was conducted by another two independent reviewers with access to the full-text access to ensure all inclusion and exclusion criteria were met and ensure any duplicates were identified, leaving 24 total studies. Any discrepancies were resolved with a fifth independent reviewer acting as a tiebreaker. Information on patient characteristics collected from each study was collected in excel and include the:

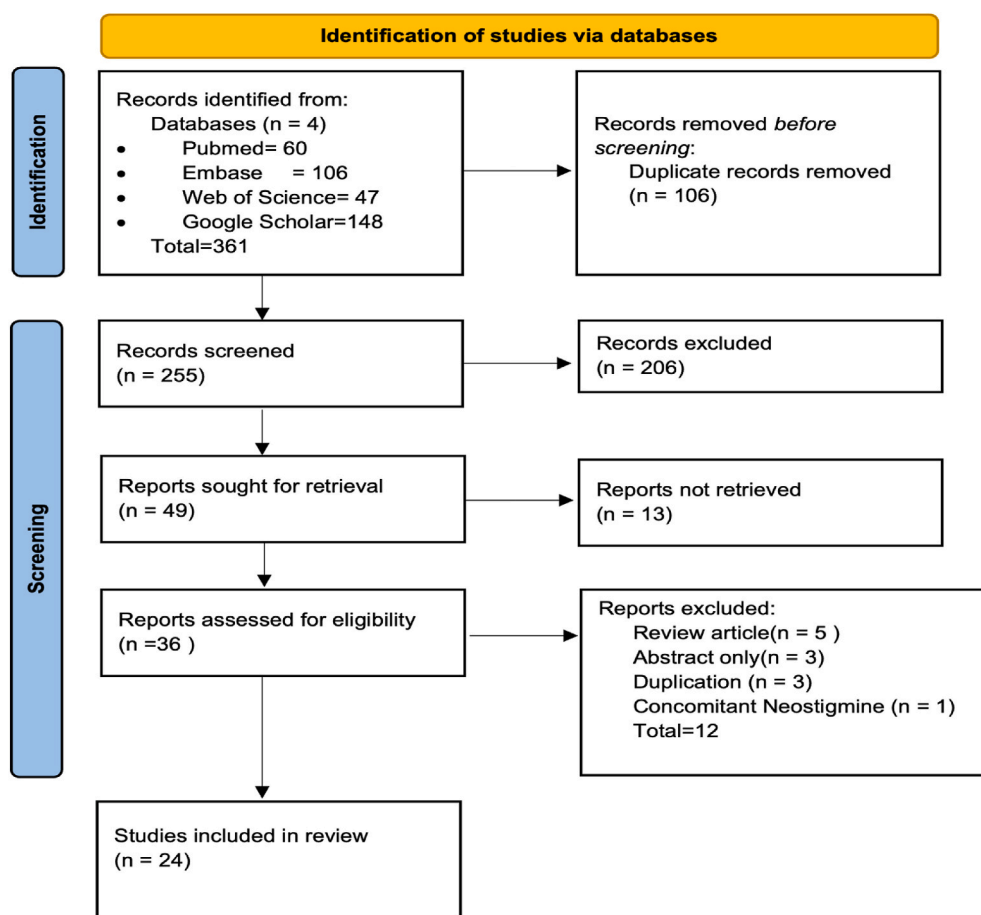


Fig. 1. Study selection flowchart.

(i) type of study, (ii) mean age, (iii) gender and (iv) subgroups of type of surgical encounter. Outcome information collected included (i) time from administration of sugammadex to 90 % recovery of ToF ratio, (ii) time from administration of sugammadex to extubation, (iii) time from administration of sugammadex to spontaneous breathing, (iv) number of in-hospital deaths, (v) use of plasma exchange and immunoglobulins following surgery, (vi) number of postoperative myasthenic crises. Quality appraisal of each study involved utilization of the JBI Critical Appraisal Checklist for the respective study design.

3. Results

3.1. Study selection and characteristics

The selection process (Fig. 1) began with a search of PubMed, Embase.com, Web of Science, and Google Scholar. All results of the search of these programs (resulting in 361 results) were downloaded on March 27th, 2024. Systematic Review Accelerator's "Deduplicator" was used to eliminate duplications, leaving a residual 255 citations which were then uploaded into Rayyan for screening.

The remaining citations underwent two rounds of screening, with two reviewers for each screen. For the first screen, the reviewers were given access to the title and abstract of each citation. After this round was complete, the second round of reviewers was given full access to each complete article. The criteria used in the screening process is as follows:

Inclusion criteria:

- Articles published from 2010 to present (2024)
- Eligible patients diagnosed with MG undergoing general anesthesia, regardless of patient age, country, race, and gender
- Investigated interventions including neuromuscular blockade reversal with sugammadex alone or in comparison to neostigmine, specifically the safety and efficacy of sugammadex

Exclusion criteria:

- Articles written in a Non-English language
- Articles without full-text access, or abstract-only papers
- Studies focused on non-human subjects

There were several studies which would appear to meet the inclusion and exclusion criteria, yet were unable to be accessed. There were several articles that met our criteria upon reading the title and abstract, but the full text was in a non-English language. There

Table 2
Patient characteristics.

Citation	Study Type	Number Treated	Age	Gender (M: F)	Subgroup
No et al. [7]	Retrospective analysis	83	45 ± 8.6	26:57	Thymectomy
Fernandes et al. [8]	Case report	1	27	F	–
Soyoral et al. [9]	Case report	1	28	F	C-section
Tsukada et al. [10]	Retrospective cohort	873	55.3 ± 15.1	369:504	Thymectomy
Mouri et al. [11]	Retrospective observational	506	55 ± 14.1	235:271	–
Shah & Dharmarajah [12]	Case report	1	87	M	–
Vymazal et al. [13]	Case series	117	41.6 (32–68)	50:67	–
de Boer et al. [14]	Case series	21	56 (26–80)	8:13	–
Sungur Ulke et al. [15]	Case series	10	31 ± 12	–	Thymectomy [16]
Kiss et al. [16]	Case report	1	25	F	–
Garcia et al. [17]	Case report	1	35	F	C-section
Jakubiak et al. [18]	Case report	1	38	F	Obese
Petrut et al. [19]	Case study	1	40	F	Laparoscopic abdominal surgery
Unterbuchner et al. [20]	Case report	1	72	M	–
Casarotti et al. [21]	Case report	2	48, 71	M	Rapid sequence induction
Rudzka-Nowak & Piechota [22]	Case report	1	85	M	Abdominal surgery
Argiriadou et al. [23]	Case report	1	31	F	Thymectomy, Obese
Saylon [24]	Retrospective study	30	45.27 ± 15.31	13:17	Thymectomy, MG vs nonMG
Dontukurthy et al. [25]	Case report	1	13	F	JMG
Lai et al. [26]	Case report	1	–	M	Ocular MG
Ertürk et al.	Case report	1	31	F	–
Sugi et al. [27]	Case report	1	26	F	–
Misiolek et al. [28]	Prospective randomized study	22	44.46 ± 17.88 (Group S)	–	Thymectomy
			41.5 ± 15.41 (Group P)		
Rubin & Ramamurthi [29]	Case report	1	3 weeks	M	–

were also several abstract-only papers which were excluded.

Following two rounds of citation screening, 36 citations were selected for further data extraction and quality appraisal. There were several studies here that, following a deep dive, were excluded. One article met our criteria involving sugammadex, but neostigmine was used concomitantly which we believed could confound results [6]. There were also several citations which, upon further investigation, were found to be a review of the literature. Following quality appraisal using JBI Critical Appraisal Checklists, 24 articles were included, and patient characteristics were extracted for each (Table 2).

3.2. Risk of bias assessment

A risk of bias assessment was conducted following the initial screening process, at the time of data extraction and quality appraisal. The remaining 36 citations were divided amongst five reviewers, with each thoroughly reading their given articles and assessing risk. As the majority of citations included in this review were case studies or reports, a certain level of selection bias is unavoidable. This could lead to a lack of generalizability in post operative outcomes of patients with MG who are given sugammadex, as well as overestimate the likelihood of a positive outcome.

Other than the inherent selection bias of case reports, there were a few other instances of bias that contributors to the article made a point to mention. For instance, one study acknowledged the limitations of being unable to adjust for unmeasured confounders such as symptoms, severity, duration of MG, pulmonary function tests, and antibody test results, which could potentially introduce bias in the association between sugammadex and postoperative outcomes [11]. They also mentioned the use of a Japanese nationwide database could limit generalizability as opposed to using a database that is worldwide, or even including information from one other country [11]. Another study included patients from 2007 to 2020, which is a broad range, but this could introduce selection bias if there were any changes in patient characteristics or management strategies over time. They also limited their study to only patients undergoing VATS-thymectomy, which may limit generalizability [7].

There were a few studies where bias appeared transparent but was not mentioned in the limitations. For example, one study had two patients in whom neostigmine was used that did not recover muscle strength sufficient for breathing and had to be mechanically ventilated. These two patients were not included in data analysis, which may underestimate the difference between sugammadex and the control. In this study, the information regarding these patients was included, but the bias was not discussed [28]. This study received a moderate risk of bias but was still included due to high power of the study. Overall, the majority of the citations selected for our review received a low risk of bias.

Table 3
Sugammadex efficacy and complications.

Citation	Time to TOF Recovery	Time to Extubation	Plasma Exchange or Immunoglobulin	Myasthenic Crisis
No et al. [7]	–	–	–	3
Fernandes et al. [8]	~60–70 min	45 min	–	0
Soyoral et al. [9]	–	2 min	–	0
Tsukada et al. [10]	–	–	39 plasma exchange, 17 immunoglobulin	0
Mouri et al. [11]	–	–	–	22
Shah & Dharmarajah [12]	–	–	–	0
Vymazal et al. [13]	117s avg	276s avg	0	0
de Boer et al. [14]	79.1s avg for moderate NMB, 165s avg for deep	–	0	0
Sungur Ulke et al. [15]	111s avg	–	0	0
Kiss et al. [16]	Unsuccessful, given Pyridostigmine after 8 min	–	–	0
Garcia et al. [17]	4 min	48 h, difficulty weaning, undiagnosed MG	–	1
Jakubiak et al. [18]	2 min 48 s	7 min	–	0
Petrún et al. [19]	4 min	10 min	–	0
Unterbuchner et al. [20]	3.5 min	13.5 min	–	0
Casarotti et al. [21]	3 min, 2 min	33 min, 3 h	–	0
Rudzka-Nowak & Piechota [22]	–	6 min	–	0
Argiriadou et al. [23]	3 min	10 min	–	0
Saylon [24]	–	–	–	0
Dontukurthy et al. [25]	10 min	–	–	0
Lai et al. [26]	–	Required reintubation	5x plasma exchange	1
Ertürk et al.	–	4 min	–	0
Sugi et al. [27]	Unsuccessful, given Neostigmine	–	–	0
Misiolek et al. [28]	–	35s avg (Group S) 174.29s avg (Group P)	0conf	0
Rubin & Ramamurthi [29]	5 min	–	–	0

3.3. Safety and efficacy of sugammadex

Our systematic review helped to shed some light on the safety and efficacy of sugammadex, particularly in the context of its application in neuromuscular blockade reversal in myasthenic patients (Table 3). Sugammadex is noted for its rapid action in reversing neuromuscular blockades, with several instances showing significant efficacy. For instance, the time to Train-of-Four (ToF) recovery, a critical measure of neuromuscular function, averaged anywhere from 79.7s for moderate neuromuscular blockade [14] to 10 min in a child with juvenile myasthenia gravis [25]. Similarly, the average time to extubation, another critical measure of recovery post-surgery, is relatively short, highlighting the rapid onset of sugammadex's effects. The reported times range from as quick as 2 min for a caesarean section [9] to an average of approximately 276 s in a case series of 117 patients [13], emphasizing its swift action in facilitating spontaneous breathing and extubation.

In terms of safety, the data indicates that sugammadex does not significantly increase the risk of myasthenic crisis, a severe exacerbation of myasthenia gravis symptoms. One case required reintubation after administration, which was managed with plasma exchange, a standard treatment for myasthenic crisis [26]. One patient was discovered to have undiagnosed myasthenia and experienced a delay in weaning off of the ventilator of 48 h [17]. In a retrospective cohort study of 873 patients, 39 patients required plasma exchange therapy and 17 needed immunoglobulin therapy following reversal of neuromuscular blockade [10]. Most importantly, there were no instances of mortality reported, underscoring the overall safety of sugammadex. The absence of major adverse effects or mortality in the documented cases suggests that sugammadex is a safe and effective agent for reversing neuromuscular blockade, particularly in patients with underlying conditions such as myasthenia gravis. The consistent and rapid recovery times, coupled with the low incidence of severe complications, make sugammadex a reliable choice in clinical settings requiring prompt and safe reversal of neuromuscular blockades.

4. Discussion

The anesthetic management of patients with myasthenia gravis (MG) is uniquely challenging as these patients have been shown to have widely varied responses to neuromuscular blocking agents (NMBAs), with a marked resistance to depolarizing agents like succinylcholine and exquisite sensitivity to non-depolarizing agents such as rocuronium and vecuronium [30,31]. The use of NMBAs in patients with MG has also been associated with higher rates of transfers to intensive care unit postoperatively and delayed extubation [32,33]. As such, anesthesiologists commonly avoid or significantly limit the use of NMBAs in patients with MG when possible. Unfortunately, there are many surgical procedures in which neuromuscular blockade is required and thus use of NMBAs is unavoidable. In these cases, patients with MG should be carefully monitored for the level of neuromuscular blockade both during and after the procedure. Reversal agents for NMBAs, most commonly anticholinesterase agents such as neostigmine, also pose an additional threat to the safety of MG patients and therefore need to be carefully considered. Anticholinesterase agents can be ineffective in the setting of chronic anticholinergic therapy which is common within the MG population. This can result in postoperative residual neuromuscular block, a feared complication of using NMBAs that can cause complications including respiratory failure. Additionally, anticholinesterase agents come with the risk of cholinergic crisis as the mechanism of action involves the alteration of acetylcholine within the neuromuscular junction.

The emergence of sugammadex, a novel reversal agent for steroidal NMBAs that works by encapsulating and inactivating the blocking agent, has the potential to change the current management of muscular blockade in the setting of MG. Currently, the application of sugammadex in reversal of steroidal NMBAs in MG patients is gaining traction however most of the literature surrounding its use consists of case studies or series. In an effort to gain a better understanding of both the efficacy and safety of this drug we conducted a systematic review of the current literature.

Time from sugammadex administration to return of neuromuscular function, measured by TOF recovery, can be used in the appraisal of drug efficacy. Out of the 24 articles included, 14 reported time to TOF recovery. When reversal with sugammadex was successful, TOF recovery was extremely swift often returning to TOF baseline within minutes of administration. However, within these 14 articles, three reported cases in which TOF recovery did not occur despite sugammadex administration and ultimately required additional pharmacotherapy with anticholinesterase inhibitor. These findings highlight one of the major advantages of sugammadex, its quick onset of action. However, further research is needed to elucidate potential causes or factors that may contribute to the variability in efficacy between patients that appears to be present.

Our review collected data regarding need for plasma exchange or immunoglobulin and incidence of myasthenic crisis for appraisal of sugammadex safety. Previously reported incidences of myasthenic crisis post thyroidectomy ranges from 6.2 % to 30.3 % [34]. Among 1679 patients treated with sugammadex, only 27 cases of postoperative myasthenic crisis were reported, highlighting its safety profile. While it is reasonable to suspect the low rate of myasthenic crisis is likely owed to its unique mechanism of action that does not directly modulate acetylcholine levels as compared to reversal agents like anticholinesterases, more research directly comparing rates between different reversal agents in a controlled randomized manner is needed to confirm. It is also crucial to recognize that while sugammadex may not further increase risk of crisis, it may not prevent or decrease the rate crisis, as previous research has found that MG disease severity rating, BMI and previous history of crisis were all independent risk factors in the development of post-operative crisis [35]. A patient's postoperative myasthenic status and risk of myasthenic crisis depend heavily on their pre-surgical condition; therefore, patients undergoing planned procedures should receive thorough preparation well in advance. Similar to crisis rate, treatment with plasma exchange was required in only 40 patients and treatment with immunoglobulin was required in 17 patients. Perhaps the most impressive outcome was the lack of patient deaths reported in all of the 1679 cases of sugammadex use.

Among the case series studies reviewed, the work of Vymazal et al. stands out as particularly relevant to clinical anesthesiologists.

Their study addressed several key concerns in the management of MG patients. First, they used rocuronium at the usual dose and measured the Train of 4 (TOF) ratio using accelerometer response at the abductor pollicis muscle. Second, they followed the accepted dosing regimen for sugammadex administration. Third, they monitored the accelerometer response at the abductor pollicis muscle until a TOF ratio of 0.9 was obtained, which is the standard for adequate reversal of neuromuscular blockade. Fourth, they monitored all their patients for re-intubation within 48 h and for acquired bronchopneumonia within the 120 h after surgery, which are clinical indicators of inadequate neuromuscular blockade reversal. These methodological strengths provide valuable insights into the practical application of sugammadex in MG patients. However, it's important to note that the study's primary limitation was the small number of patients enrolled, which underscores the need for larger, more comprehensive studies in this area [13].

Overall, our assessment of sugammadex falls in line with what previous literature has suggested: sugammadex is a safe and effective choice for reversal of steroid NMBAs in patients with MG. However, future research needs to be directed toward studies such as Vymazal et al., incorporating larger patient populations and exploring sugammadex's use in diverse cases involving MG patients. These larger studies could also elucidate whether the need for plasma exchange or immunoglobulin therapy or the incidence of myasthenic crisis is as large as the retrospective studies indicate.

5. Limitations

This review is limited by the scarcity of randomized control trials and other high-quality study designs with a large sample size, and rather was largely composed of case reports and case series. The lack of large sample size lends to decreased power of the study. While case series studies lack randomization and the use of a control group, they do control for confounding variables much better than retrospective studies or case reports. Additionally, the novelty of sugammadex for reversing neuromuscular blockades in patients with comorbidities limited the quantity of studies found in the initial search. Another significant limitation is the lack of information regarding the serological status of the patients, specifically the presence of acetylcholine receptor antibodies (AChRab) or muscle-specific kinase (MuSK) antibodies. This information is crucial as it could influence the patients' responses to sugammadex and their overall outcomes. Furthermore, while most of the studies included had minor limitations, some did not adequately address potential biases, further increasing the risk of bias within the collected data.

6. Conclusion

This systematic review focuses on the use of sugammadex for reversing neuromuscular blockades in patients with Myasthenia Gravis (MG), a condition that presents unique challenges in anesthetic management. The importance of this topic lies in the need for effective and safe reversal agents for neuromuscular blockades, especially in vulnerable populations like those with MG, where traditional agents may pose significant risks.

Our systematic review highlights that sugammadex is both an effective and safe option for reversing neuromuscular blockades in patients with Myasthenia Gravis. Sugammadex demonstrates a rapid and effective reversal of neuromuscular blockades, often restoring neuromuscular function within minutes. The safety profile of sugammadex is favorable, with a low incidence of postoperative myasthenic crisis and no reported mortalities in the cases reviewed. Despite its promising efficacy and safety, most existing literature consists of case reports or small series, indicating a need for more large-scale studies to confirm these findings. Further research is essential to fully establish its benefits and elucidate any factors contributing to variability in patient responses.

In conclusion, this review supports the potential of Sugammadex as an effective and safe reversal agent for neuromuscular blockades in MG patients. While preliminary findings are promising, more extensive studies are needed to validate its superiority and ensure its broad applicability in clinical settings.

CRedit authorship contribution statement

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Ethics approval

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Availability of data and material

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References

- [1] A. Beloor Suresh, R.M.D. Asuncion, Myasthenia gravis, in: StatPearls, StatPearls Publishing, 2024. <http://www.ncbi.nlm.nih.gov/books/NBK559331/>. (Accessed 27 July 2024).
- [2] H. Tireli, G. Yuksel, T. Okay, K. Kutkavul, Role of thymus on prognosis of myasthenia gravis in Turkish population, *North Clin Istanbul*. 7 (5) (2020) 452–459, <https://doi.org/10.14744/nci.2020.51333>.
- [3] A. Neuman, B. Granlund, Anesthesia for patients with myasthenia gravis, in: StatPearls, StatPearls Publishing, 2023. <http://www.ncbi.nlm.nih.gov/books/NBK572091/>. (Accessed 15 January 2024).
- [4] A. Adeyinka, N.P. Kondamudi, Cholinergic crisis, in: StatPearls, StatPearls Publishing, 2024. <http://www.ncbi.nlm.nih.gov/books/NBK482433/>. (Accessed 27 July 2024).
- [5] H.J. No, Y.C. Yoo, Y.J. Oh, et al., Comparison between sugammadex and neostigmine after video-assisted thoracoscopic surgery–thymectomy in patients with myasthenia gravis: a single-center retrospective exploratory analysis, *J. Personalized Med.* 13 (9) (2023) 1380, <https://doi.org/10.3390/jpm13091380>.
- [6] Haddad D, Hanna AJ, Russo L. Successful neuromuscular blockade reversal using sugammadex and neostigmine failed to prevent myasthenic crisis after emergency surgery: a case report. *Cureus*. 14(7):e27366. doi:10.7759/cureus.27366.
- [7] H.J. No, Y.C. Yoo, Y.J. Oh, et al., Comparison between sugammadex and neostigmine after video-assisted thoracoscopic surgery–thymectomy in patients with myasthenia gravis: a single-center retrospective exploratory analysis, *J. Personalized Med.* 13 (9) (2023) 1380, <https://doi.org/10.3390/jpm13091380>.
- [8] H.D.S. Fernandes, J.L.S. Ximenes, D.I. Nunes, H.A. Ashmawi, J.E. Vieira, Failure of reversion of neuromuscular block with sugammadex in patient with myasthenia gravis: case report and brief review of literature, *BMC Anesthesiol.* 19 (1) (2019) 160, <https://doi.org/10.1186/s12871-019-0829-0>.
- [9] L. Soyoral, U. Goktas, M.B. Cegin, V. Baydi, Successful use of sugammadex for caesarean section in a patient with myasthenia gravis, *Braz J Anesthesiol Elsevier* 67 (2) (2017) 221–222, <https://doi.org/10.1016/j.bjane.2014.08.008>.
- [10] S. Tsukada, S. Shimizu, K. Fushimi, Rocuronium reversed with sugammadex for thymectomy in myasthenia gravis: a retrospective analysis of complications from Japan, *Eur. J. Anaesthesiol.* 38 (8) (2021) 850–855, <https://doi.org/10.1097/EJA.0000000000001500>.
- [11] H. Mouri, T. Jo, H. Matsui, K. Fushimi, H. Yasunaga, Effect of sugammadex on postoperative myasthenic crisis in myasthenia gravis patients: propensity score analysis of a Japanese nationwide database, *Anesth. Analg.* 130 (2) (2020) 367–373, <https://doi.org/10.1213/ANE.0000000000004239>.
- [12] D. Shah, A. Dharmarajah, Use of Sugammadex in an octagenarian with Myaesthesia Gravis undergoing emergency laparotomy, *J. Clin. Anesth.* 37 (2017) 109–110, <https://doi.org/10.1016/j.jclinane.2016.11.008>.
- [13] T. Vymazal, M. Krecmerova, V. Bicek, R. Lischke, Feasibility of full and rapid neuromuscular blockade recovery with sugammadex in myasthenia gravis patients undergoing surgery – a series of 117 cases, *Ther Clin Risk Manag* 11 (2015) 1593–1596, <https://doi.org/10.2147/TCRM.S93009>.
- [14] H.D. de Boer, M.O. Shields, L.H.D.J. Booij, Reversal of neuromuscular blockade with sugammadex in patients with myasthenia gravis: a case series of 21 patients and review of the literature, *Eur. J. Anaesthesiol.* 31 (12) (2014) 715–721, <https://doi.org/10.1097/EJA.0000000000000153>.
- [15] Ulke Z. Sungur, A. Yavru, E. Camci, B. Ozkan, A. Tokar, M. Senturk, Rocuronium and sugammadex in patients with myasthenia gravis undergoing thymectomy, *Acta Anaesthesiol. Scand.* 57 (6) (2013) 745–748, <https://doi.org/10.1111/aas.12123>.
- [16] G. Kiss, A. Lacour, A. d'Hollander, Fade of train-of-four ratio despite administration of more than 12 mg kg⁻¹ sugammadex in a myasthenia gravis patient receiving rocuronium, *Br. J. Anaesth.* 110 (5) (2013) 854–855, <https://doi.org/10.1093/bja/aet098>.
- [17] V. Garcia, P. Diemunsch, S. Boet, Use of rocuronium and sugammadex for caesarean delivery in a patient with myasthenia gravis, *Int. J. Obstet. Anesth.* 21 (3) (2012) 286–287, <https://doi.org/10.1016/j.ijoa.2012.02.006>.
- [18] J. Jakubiak, T. Gaszynski, W. Gaszynski, Neuromuscular block reversal with sugammadex in a morbidly obese patient with myasthenia gravis, *Anaesthesiol. Intensive Ther.* 44 (1) (2012) 28–30.
- [19] A.M. Petrun, D. Mekis, M. Kamenik, Successful use of rocuronium and sugammadex in a patient with myasthenia, *Eur J Anaesthesiol EJA* 27 (10) (2010) 917, <https://doi.org/10.1097/EJA.0b013e3283392593>.
- [20] C. Unterbuchner, H. Fink, M. Blobner, The use of sugammadex in a patient with myasthenia gravis, *Anaesthesia* 65 (3) (2010) 302–305, <https://doi.org/10.1111/j.1365-2044.2009.06236.x>.
- [21] P. Casarotti, C. Mendola, G. Cammarota, F. Della Corte, High-dose rocuronium for rapid-sequence induction and reversal with sugammadex in two myasthenic patients, *Acta Anaesthesiol. Scand.* 58 (9) (2014) 1154–1158, <https://doi.org/10.1111/aas.12391>.
- [22] A. Rudzka-Nowak, M. Piechota, Anaesthetic management of a patient with myasthenia gravis for abdominal surgery using sugammadex, *Arch Med Sci AMS* 7 (2) (2011) 361–364, <https://doi.org/10.5114/aoms.2011.22094>.
- [23] H. Argiriadou, K. Anastasiadis, E. Thomaidou, D. Vasilakos, Reversal of neuromuscular blockade with sugammadex in an obese myasthenic patient undergoing thymectomy, *J. Anesth.* 25 (2) (2011) 316–317, <https://doi.org/10.1007/s00540-011-1101-z>.
- [24] Sedat Saylan AAD of A and ICM, Anesthesia and neuromuscular block management in thymectomies performed in cases of thymoma and myasthenia gravis: a retrospective study. <http://archive.org/details/anesthesia-and-neuromuscular-block-management-in-thymectomies-performed-in-cases>, 2021. (Accessed 12 July 2024).
- [25] S. Dontukurthy, C. Wisler, V. Raman, J.D. Tobias, Myasthenia gravis and sugammadex: a case report and review of the literature, *Saudi J. Anaesth.* 14 (2) (2020) 244–248, <https://doi.org/10.4103/sja.SJA.721.19>.
- [26] H.C. Lai, T.W. Huang, W.C. Tseng, T.S. Wu, Z.F. Wu, Sugammadex and postoperative myasthenic crisis, *J. Clin. Anesth.* 57 (2019) 63, <https://doi.org/10.1016/j.jclinane.2019.02.026>.

- [27] Y. Sugi, K. Nitahara, T. Shiroshita, K. Higa, Restoration of train-of-four ratio with neostigmine after insufficient recovery with sugammadex in a patient with myasthenia gravis, *Case Rep* 1 (3) (2013) 43–45, <https://doi.org/10.1097/ACC.0b013e3182953053>.
- [28] H. Misiólek, D. Czyżewski, J. Karpe, A. Tomala, P. Palaczyński, J. Chelchowski, The use of sugammadex for the reversal of neuromuscular blockade after thymectomy with videothoracoscopy in myasthenia gravis patients – a preliminary report, *Kardiochirurgia Torakochirurgia Pol J Thorac Cardiovasc Surg* 10 (3) (2013) 239–243, <https://doi.org/10.5114/kitp.2013.38099>.
- [29] J.E. Rubin, R.J. Ramamurthi, The role of sugammadex in symptomatic transient neonatal myasthenia gravis: a case report, *Case Rep* 9 (9) (2017) 271–273, <https://doi.org/10.1213/XAA.0000000000000590>.
- [30] E. Gilhus Nils, Myasthenia gravis, *N. Engl. J. Med.* 375 (26) (2016) 2570–2581, <https://doi.org/10.1056/NEJMra1602678>.
- [31] A.P. Wainwright, P.M. Brodrick, Suxamethonium in myasthenia gravis, *Anaesthesia* 42 (9) (1987) 950–957, <https://doi.org/10.1111/j.1365-2044.1987.tb05365.x>.
- [32] P. Gritti, M. Sgarzi, B. Carrara, et al., A standardized protocol for the perioperative management of myasthenia gravis patients. Experience with 110 patients, *Acta Anaesthesiol. Scand.* 56 (1) (2012) 66–75, <https://doi.org/10.1111/j.1399-6576.2011.02564.x>.
- [33] Y. Fujita, S. Moriyama, S. Aoki, et al., Estimation of the success rate of anesthetic management for thymectomy in patients with myasthenia gravis treated without muscle relaxants: a retrospective observational cohort study, *J. Anesth.* 29 (5) (2015) 794–797, <https://doi.org/10.1007/s00540-015-1999-7>.
- [34] Y. Geng, H. Zhang, Y. Wang, Risk factors of myasthenia crisis after thymectomy among myasthenia gravis patients: a meta-analysis, *Medicine (Baltim.)* 99 (1) (2020) e18622, <https://doi.org/10.1097/MD.00000000000018622>.
- [35] G. Leuzzi, E. Meacci, G. Cusumano, et al., Thymectomy in myasthenia gravis: proposal for a predictive score of postoperative myasthenic crisis, *Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg* 45 (4) (2014) e76–e88, <https://doi.org/10.1093/ejcts/ezt641>, discussion e88.