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Brief Communication

Benefits and quick adoption of the use of Sugammadex in a busy practice setting

Vincent Devito[1*], Fiore Toscano[2], Rany Makaryus[2*]

[1]Department of Surgery, NYU Langone Long Island, Mineola, NY, USA; [2]Department of Anesthesiology, NYU Langone Long Island, Mineola, NY, USA. [*]Equal contributors.

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Abstract: The everyday clinical practice of anesthesia has been transformed by the new reversal agent Sugammadex. With multiple benefits to this agent, including immediate reversibility of certain neuromuscular blocking agents, a more robust reversal, and the ability to keep a deeper plane of paralysis throughout surgical procedures, this medication has provided anesthesiologists with a new and improved ability to provide high quality care to their patients. The effectiveness of the reversal provided by this agent has also improved the incidence of post-operative complications relating to improper reversal and the need for reintubations. With the new American Society of Anesthesiologists (ASA) guidelines on neuromuscular blockade and its reversal, Sugammadex has been easily and quickly adopted into everyday clinical practice.

Keywords: Sugammadex, neuromuscular blocking agents, reversal agents

Introduction

The approval of the new reversal agent Sugammadex for clinical use changed the everyday practice of anesthesia. There are multiple benefits to the use of this medication that give anesthesiologists another impressive tool in their toolbox for the benefit of their patients. Embracing the use of this medication has been rather quick for many practices, and that is certainly a testament to the multiple benefits and ease of use of this medication. In fact, in some practices, use of this medication has been adopted so quickly that these practices face the opposite problem of trying to restrict the use of Sugammadex. Given the current high cost of the medication, it is important to use it judiciously; however, it is difficult to ignore the many advantages that make this a superior reversal agent than the other available options [1].

First and foremost among these advantages is the ability to use rocuronium as an alternate paralytic agent to succinylcholine without being overly concerned about extended paralysis in an airway emergency [2]. Previously, the standard of care was to use succinylcholine in a situation where there was concern over the possibility of a difficult intubation. As opposed to rocuronium, a nondepolarizing neuromuscular blocking agent, succinylcholine is a depolarizing neuromuscular blocking agent that has a very fast and obvious onset, provides great intubating conditions, and, barring the presence of pseudocholinesterase deficiency, has a very short duration of action. Succinylcholine, as a depolarizing agent, binds the nicotinic receptors in the neuromuscular junction resulting in a disorganized depolarization of these receptors seen clinically as fasciculations. Because repolarization is prevented, the muscles remain flaccid until the succinylcholine is metabolized [3]. As a result of this mechanism of action, there are some drawbacks to the use of this medication. It should not be used in patients who have muscle weakness from upper motor neuron lesions, such as in stroke patients. It is not the best option in patients who have been bed bound for quite some time given the possibility of having upregulated acetylcholine receptors along the neuromuscular junction [3]. With rocuronium, on the other hand, the most important clinical concern is giving the medication in

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patients with renal failure, as they would metabolize it slowly, relying more on hepatic elimination than renal [4]. When using the higher intubating dosing, onset is quick, reliable, provides good intubating conditions [5], and now with Sugammadex, can be reversed even faster than waiting for succinylcholine effects to wear off [2, 6].

Sugammadex can provide a faster and more robust reversal than neostigmine [7]. The time to full effectiveness of neostigmine reversal can take more than 10 minutes, whereas with Sugammadex, it takes only 1 to 3 minutes [8]. While these 10 minutes may not be a major difference, the reality is that the reversal with Sugammadex is also much more robust than with neostigmine, especially when deep neuromuscular blockade is needed to provide more intense muscle paralysis for optimal surgical conditions [9]. With new advancements in robotic surgery, there has been an even greater push towards use of minimally invasive surgery, particularly laparoscopic surgery. With such surgeries, the improved surgical conditions provided by deep neuromuscular blockade helps surgeons with visualization and operating conditions, which can possibly translate to shorter operating times and improved outcomes [9, 10]. In fact, patients given sugammadex as a neuromuscular blockade reversal agent had a shorter total time spent in the operating room and a shorter PACU stay when compared to neostigmine. This reduction in time spent in the OR and in the PACU can actually offset the higher acquisition cost of sugammadex resulting in it being a more cost-effective option over neostigmine [11].

In addition, with neostigmine, not only do clinicians have to consider the onset of action, but also the duration of action, since the possibility of postoperative residual curarization with neostigmine can be a major issue. Since the duration of action of rocuronium can be as long as 90 minutes while that of neostigmine is typically shorter [12], the concentration of the nondepolarizing agent can theoretically remain high after neostigmine effects have already dissipated leading to recurarization or a residual paralysis. Sugammadex, on the other hand, irreversibly binds to the steroidal nondepolarizing agents (e.g., rocuronium, vecuronium), and that molecule is then renally excreted [13, 14]. This property of irreversible binding by Sugammadex is why studies have found a reduction in overall signs of postoperative residual paralysis when Sugammadex is used compared to neostigmine [15].

The theoretical benefit gained by the irreversible binding to the paralytic agent would be that the need for reintubations in the postoperative period would be greatly reduced. Anesthesia providers do their best to quickly and effectively reverse the effects of the anesthetic agents given intra-operatively, especially when it comes to paralytic agents. Paying close attention to the twitch count is very important to being able to adequately reverse these effects in a short time leading to extubation as the procedure is completed. Admittedly, following twitches alone, or even in conjunction with clinical signs such as a 5 second head lift or hand grip strength, does not fully reveal if a patient will do well enough for extubation every single time. There is always a small chance for recurarization as described above, inadequate reversal dosing, or even misidentifying the adequacy of the reversal. Despite all the advantages of Sugammadex, until recently the effects of Sugammadex on postoperative pulmonary complications remained controversial. In a recent meta-analysis comparing postoperative pulmonary complications after reversal with Sugammadex versus neostigmine, Sugammadex was noted to be more effective at reducing the incidence of postoperative pulmonary complications including pneumonia, atelectasis, non-invasive ventilation, and reintubation [16]. Specifically, this meta-analysis demonstrated a significant relative risk reduction for each of these pulmonary complications, including a reduction in reintubation. This is quite important as reducing pulmonary complications not only renders a great benefit to patients but can also reduce the overall health care costs in the perioperative period.

Our local anesthesia group works at a 591-bed hospital that is a level 1 trauma center, with 20 operating rooms on the hospital campus, 6 operating rooms at an ambulatory center, 6 endoscopy rooms, and 3 cardiac electrophysiology lab rooms, in addition to other off-site anesthesia locations such as the cardiac cath lab, MRI suite, and interventional radiology. In this busy practice, there was a notable trend for

reduction in the number of patients requiring reintubation in the postoperative period after sugammadex was brought to the practice and was made readily available. Though the data is not recorded, the anecdotal evidence for this is quite convincing. Prior to the introduction of sugammadex, there was a task force set up, whose primary goal was to identify all occurrences of reintubations after general anesthesia to learn how to improve the quality of care and reduce these occurrences. Each month there would be a meeting to review all such cases requiring reintubations, and on average there would be 1-3 cases to go through. Since the group incorporated the use of sugammadex into their practice, however, the number of meetings per year for this task force has decreased significantly as there were barely any cases to report on or to review. In fact, there have been only 2-3 cases of reintubations per calendar year since the group incorporated the use of sugammadex. Admittedly, this anecdotal evidence does not prove this point; however, there is a trend for improved patient care and outcomes with this new reversal agent.

One of the biggest drawbacks regarding the use of sugammadex is the question of what agent to use in the case where a patient who is just reversed needs to be given additional paralysis. At that point, the use of steroidal agents will not be effective in typical doses; however, other nondepolarizing agents in the class of benzylisoquinoliniums (e.g., cisatracurium), or even succinylcholine would not be affected by sugammadex and will continue to work normally in the typical doses. Given that a solution to this concern exists, and that this possibility is quite rare, it is not regarded to be a high consideration in deciding which reversal agent to use.

Summary

What does this all translate to clinically? With the vast amount of supporting evidence for the use of sugammadex over its counterparts, the ASA has released guidelines that recommends the use of sugammadex for deep, moderate, and shallow levels of neuromuscular blockade that is induced by either rocuronium or vecuronium, while the use of neostigmine being categorized as a reasonable alternative for minimal blockade only [17]. Deep neuromuscular blockade is described as a train of four count of 0; moderate blockade is equal to a train of four count of 1 to 3 twitches; shallow blockade is equal to a train of four count of 4 with a ratio less than 0.4; and a minimal blockade is equal to a train of four ratio of 0.4 to 0.9. The ensuing question regarding the ideal dosing of sugammadex is one that needs further examination, especially as Sugammadex has a greater affinity for rocuronium than vecuronium [17]. Currently, there is only dosing recommendations of Sugammadex for deep and moderate neuromuscular blockade, and not for shallow and minimal blockade. The dosing guidelines that do exist also do not specify between reversing rocuronium versus vecuronium, as currently only depth of block affects sugammadex dosing recommendations and not the choice of anesthetic agent for neuromuscular blockade [17]. Future studies and guidelines should focus on identifying the appropriate dosing for rocuronium and vecuronium separately to ensure adequate reversal, avoid any residual paralysis and limit any overdosing with sugammadex. Given the evidence now accumulated on this topic, it is clear that Sugammadex is the superior reversal agent and has not only been improving patient outcomes, but also has shown to be the more cost-effective approach.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Rany Makaryus, NYU Langone Hospital-Long Island, 259 1st Street, Hoag 3, Mineola, NY 11501, USA. Tel: 516-424-9834; Fax: 516-663-8585; E-mail: Rany.Makaryus@nyulangone.org

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