Sugammadex Dosing in Bariatric Patients

To the Editor:

We read with interest the article by Llauradó *et al.*[1] focusing on the efficiency of ideal body weight–adjusted sugammadex dosing in patients undergoing bariatric surgery. The authors report a high incidence of slow responders and outliers leading to a potential risk of recurarization; they consider ideal body weight–adjusted dosing of sugammadex as unsafe. However, we feel that a significant lack of clarity in both design and methods makes it difficult to draw any conclusion from that study.

First, patients in the deep-block group had a posttetanic count (PTC) ≤ 2, thus including also those with no response to PTC. According to the good clinical research practice for pharmacodynamic studies of neuromuscular blocking agents, deep block is defined as no response to train-of-four stimulation but at least one response to the 15 PTC stimulations.[2] This definition is used because PTC1 is the deepest neuromuscular block that can be precisely defined; as soon as no response to PTC is detectable, neuromuscular block can no longer be quantified. Indeed, it may be close to return of the first PTC response, but it may also be much more intense, with no return to the first PTC answer for a long period. This heterogeneous group of neuromuscular blockade with no response to PTC is summarized as intense blockade.[2] Although the recommended dose of sugammadex to antagonize moderate or deep block is 2 and 4 mg/kg, respectively, only a few studies focused on sugammadex dosing for intense neuromuscular block, *i.e.*, when no response to PTC can be detected.[3,4] They proposed a dose between 8 and 16 mg/kg depending on the elapsed time interval between rocuronium injection and start of reversal. In the present study, however, these patients were also treated with 4 mg/kg ideal body weight sugammadex. Thus, independently of whether sugammadex dosing is based on real or ideal body weight, it was significantly underdosed in patients with no response to PTC. This may have contributed to the "outliers" observed by Llauradó *et al.* Second, all patients in the present study had either a PTC ≤ 2 or a train-of-four count ≥ 2. Not 1 of the 120 patients included in this observational study has a neuromuscular block level in between, that is, corresponding to 3–15 PTC or a train-of-four count of 1. This is at least surprising and let suppose an active control rather than a real observation. Third, induction of anesthesia was not standardized; some patients received succinylcholine, whereas others did not. This, however, does not facilitate the interpretation of the results. How can the authors exclude that some of the patients in their study were "slow responders" or "outliers" because of impaired plasmacholinesterase activity leading to slow succinylcholine metabolism rather than a delayed response to sugammadex-induced reversal? Fourth, there may be a bias in the patient's group assignment. According to the authors, the level of neuromuscular block at the end of surgery determined whether the patients were assigned to deep or moderate block group. However, the total dose of rocuronium was identical in both groups, and surgical time was slightly longer in the deep-block group. Thus, despite the same dose of rocuronium and somewhat longer surgical procedure, 43 patients had a profound block, whereas the remaining 77 patients had a shorter duration but only a moderate neuromuscular block. Interindividual variability to neuromuscular blocking agents is large and the group assignment let suppose that patients more "resistant" to rocuronium were assigned to the moderate group, whereas patients more "sensitive" to rocuronium were assigned to the deep group. Finally, if the train-of-four ratio did not reach 0.9 within 2 or 3 min, respectively, a second dose of sugammadex was given. This, however, did not allow to draw any conclusions on either the risk of recurarization or the time course of an ideal body weight–adjusted sugammadex dosing.

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In Reply:

We read with interest the valuable comments of Schmartz *et al.*, which require some clarifications.

Succinylcholine was used in 14 patients (three in deep blockade [DB] and 11 in moderate blockade [MB]). After excluding patients administered succinylcholine, main data, expressed as median (range) and [percentile 10–90] were total dose of rocuronium (mg), 107.5 (70–290) [85.5–148.7] DB *versus* 100 (50–180) [68–157] MB, $P = 0.169$; total dose of sugammadex (mg), 250 (120–520) [200–454] DB *versus* 150 (100–320) [110–273] MB, $P < 0.001$; dose of sugammadex per real body weight (mg/kg), 2.30 (1.12–4.42) [1.51–3.925] DB *versus* 1.2272

(0.88–3.37) [1.0224–2.3638] MB, $P < 0.001$; time to train-of-four ratio of 0.9 s, 168.5 (20–460) [80–338] DB *versus* 111.5 (28–300) [49.7–213] MB, $P < 0.001$. In DB, 16 (40%) patients required a second dose of sugammadex and 14 (21%) in MB, $P = 0.047$. These results are not different from data presented.[1] Even if some activity of succinylcholine would be present, it was not determining the results of the study.

Sugammadex is able to quickly reverse a neuromuscular blockade (by <2 min); increasing the dose does not hasten recovery.[2] In our protocol, if the train-of-four ratio was less than 0.9, a second dose of sugammadex was administered after 3 min for DB and 2 min for MB. More than 20% and approximately 40% of patients with MB and DB, respectively, required a second dose. Delayed response to sugammadex is pointed out in most of the publications related to sugammadex administration to lean patients. In addition, the combination of underdose and delayed response has been associated with recurarization.[3] In favor of safety, tracheal extubation has to be performed when the train-of-four ratio 0.9 target is achieved. A delayed response to sugammadex (target not achieved at the expected time) makes tracheal extubation more challenging, especially in the morbid obese, who are at risk of potential airway serious complications; therefore, requiring close surveillance and neuromuscular monitoring.

In the first draft to Anesthesiology, "Profound Blockade" was defined as "posttetanic count ≥ 1 to T1 appearance," literal translation of the text in the observational study protocol (approval reference SAB-SUG-2011-01). Reviewers asked for a better description of DB, so we remade figure 1, modifying the definition of DB by using the number of twitches in the posttetanic count (posttetanic count = 0–12 twitches); however, on the draft we send and in the final draft version, "posttetanic count = 0–2 twitches" were written (this error was also reproduced in the text). This has created difficulty in interpreting methods. We apologize for that. Reviewing our database, all patients with DB had almost one twitch at posttetanic response count; therefore, no patient had intense neuromuscular blockade.

Even not significant, slightly more rocuronium was administered to patients with DB (even more after excluding patients administered succinylcholine). As it has been indicated, the interindividual variability to neuromuscular blocking agents is large, even more for rocuronium.[4] This variability could be facilitated by the association with sevoflurane in our patients.

When large doses of rocuronium have been used, we do not know how much rocuronium is still available after sugammadex administration. Redistribution of rocuronium might explain delayed response, or even outliers; however, this statement remains to be demonstrated.

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ERRATUM

Sugammadex Ideal Body Weight Dose Adjusted by Level of Neuromuscular Blockade in Laparoscopic Bariatric Surgery: Erratum

In the article on page 93 of the July 2012 issue, there are three places where errors occur related to the number of twitches given:

1. In the abstract (p. 93), the second sentence of the Methods section should read: "To reverse a deep blockade (12 or fewer posttetanic twitches), a dose of sugammadex of 4 mg/kg ideal body weight (IBW) was followed by a second dose of 2 mg/kg IBW if the TOFR was less than 0.9 after 3 min."
2. In the section Neuromuscular Monitoring and Sugammadex Administration Protocol (p. 94), the second sentence should read: "To confirm a deep blockade, we applied a titanic stimulus (of 50 Hz for 5 s) and counted the posttetanic twitches 3 s later; the block was considered deep if zero to 12 posttetanic twitches were detected."
3. In figure 1 (p. 95), text should read: "Deep Blockade (from PTC = 0 to 12 Twitches)" instead of "Deep Blockade (from PTC = 0 to 2 Twitches)."

The publisher regrets these errors.

Reference

Llauradó S, Sabaté A, Ferreres E, Camprubí I, Cabrera A: Sugammadex ideal body weight dose adjusted by level of neuromuscular blockade in laparoscopic bariatric surgery. Anesthesiology 2012; 117:93–8