

## Sugammadex after the Reappearance of Four Twitches during Train-of-four Stimulation: Monitoring and Dose Considerations

### To the Editor:

I read with great interest the article by Pongrácz *et al.*<sup>1</sup> evaluating the appropriate dose of sugammadex to reverse neuromuscular blockade (NMB) after the reappearance of four twitches during train-of-four (TOF) stimulation. It is a welcome addition to previous studies that have demonstrated the superiority of sugammadex over anticholinesterases in completely, safely, and quickly reversing rocuronium-induced NMB of any magnitude.<sup>1,2</sup> This study raises two important issues, which deserve comment.

To my knowledge, this is the first clinical trial that has considered a TOF ratio of 1.0, instead of 0.9 or greater, as the goal for reversal of NMB.<sup>1</sup> A TOF ratio of 0.9 or greater may not indicate full recovery, as this ratio can be associated with impaired neuromuscular transmission,<sup>3</sup> inhibition of the hypoxic-ventilatory response, and upper airway or pharyngeal dysfunction.<sup>4</sup> Acceleromyography studies have confirmed the potential for inadequate reversal at a TOF ratio of 0.9 or greater, leading to the recommendation that a TOF ratio of 1.0 or greater be used to confirm complete recovery from NMB.<sup>2,4</sup> With the introduction of sugammadex into clinical practice, obtaining a TOF ratio of 1.0 or greater is now a relatively easy goal to achieve, and it is hoped that future research and clinical practice will follow the example shown by Pongrácz *et al.*<sup>1</sup> by insisting on the use of this ratio as the goal for NMB reversal.

Although Pongrácz *et al.*<sup>1</sup> found that 1.0 mg/kg was sufficient to achieve a TOF of 1.0 after the reappearance of four twitches on TOF stimulation, I have some concern to recommend it as the optimal dose of sugammadex in this situation. A dose of sugammadex is just sufficient to liberate approximately 30% of the postjunctional nicotinic receptors, a condition necessary for the complete reversal.<sup>5</sup> So, even with complete reversal of NMB by sugammadex, up to 70% of the postjunctional nicotinic receptors may remain occupied by steroidal neuromuscular-blocking agent.<sup>5</sup> Therefore, a larger dose of sugammadex, such as 2 mg/kg, may be more appropriate, as it will create a greater rocuronium tissue to plasma concentration gradient, thereby causing more free rocuronium molecules to move into the circulation, where they are promptly encapsulated.<sup>5</sup> Reducing the number of postjunctional nicotinic receptors occupied by rocuronium may reduce the risk of recurarization<sup>6</sup> and the neuromuscular-blocking effects of agents that decrease acetylcholine release,<sup>5</sup> thus further improving patient safety.<sup>4-6</sup>

With its unique mechanism of action, proven efficacy in reversing NMB, fast onset of action, and minimal adverse effects, sugammadex has become an important tool in modern-day anesthesia practice.<sup>2,4,5</sup> By using a TOF ratio of 1.0 or greater as the goal for NMB reversal and administering the most appropriate dose for the degree of blockade, full potential of sugammadex for improving patient care and safety may be achieved.

### Competing Interests

The author has received payment for lecture from Merck Sharp & Dohme (Italy).

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### References

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### In Reply:

In his letter to the Editor, Dr. Carron raises two important issues referring to the published data by Pongrácz *et al.*<sup>1</sup> evaluating low doses of sugammadex to reverse rocuronium-induced neuromuscular blockade (NMB) after the reappearance of four twitches during train-of-four (TOF) stimulation.

First, Dr. Carron emphasizes the importance of having considered a TOF fade ratio of 1.0 or greater as an adequate reversal in our study, unlike 0.9 or greater used by other investigators. Indeed, to date in all published studies investigating sugammadex, the primary outcome parameter was a nonnormalized TOF ratio of 0.9. However, a recorded TOF fade ratio of 0.9 does not equal full recovery of the NMB, because after sugammadex the TOF ratios regularly reach a final value of 1.0 or greater. Therefore, we considered a