Sugammadex: a game-changer for reversing neuromuscular blockade

MARILYN ARCHAMBEAULT, CAA, MSA
CERTIFIED ANESTHESIOLOGIST ASSISTANT
WASHINGTON, D.C., USA

Sugammadex is a relatively new medication used in anesthesiology, particularly in reversing neuromuscular blockade induced by neuromuscular blocking agents (Thilen et al., 2023). Neuromuscular blocking agents (NMBAs) are drugs that inhibit muscle contraction and are used to facilitate intubation and decrease patient movement during surgical procedures. Although effective in facilitating surgery, NMBAs also paralyze the diaphragm and other respiratory muscles, increasing the risk of respiratory complications postoperatively (Beltran et al., 2022). Sugammadex was developed as a novel, selective, and reversible antagonist for NMBAs to help overcome these challenges.

Sugammadex was developed to address some limitations of traditional reversal agents such as neostigmine, including

delayed onset, unpredictable response, and muscarinic side effects (Chen et al., 2022). Sugammadex was approved by the United States Food and Drug Administration (FDA) in December 2015 to reverse NMB in adult patients. Since then, it has been approved for use in pediatric patients aged two years and older (Thilen et al., 2023).

Sugammadex selectively targets and encapsulates NMBAs, specifically rocuronium and vecuronium, with high affinity and rapid action (Irani et al., 2022). This encapsulation is facilitated by a cyclodextrin molecule within sugammadex's structure, which creates a cavity that can trap the NMBA molecule. Once the NMBA molecule is encapsulated, it can no longer bind to the receptors at the neuromuscular junction, which leads to the restoration of neuromuscular function. Sugammadex is administered intravenously, usually at the end of a surgical procedure, with the dose determined based on the level of neuromuscular blockade and the desired speed of reversal (Duranteau et al., 2021).

Interestingly, the structure of sugammadex shares similarities with the titular air freshener, Febreze ®. Both sugammadex and Febreze ® contain cyclodextrin components which help to encapsulate specific molecules. However, whereas sugammadex encapsulates NMBA molecules, Febreze ® captures odor molecules by trapping them within the cyclodextrin cavity. This suggests that cyclodextrins may have various applications beyond the field of anesthesia, and this area of research could lead to the development of new treatments for various diseases and conditions (Beltran et al., 2022; Chen et al., 2022; Irani et al., 2022).

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Sugammadex is contraindicated in patients with known hypersensitivity or allergy to sugammadex or any of its components (Thilen et al., 2023). Sugammadex is not recommended in patients with renal impairment, as the kidneys primarily eliminate it. In patients with severe renal dysfunction (creatinine clearance less than 30 mL/min), sugammadex may not effectively reverse NMB (Thilen et al., 2023).

Compared to neostigmine, using sugammadex for NMB reversal is associated with a lower incidence of muscarinic side effects (Beltran et al., 2022; Li et al., 2021; Ruetzler et al., 2022; Suleiman et al., 2022). Neostigmine administration can solicit unwanted muscarinic side effects which are mediated by the activation of muscarinic receptors in various organs and tissues. These side effects include bradycardia, hypotension, bronchospasm, salivation, lacrimation, sweating, defecation, and urinary incontinence (Carvalho et al., 2020; Lee & Jung, 2020; Thilen et al., 2023). Glycopyrrolate (or, less frequently, atropine) is co-administered with neostigmine to minimize these muscarinic side effects. Therefore, the choice of reversal agent should be based on the individual patient's characteristics and the clinical situation (Blobner et al., 2022; Duranteau et al., 2021; Hirsch et al., 2022).

Sugammadex is generally well-tolerated, with few reported adverse effects. The most common side effects include nausea, vomiting, and headache. These side effects are usually mild and self-limiting, resolving within a few hours. However, more severe side effects have been reported, including anaphylaxis, bronchospasm, hypotension, and bradycardia (Goodman et al., 2022; Teng et al., 2021; Trivedi et al., 2021). Anaphylaxis is a rare but potentially life-threatening reaction that can occur within minutes of administration. Therefore, the dosing of sugammadex should be carefully considered in patients with preoperative risk factors for sugammadex-induced anaphylaxis (Kotake et al., 2022). Furthermore, bronchospasm can develop in patients with a history of asthma or chronic obstructive pulmonary disease (COPD), and hypotension and bradycardia can occur in patients with pre-existing cardiovascular disease (Teng et al., 2021; Trivedi et al., 2021).

A prospective observational study conducted by Devoy, Hunter, and Smith (2022) raised concerns about using sugammadex with concurrent oral contraceptive use. The study found that sugammadex administration decreased the levels of estrogen and progesterone hormones in women who take hormonal contraception. The authors suggest that this could lead to contraceptive failure and

unintended pregnancy; thus, caution should be exercised when administering sugammadex to women of reproductive age who use or could be using hormonal contraception. Additionally, Hirsch, Chia, and Jahr (2022) recommend that healthcare providers discuss sugammadex administration's potential risks and benefits with their patients, especially women of childbearing age who use oral contraceptives, to facilitate informed decision-making. Limited research is available on the safety and efficacy of sugammadex use during pregnancy. However, a case series study of pregnant women who received sugammadex during surgery reported favorable maternal and fetal outcomes (Singh et al., 2021).

According to the 2023 American Society of Anesthesiologists Practice Guidelines for Monitoring and Antagonism of Neuromuscular Blockade, sugammadex dosing is based on the patient's weight, depth of NMB and dose of NMBA used (Thilen et al., 2023). For adults, the recommended dose of sugammadex is 2 mg/kg for moderate NMB (train-of-four [TOF] ratio 0.1-0.4) and 4 mg/kg for deep NMB (TOF ratio < 0.1) induced by rocuronium or vecuronium (Dubois et al., 2023). A randomized placebo-controlled trial by Duranteau et al. (2021) found that earlier and lower dose administration of sugammadex was safe and effective in reversing moderate NMB.

In recent years, qualitative neuromonitoring (QNM) has gained attention as a complementary technique for monitoring NMB during anesthesia, especially in patients with neuromuscular disease or those undergoing surgery with a high risk of postoperative respiratory complications (Naguib et al., 2017). Postoperative complications resulting from residual paralysis include muscle weakness, pulmonary complications, and increased healthcare utilization (Dubois et al., 2023; Li et al., 2021; Suleiman et al., 2022). These complications may be influenced by choice of neuromuscular blockade reversal agents, such as sugammadex or neostigmine, and their administration practices (Bash et al., 2021; Beltran et al., 2022; Ruetzler et al., 2022).

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QNM measures the transmission of nerve impulses at the neuromuscular junction and objectively measures the degree of muscle relaxation. QNM is used to ensure that the level of muscle relaxation is appropriate for the surgical procedure and can be measured through various methods, such as electromyography, acceleromyography, or kinemyography. These techniques use sensors and electrodes to measure muscle activity, response, and contraction. QNM allows for precise titration of NMBAs and their reversal agents, which can prevent postoperative residual paralysis and associated complications (Blobner et al., 2022). The use of QNM is beneficial in various clinical settings, including outpatient surgery, pediatric surgery, and colorectal surgery (Bash et al., 2021; Beltran et al., 2022; Chen et al., 2022).

According to Lentz et al. (2021), sugammadex can be used in a difficult airway situation by rapidly reversing NMB, which can help to restore airway patency, potentially avoiding the need for more invasive interventions. In such situations, a bolus dose of sugammadex 16 mg/kg can be administered to reverse NMB immediately (Lentz et al., 2021). Many institutions have included and stocked sugammadex in their difficult airway emergency carts for this reason.

The relative cost of sugammadex is significantly higher than that of neostigmine (Beltran et al., 2022). A systematic review and meta-analysis of studies on the use of sugammadex in colorectal surgery found that the cost of sugammadex was significantly higher than that of neostigmine and that the increased cost may limit its use in some settings (Chen et al., 2022). However, other studies have suggested that using sugammadex may be cost-effective in certain situations, such as when it reduces the incidence of postoperative pulmonary complications (Li et al., 2021). It is essential to weigh the clinical benefits of sugammadex against its financial impact, taking into account patient-specific factors and institutional resources, to optimize patient outcomes and healthcare expenditure. Further research is needed to determine its cost-effectiveness across different clinical settings.

In conclusion, sugammadex represents a valuable addition to anesthesiology, and its unique properties hold promise for future research in other areas of medicine. However, careful

consideration of dosing, contraindications, and potential side effects is necessary for safe and effective administration. The use of QNM can further optimize the administration of sugammadex. While the cost of sugammadex remains a consideration, its benefits in certain situations may outweigh the increased expense. As anesthesia continues to evolve, sugammadex administration should be guided by individual patient characteristics and clinical circumstances to ensure optimal outcomes.

The author declares that she has no competing interests, financial or otherwise, and that no commercial or industrial affiliations influenced the preparation or presentation of this manuscript.

Marilyn Archambeault, CAA, MSA
Certified Anesthesiologist AssistantCertified Anesthesiologist Assistant
Washington, D.C., USA

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Continuing Education Quiz

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1. **What is the primary purpose of sugammadex in anesthesiology?**
   A. To induce anesthesia
   B. To increase patient movement during surgery
   C. To reverse neuromuscular blockade
   D. To improve postoperative recovery

2. **How does sugammadex differ from traditional reversal agents like neostigmine?**
   A. Faster onset
   B. More predictable response
   C. Fewer muscarinic side effects
   D. All of the above

3. **Which of the following molecules does sugammadex selectively target and encapsulate?**
   A. Rocuronium
   B. Neostigmine
   C. Febreze®
   D. Glycopyrrolate

4. **What component within sugammadex's structure is responsible for encapsulating neuromuscular blocking agents?**
   A. Febreze® molecule
   B. Cyclodextrin molecule
   C. Muscarinic molecule
   D. Acetylcholine molecule

5. **What is the potential risk of sugammadex administration for women of reproductive age using hormonal contraception?**
   A. Increased risk of blood clots
   B. Decreased levels of estrogen and progesterone hormones
   C. Increased risk of anaphylaxis
   D. Increased risk of postoperative complications

6. **What factor influences the recommended dose of sugammadex for adults?**
   A. Patient's weight
   B. Depth of neuromuscular blockade
   C. Dose of neuromuscular blocking agent used
   D. All of the above

7. **Compared to neostigmine, what is a significant disadvantage of sugammadex?**
   A. Lower efficacy
   B. Greater risk of side effects
   C. Slower onset of action
   D. Higher cost

8. **Which technique does qualitative neuromonitoring (QNM) NOT use to measure muscle activity, response, and contraction?**
   A. Electromyography
   B. Acceleromyography
   C. Kinemyography
   D. Capnography

9. **In what clinical scenario is a bolus dose of sugammadex 16 mg/kg recommended?**
   A. When the patient has moderate neuromuscular blockade
   B. In a difficult airway situation
   C. When the patient has deep neuromuscular blockade
   D. To reverse patients with renal impairment

10. **Which of the following is NOT a muscarinic side effect associated with neostigmine?**
    A. Tachycardia
    B. Salivation
    C. Hypotension
    D. Urinary incontinence

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