Recommendations for Sugammadex Administration in Standard and Special Populations

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Executive Summary

Introduction of the Problem

Neuromuscular blocking medications are frequently administered by anesthesia providers during the intraoperative period. Inadequate reversal of these medications can lead to respiratory depression in the post-anesthesia period. Neostigmine has traditionally been the drug of choice used to reverse nondepolarizing muscle relaxants (NDMRs) (Luo et al., 2018). Sugammadex, also known as Bridion, was approved for clinical use by the FDA in December 2015 (Fink & Schaller, 2013). In recent years, sugammadex has gained popularity due to several important pharmacokinetic and pharmacodynamic properties, most notably, an extremely predictable and reliable reversal course for certain NDMRs.

Due to the lack of standardization and evidence-based information for the use of sugammadex at Memorial Hospital Belleville, anesthesia providers requested more information on its use in both standard and selected special populations, including renal failure, pregnancy, breastfeeding, and pediatrics. Lack of evidence-based resources, potential knowledge deficits, and lack of quick references have led to limited use of sugammadex in current clinical practice. This project aimed to bridge the knowledge gap, provide a cost analysis, and produce evidence-based resources for the administration of sugammadex for anesthesia providers at this facility.

Literature Review

Dosing

A peripheral nerve stimulator is used to assess the train-of-four (TOF count) in patients who have received NDMRs (Naguib et al., 2017). A TOF ratio of \( \geq 0.9 \) indicates an adequate reversal in a patient who has received NDMRs (Naguib et al., 2017). If the second twitch has returned, 2 mg/kg of sugammadex will fully reverse the neuromuscular blockade (Merck & Co,
If zero twitches are noted, a 4 mg/kg dose of sugammadex will be necessary (Merck & Co, 2022; Swerdlow & Osborne-Smith, 2022). In cannot intubate/cannot ventilate situations, a dose of 16 mg/kg of sugammadex should be administered (Merck & Co, 2022). The dosing for sugammadex is based on actual body weight (Merck & Co, 2022). When compared to the reversal time of neostigmine with its peak effect not occurring for seven to eleven minutes, sugammadex takes on average 1.8 minutes to fully reverse neuromuscular blockade (Brull & Kopman, 2017; Merck & Co, 2022).

**Side Effects and Interactions**

The most common side effects noted with sugammadex administration are anaphylaxis, bradycardia, hypotension, prolonged clotting times, nausea and vomiting, and rash. The risk of side effects increases as the dose of the medication increases (Merck & Co, 2022; Swerdlow & Osborne-Smith, 2022). Side effects are more likely when doses of 16 mg/kg are used (Merck & Co, 2022).

It is important to note that toremifene, a chemotherapy medication used in breast cancer patients, can displace the steroidal NDMR from the NDMR-sugammadex complex (Nag et al., 2013; Merck & Co, 2022). If toremifene is taken on the day of surgery, it can delay the reversal time of sugammadex (Swerdlow & Osborne-Smith, 2022; Merck & Co, 2022). Additionally, sugammadex is incompatible with verapamil, ondansetron, and ranitidine. When administering these medications in combination, the provider must ensure the intravenous line is completely flushed with 0.9% sodium chloride before administering sugammadex (Merck & Co, 2022).

**Use in Special Populations**

Although sugammadex is not FDA approved for patients with end-stage renal disease (ESRD), it can be used in renal failure patients with a few special considerations. If the patient
presents with a creatinine clearance ≤ 30 ml/min, sugammadex should be avoided (Swerdlow & Osborne-Smith, 2022; Paredes et al., 2020). With a creatinine clearance above 30 ml/min, no dose reduction is necessary (Swerdlow & Osborne-Smith, 2022). If sugammadex is administered and the patient currently receives dialysis, Cammu et al. (2012) recommends that the patient receive a dialysis treatment with a high-flux filter within 24 to 48 hours after administration. Paredes et al. (2020) noted that the TOFR median recovery time was 3.1 minutes compared to 1.8 minutes in patients with normal renal function. In addition, despite prolonged plasma concentrations of sugammadex, no signs of recurarization were noted in the post-anesthesia period (Kim et al., 2021).

SOAP recommends strict avoidance of sugammadex during the first trimester of pregnancy (12 weeks) due to the necessity of progesterone to maintain a viable pregnancy. Sugammadex binds to progesterone and can decrease levels by up to 34%, potentially threatening an early pregnancy (Willett et al., 2019). SOAP states that it is safe to use in pregnant mothers when they are near-term or at-term (37-40 weeks) (Willett et al., 2019).

Additionally, the direct effects of sugammadex on lactation are unknown. Sugammadex and the sugammadex-rocuronium complex are large hydrophilic molecules that suggest an unlikelihood of entering breastmilk (Willett et al., 2019). SOAP states that after the establishment of breastmilk or after 10 days, sugammadex can be used with caution, and the patient should be informed that the effects are unknown (Willett et al., 2019). Willett et al. (2019) recommends using traditional reversal methods (neostigmine and glycopyrrolate) if lactation status is unknown.

Due to the effects of sugammadex on progesterone, SOAP recommends that female patients of childbearing age use a non-hormonal method of contraception for seven days after
administration (Willett et al., 2019). Hormonal birth control includes anything that contains progesterone only or progesterone in combination with estrogens, such as birth control pills, intrauterine devices (IUDs), vaginal rings, and implants (Willett et al., 2019).

Lastly, the use of sugammadex in pediatrics under two years of age has not been FDA approved. Current studies state that dosing for pediatrics remains the same as adult patients. Studies show that sugammadex reverses neuromuscular blockade faster in pediatric patients than in adults (Matsui et al., 2019). Adult doses (2 mg/kg and 4 mg/kg) of sugammadex have been used in pediatrics with no significant adverse effects (Franz et al., 2019; Voss et al., 2021). Sugammadex should be diluted to increase the accuracy of dosing in pediatrics (Merck & Co, 2022).

Cost Analysis

A cost analysis includes more than just the price of the medication. In a 2020 study by Deyhim et al., the average cost of a 2ml (200mg) vial of sugammadex was $119.69. A 10ml (10mg) vial of neostigmine, on average, is $22.03, while a 1ml (0.2mg) vial of glycopyrrolate is $8.40 (Deyhim et al., 2020). With the average cost of OR time being $37 in 2018, saving OR time becomes an important factor in the analysis. Individuals receiving sugammadex spend an average of 12 fewer minutes in the OR (Moss et al., 2022). This information shows that despite a higher unit price, sugammadex may decrease time in the OR and/or PACU, thereby indirectly saving money while potentially improving patient outcomes.

Project Methods

Purpose and Goals

The purpose of this project was to increase provider knowledge about sugammadex and confidence in using the medication in standard and special patient populations. The reference
card's purpose was to supply anesthesia providers with a quick reference tool to use when they are unsure of the dosing or appropriate use of the medication in a special population while in the operating room.

**Project Setting**

The project was implemented in the anesthesia break room at Memorial Hospital Belleville. A nonexperimental single-group design was used. The sample included Certified Registered Nurse Anesthetists (CRNA), Student Registered Nurse Anesthetists (SRNA), and Anesthesiologists.

**IRB Approval**

Approval was obtained from the Belleville Community Institutional Review Board (IRB) on May 15, 2023. The project was determined to be IRB exempt on June 5, 2023, by the Southern Illinois University of Edwardsville board.

**Evaluation**

**Tools and Measures**

A posterboard, PowerPoint presentation, and quick reference card were provided to the anesthesia staff on August 29, 2023. A post-implementation survey was made available to all anesthesia providers through a QR code link. Five questions of the survey were presented in a multiple-choice format and addressed the number of years the provider had been practicing and their current use of sugammadex. An additional five questions used a Likert scale to evaluate the effectiveness of the overall presentation and quick reference. These questions allowed providers to choose a number from 1 to 10, with 1 being not at all, 5 being neutral, and 10 being very much, based on the knowledge gained from the presentation. Additionally, the staff provided feedback on whether the quick reference card was user friendly and if they would be more likely
to use sugammadex if a Pyxis was available in each operating room. Although there was a larger participation in the presentation, only thirteen providers responded to the survey.

**Results**

The results obtained from the post-implementation survey showed an overall increase in provider knowledge about the use of sugammadex. While all survey participants currently use sugammadex, only five (38.5%) use it 100% of the time. Barriers to the use of sugammadex included providers being more comfortable with the use of neostigmine and neostigmine being more accessible than sugammadex in the operating room. Overall, most providers (84.6%) indicated that their knowledge of sugammadex in standard and special patient populations was increased after the presentation. Additionally, 84.6% of the providers felt that the presentation increased their confidence in the use of the medication. After receiving a quick reference badge card, 100% of the providers who participated in the survey felt as though it was user friendly. Lastly, all 13 (100%) providers agreed that they would very likely increase their use of sugammadex if there was a Pyxis and sugammadex in each operating room.

**Limitations**

Due to the small number of anesthesia providers within the hospital, a smaller sample was inevitable. In addition, not all providers who participated in the presentation chose to participate in the survey. The poster remained available to providers for a week following the project's implementation, with the survey link also open during this time. These factors may limit the ability to generalize the results of this project to the larger population.

**Impact on Practice**

After the project's results were finalized, it was concluded that they produced a positive outcome. Survey responses provided by the anesthesia staff showed an increase in knowledge
and comfort when using sugammadex in standard and special patient populations. A long-term goal of this project is for providers to use sugammadex in all cases where it is clinically appropriate.

As current research on sugammadex continues to grow and improve, this project could be researched and implemented at other facilities. It would be most beneficial to implement this project at a facility where sugammadex use is minimal. In addition to anesthesia providers, PACU nurses, pharmacy, and purchasing staff involvement in the project would help provide a solid foundation of knowledge across the multi-disciplinary team. A further in-depth cost analysis could provide a clear picture of the benefits of adequate neuromuscular blockade reversal.

**Conclusion**

Adequate reversal of neuromuscular blockade is necessary to reduce the incidence of postoperative complications. Correct use of sugammadex in standard and special patient populations has been proven to reduce postoperative complications (Kheterpal et al., 2020). Per the request of the host site, research on sugammadex was presented to the anesthesia staff in the form of posters, laminated PowerPoint presentations, and quick reference badge cards. The overall results of the project showed a positive increase in provider knowledge. As providers continue to follow current guidelines, patient safety and outcomes can be improved.

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