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LETTER TO THE EDITOR

Sugammadex-Is Cost the Only Drawback?

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Sugammadex first underwent clinical trials as a proposed reversal agent for rocuronium in 1999. After almost a decade of promising results, it received its first regulatory approval in 2008 by the European Union. Several years later, sugammadex was approved in 57 countries, and over 10 million patients had received the drug. In 2015, the FDA followed suit and approved sugammadex for the "...reversal of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adults...". This new reversal agent is impressive because it utilizes a novel, selective, and specific mechanism of action. The modified cyclodextrin works as a direct antagonist, encapsulating rocuronium (and to a lesser degree vecuronium), resulting in the clinical reversal of muscle paralysis. Sugammadex's characteristics and flexibility is a game-changer in the prevention of residual muscle paralysis.

Residual muscle paralysis is an important safety issue, with multiple studies demonstrating an association with increased postoperative complications. The pathophysiology of these complications isn't difficult to explain. One can only imagine the signs and symptoms in an awake patient (i.e. the panic from not having the strength to take a deep breath or move at full strength; the anxiety of not controlling one's body movement). A study by the Cleveland Clinic demonstrated that major complications such as reintubation, myocardial infarct, CHF, stroke, were 2.1% higher in sufficiently unreversed patients [1]. In addition, minor complications such as hypotension/hypertension, bradycardia, and nausea/ vomiting were 35% higher. Even with such high stakes, residual muscle paralysis remains a reality today. The RECITE-US study looked at 328 patients over ten hospitals and showed that 31% of the patients had a train of four less than 0.6 [2].

The adequate reversal of neuromuscular blocking agents has been challenging for several reasons: 1) Monitoring neuromuscular paralysis reversal for the most part is by visual inspection, 2) The capital cost of acquiring a quantification monitoring, 3) Production pressures of the OR environment (i.e., workplace efficiency by minimizing turnover time), 4) The increase incidence of surgical patients with co-morbidities (i.e. obesity, obstructive sleep apnea, elderly - all factors that increase residual blockade), 5) The shift towards minimally invasive surgical technique requiring intense muscle relaxation until the end of surgery, and 6) The increase incidence of the arm tucked position which precludes peripheral nerve monitoring.

Our thought is that the risk of residual blockade can be decreased with the routine use of rocuronium and sugammadex. Rocuronium is a preferred paralysis agent due to its predictable duration and rapid onset. Although many argue that succinylcholine is safer because it has the fastest onset and shortest duration of action, succinylcholine does not have a direct antagonist. Since sugammadex is a direct antagonist to rocuronium, the reversal of rocuronium is more reliable which is a serious consideration since a significant number of providers do not monitor for muscle paralysis. In a study, up to 40% of anesthesia practitioners did not utilize a qualitative monitor, and a far higher percentage did not have access to a quantitative monitor [3]. Although using sugammadex does not negate the need for monitoring, it can boost confidence in minimizing residual paralysis.

The case can be made that the use of rocuronium and sugammadex should be the rule and not the exception. This standardization potentially can improve



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safety while minimizing waste and error. In 2016, Martinez, et al. concluded that patients who either were not reversed or reversed with neostigmine had a residual block in 30% of cases, whereas those reversed with sugammadex only had 1.2%. Not surprisingly, the incidence of major complications was 7.2% in the neostigmine group and 1.1% in the sugammadex group [4]. Furthermore, a study in 2019 compared neostigmine to sugammadex, with endpoints being the incidence of 30-day unplanned readmission rates, hospital length of stay, and hospital charges. The sugammadex group was 34, 20, 24% lower than the neostigmine group, respectively [5]. So, is it the acquisition cost which is the only factor limiting the use of sugammadex? The additional cost can be justified from the standpoint of patient safety, OR efficiency, and quality of care. Are we currently sacrificing safety for cost (which will be a moot point once this drug's patent expires)? Impactful advances in medicine (i.e. propofol, 5HT3 antagonists) require costs for research and development to improve patient care. Assuming residual blockade is on that par, if not more so, the case can be made for the routine use of sugammadex.

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