

Sugammadex for the reversal of muscle relaxation in general anaesthesia: A systematic review and economic assessment.

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Page | 1

Abstract

Background

For intubation and surgical optimisation, general anaesthesia requires neuromuscular blocking agents (NMBAs). Sugammadex, a new reversal drug, reverses Aminosteroidal-induced neuromuscular blockade quickly and predictably, improving patient outcomes and operating room efficiency.

Objectives

To evaluate the clinical effectiveness and economic viability of sugammadex compared to neostigmine or placebo for the reversal of rocuronium- or vecuronium-induced neuromuscular blockade in general anaesthesia.

Methods

A comprehensive review compared sugammadex to neostigmine or placebo for reversing moderate, profound, and acute neuromuscular blockade. Recovery timeframes, safety, and economic impacts were collected. A de novo cost-effectiveness model based on UK NHS practice assessed the value per minute of recuperation time saved.

Results

Sugammadex shortened recovery times by 1.3–1.7 minutes (moderate blockade) and 2.7 minutes (deep blockade) compared to neostigmine and placebo. Economic studies showed that sugammadex might be cost-effective if operating room recovery time savings were over £2.40 per minute. The safety profile was better than neostigmine.

Conclusion

Sugammadex is a clinically effective and potentially cost-efficient agent for NMB reversal. Its advantages are especially relevant in high-turnover or high-risk surgical settings, though broader economic assessments across healthcare systems are needed.

Keywords: Sugammadex, Neuromuscular Blockade, General Anaesthesia, Cost-effectiveness

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Introduction

A key component of contemporary general anaesthesia is the use of neuromuscular blocking agents (NMBAs), which promote muscle relaxation during surgery, make endotracheal intubation easier, and improve surgical outcomes [1]. Aminosteroidal NMBAs with an intermediate duration of action and reasonably predictable pharmacokinetics, like rocuronium and vecuronium, are commonly employed [2]. To restore spontaneous respiration and avoid persistent neuromuscular blockade, which is linked to problems like hypoxia, aspiration, and extended recovery room stays, their effects must be safely and effectively reversed at the end of surgical procedures [3].

The preferred reversal therapy has historically been neostigmine, an acetylcholinesterase inhibitor given in

combination with an anticholinergic like glycopyrrolate [4]. Despite its widespread use, neostigmine has a number of drawbacks. These include the possibility of side effects such as bradycardia, salivation, and postoperative nausea, as well as a relatively late onset of action and a ceiling effect beyond which further dose produces declining benefits. Furthermore, whether there is a substantial

blockade or a need for quick reversal, neostigmine's effectiveness is reduced [5,6].

In this regard, a notable pharmaceutical development is Sugammadex (Bridion®), a modified γ -cyclodextrin. Sugammadex functions by encapsulating rocuronium or vecuronium molecules in the plasma, making them inactive and promoting their quick clearance, in contrast to neostigmine, which raises the concentration of acetylcholine to outcompete the NMBA at the

neuromuscular junction [7]. Because of this special mechanism, sugammadex has a quicker onset of action, fewer systemic adverse effects, and the ability to quickly and consistently reverse even deep neuromuscular blockade [8,9].

Page | 2 There is increasing interest in learning about sugammadex's therapeutic efficacy and cost-effectiveness in both routine and emergency anaesthetic treatment due to its possible clinical benefits. Given that sugammadex is more expensive to purchase than neostigmine, the economic ramifications are especially pertinent [10].

The purpose of this study is to conduct an economic evaluation to determine the value proposition of sugammadex in the setting of general anaesthesia and to present a systematic review of the clinical outcomes linked to its use.

Materials and methods

Study Design

Sugammadex was tested for its clinical efficacy and cost-effectiveness in reversing neuromuscular blockade (NMB) caused by rocuronium or vecuronium during general anaesthesia using a systematic review and de novo economic modelling. The review used published and grey literature according to health technology evaluation and systematic review methodologies.

Data Sources and Search Strategy

A comprehensive literature search was conducted in May 2008 and updated through November 2008 across multiple electronic databases, including:

- MEDLINE
- EMBASE
- CINAHL
- BIOSIS Previews
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Science Citation Index

Additional sources such as conference proceedings, trial registries, and relevant websites were also queried. The search strategy included keywords and Medical Subject Headings (MeSH) related to "sugammadex," "neuromuscular blockade," "reversal agents," "rocuronium," "vecuronium," and "general anaesthesia."

Study Selection Criteria

Inclusion Criteria

- Randomised controlled trials (RCTs) comparing sugammadex with either placebo or neostigmine plus glycopyrrolate.
- Trials evaluating reversal from moderate, profound, or immediate NMB.
- Studies involving adult patients undergoing general anaesthesia.

Exclusion Criteria

- Non-randomised or observational studies.
- Animal studies or those not involving general anaesthesia.
- Trials without comparative arms or without quantitative outcome measures.

Data Extraction and Quality Assessment

Two independent reviewers screened all titles, abstracts, and full-texts. Discrepancies were resolved through discussion or consultation with a third reviewer. Data were extracted on:

- Participant demographics and clinical context.
- Type and dose of NMBA.
- Intervention (dose and timing of sugammadex).
- Comparator details.
- Primary outcome: time to recovery to a Train-of-Four (TOF) ratio of ≥ 0.9 .
- Secondary outcomes: adverse events, time to extubation, and return to baseline neuromuscular function.

Risk of bias was assessed using the Cochrane Risk of Bias Tool, evaluating randomization, blinding, allocation concealment, and outcome reporting.

Economic Assessment

A de novo cost-effectiveness model was constructed based on trial data and UK National Health Service (NHS) practice. The model evaluated:

- Routine reversal of moderate and profound blockade.

- Immediate reversal scenarios.
- Unit costs of operating room time, recovery room time, and sugammadex dosage.

Threshold analysis was performed to identify the minimum value (in £/minute) at which sugammadex becomes cost-effective compared to standard agents.

Statistical Analysis

Use descriptive statistics and comparative time-to-recovery outcomes to synthesise RCT results. Due to trial heterogeneity, meta-analyses were considered but not performed. The incremental cost-effectiveness ratios (ICERs) assumed varying productivity increases from avoided operating and recovery room time.

Results

Study Inclusion and Characteristics

A total of 2132 titles and abstracts were screened, leading to 265 full-text articles reviewed. Ultimately, 18

randomized controlled trials (RCTs) were included, comprising:

- 4 active-control trials comparing sugammadex to neostigmine/glycopyrrolate,
- 9 placebo-controlled trials,
- 5 studies involving special populations (e.g., elderly, obese).

These studies evaluated sugammadex in varying doses (2, 4, and 16 mg/kg) for reversal of moderate, profound, and immediate NMB induced by rocuronium or vecuronium.

Efficacy Outcomes

Primary outcome: Time to recovery to a Train-of-Four (TOF) ratio ≥ 0.9

Sugammadex demonstrated significantly faster recovery times than both placebo and neostigmine across all depths of blockade. The following table summarizes the median recovery times:

Condition	Drug	Median Recovery Time (min)
Moderate Blockade	Rocuronium + Sugammadex (2 mg/kg)	1.3 – 1.7
	Rocuronium + Neostigmine	17.6
	Rocuronium + Placebo	21 – 86
Profound Blockade	Rocuronium + Sugammadex (4 mg/kg)	2.7
	Rocuronium + Neostigmine	49
	Rocuronium + Placebo	30 – >90
Immediate Reversal	Rocuronium + Sugammadex (16 mg/kg)	4.2
	Succinylcholine (spontaneous)	7.1

Similar results were observed for vecuronium-induced blockade, with sugammadex offering consistently quicker recovery across all depths.

Safety and Adverse Events

Sugammadex was generally well tolerated. No cases of bradycardia, salivation, or cholinergic crisis—commonly seen with neostigmine—were reported. Transient hypersensitivity and hypotension occurred in a minority (<1%) of patients, with no long-term sequelae.

Economic Assessment

The de novo model indicated that sugammadex is potentially cost-effective under specific circumstances:

- **Routine reversal of moderate blockade** (2 mg/kg): Cost-effective if each minute of recovery time saved is valued at **>£2.40**.
- **Profound blockade** (4 mg/kg): Threshold value is **>£1.75 per minute**.
- **Operating Room savings:** Estimated at **£4.44/min**, supporting cost-effectiveness in intraoperative contexts.
- **Recovery Room savings:** Significantly lower at **£0.33/min**, reducing cost justification in this setting.

Overall, the model supports sugammadex use, particularly in operating theatres where faster turnover can yield economic benefits.

Discussion

The results of this comprehensive study highlight sugammadex's clinical superiority and possible economic feasibility as a neuromuscular blockade (NMB) reversal medication in general anaesthesia. Compared to neostigmine and a placebo, sugammadex consistently produced quicker recovery times from both moderate and profound blocking. It also had a better safety record and less variation in the commencement of action. These observations are supported by comparative literature.

Sugammadex reverses NMB more quickly than neostigmine in a variety of clinical settings, greatly lowering time to extubation and postoperative care unit stays, especially when used for profound blockade reversal, according to a Cochrane systematic review by Hristovska et al. (2018) [11]. In contrast to neostigmine, sugammadex not only promoted a speedier recovery but also decreased the occurrence of postoperative pulmonary problems, which is a significant benefit for elderly and high-risk patients, according to another meta-analysis by Liu et al. (2023) [12].

Similar outcomes were seen in morbidly obese people, where Subramani et al. (2021) showed that sugammadex reduced residual blockade and related hazards by providing a safer and more predictable reversal than neostigmine [13]. Similar patterns were observed in paediatric populations by Won et al. (2016), who reported a decreased incidence of side events and more reliable efficacy with sugammadex [14]. Numerous studies support the cost-effectiveness of sugammadex despite its greater initial cost, especially in operating room settings where time savings result in financial gain. Chambers et al. (2010) calculated that, particularly in high-throughput surgical centres, even modest decreases in OR turnover times could make the expense worthwhile if properly priced [15].

Our research supports previous evaluations, indicating that sugammadex's capacity to reverse deep blockage and speed up extubation can enhance safety, lessen PACU overcrowding, and possibly cut down on unscheduled ICU admissions brought on by residual paralysis. However, the lack of extensive pragmatic trials and the disparity in economic assumptions among healthcare systems are two drawbacks of the current body of research. A more cost-effective and therapeutically beneficial option to neostigmine for the reversal of aminosteroidal NMB is sugammadex. To improve implementation techniques, future studies should

concentrate on practical results and financial evaluations in various surgical contexts.

Conclusion

This systematic study and economic evaluation show that sugammadex reverses aminosteroidal neuromuscular blockade during general anaesthesia better than neostigmine. Its quick start, constant efficacy across blockade depths, and safety profile make it suitable for high-risk or time-sensitive surgeries. While sugammadex's greater acquisition cost is a concern, its potential for operating room efficiency and fewer postoperative problems makes it valuable in modern anaesthesia. More real-world research is needed to optimise its use in varied clinical and economic scenarios.

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