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

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ABSTRACT

Background: Bariatric surgery patients are at risk of perioperative airway collapse. Neuromuscular blockade should be fully reversed before tracheal extubation. The optimal dosage of the reversal agent sugammadex in the morbidly obese is still unknown. This study explored the sugammadex dose adjusted according to train-of-four ratio (TOFR).

Methods: Prospective observational study of consecutive patients scheduled for laparoscopic bariatric surgery. To reverse a deep blockade (2 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. To reverse a moderate blockade (reappearance of the second twitch in the TOF), a 2 mg/kg IBW dose of sugammadex was followed by a second dose of 2 mg/kg IBW if the TOFR was less than 0.9 after 2 min. Sugammadex effectiveness was reflected by the time required to obtain a TOFr of 0.9 or more.

Results: A total of 120 patients were included. The blockade was deep at the end of surgery in 43 and moderate in 77. The median times (range) to TOFR of 0.9 or more were 167 (20–460) seconds and 113 (28–300) seconds in deep and moderate blockades, respectively (P < 0.05). The percentage of patients requiring a second dose of sugammadex were larger after deep blockades (39.5% [n = 17] vs. 23.4% [n = 18] after moderate blockades); the difference was not significant.

Conclusion: A sugammadex dose calculated according to ideal body weight is insufficient for reversing both deep and moderate blockades in a considerable number of morbidly obese patients.

What This Article Tells Us That Is New

• A sugammadex dose calculated according to ideal body weight is insufficient for reversing both deep and moderate blockades in morbidly obese patients.
depth and ensure complete recovery of pharyngeal muscles when given at doses of 2–16 mg/kg. However, for reversing deep blockade in lean patients, outliers have been identified and the optimal dosage required in the morbidly obese patient is still unknown. Our hypothesis was that calculating the sugammadex dose on the basis of ideal body weight (IBW) will lead to a higher incidence of slow response. Our objective was therefore to study the sugammadex dose required to reach a train-of-four ratio (TOFR) of 0.9 or more in these patients after scheduled laparoscopic bariatric surgery, using an anesthetic protocol that contemplated TOF-guided additional doses for slow responders.

Materials and Methods

Patient Selection
After obtaining approval from the ethics committee of Hospital Universitari de Bellvitge, Barcelona, and the Spanish Ministry of Health and Science (approval reference SAB-SUG-2011–01) for a prospective observational study, consecutive patients scheduled for laparoscopic bariatric surgery at the same hospital in January–December 2010 were recruited. Written information about the study was given to all patients and was explained orally; patients were enrolled if they gave signed consent to use of their data. Exclusion criteria were a contraindication for steroidal neuromuscular blocking agents (rocuronium or vecuronium), chronic renal failure, and reported previous use of sugammadex in order to exclude potential allergic reactions. Patients were weighed on the same day of surgery to obtain their real body weight (RBW); their IBW according to sex, height, and physical constitution was also recorded. No exclusion criteria regarding weight were established.

Study Procedures
All patients were placed in semisitting position to make ventilation and airway management easier. Standard monitoring (automated blood pressure cuff, electrocardiography, pulse oximetry, and capnography) was used and the bispectral index was analyzed. All patients were placed on a warm blanket of convection air (Warm-Touch; Mallincrod Medical, St. Louis, MO). Neuromuscular transmission was monitored according to good clinical practice recommendations, as follows: 2 mg/kg IBW was first administered and the TOFR was recorded every 20 s; and if the TOFR was less than 0.9 after 3 min, another sugammadex dose of 2 mg/kg IBW was administered. To reverse a deep blockade, sugammadex was administered as follows: 2 mg/kg IBW was first administered and the TOFR was recorded every 20 s; and if the TOFR was less than 0.9 after 2 min, another sugammadex dose of 2 mg/kg IBW was administered (fig. 1).

Variables and Statistical Analysis
The main variable of interest was the total dose of sugammadex administered to achieve a TOFR of 0.9 or more. The efficacy of sugammadex administration was reflected by the time required to obtain a TOFR of 0.9 or more and extubation after the first dose of sugammadex. Other variables recorded were patient characteristics (including comorbidity and American Society of Anesthesiologists risk classification), surgical and perioperative variables (including intra- and postoperative events), and hospital stay.

To calculate the sample size we estimated that 10% of patients would need a second dose of sugammadex and assumed that a difference of 20% in the second-dose requirement would be clinically significant. At a level of statistical significance of 0.05 for comparisons and power of 0.80, it was estimated that 120 patients should be included.

The normal distribution of continuous variables was checked with a Kolmogorov–Smirnov test; a nonparametric Mann–Whitney U test was used to compare continuous variables and a chi-square test was used to compare discontinuous variables. Statistical significance was set at $P < 0.05$. Data are presented as absolute number (%) or median and
range; because analysis of preliminary findings suggested that a substantial number of outliers would be present for some variables, we also calculated 10th–90th percentiles. SPSS software version 15.0 (SPSS, Chicago, IL) was used for all analyses.

**Results**

We enrolled 120 patients. The blockade was deep at the end of surgery in 43 and moderate in 77. Patient characteristics, comorbidity, surgical procedures, and postoperative outcomes were similar in the two groups (table 1). Two patients could not be extubated in the operating room: one (deep blockade group) awakened slowly and also had slow normalization of bispectral index values, whereas the other (moderate blockade) had a neck hematoma related to vascular puncture. Both patients recovered from the blockade after sugammadex injection and were extubated in the surgical intensive care unit without further incidents. No patients required reintubation of the trachea, and none experienced a critical airway incident. No adverse effects of sugammadex were recorded. Two patients in the deep blockade group and four in the moderate blockade group required reoperation; four patients (one in the deep blockade group and three in the moderate blockade group) required readmission to the surgical intensive care unit.

The total doses of rocuronium were similar in the two groups; however, a significantly higher median dose of sugammadex was used in patients with a deep blockade and longer times until a TOFR of 0.9 or more and extubation were also observed in that group (table 2). Likewise, the percentage of patients requiring a second dose of sugammadex tended to be larger in the deep blockade group (39.5% [n = 17] vs. 23.4% [n = 18] in the moderate blockade group), although the difference was not significant (P = 0.062, chi-square test). The patients who required a second dose of the reversal agent did not differ from the other patients with regard to age, RBW, body mass index, sex, American Society of Anesthesiologists physical classification, total dose of rocuronium, or duration of the surgical procedure (data not presented).

**Discussion**

A single IBW-based dose of sugammadex successfully achieved a TOFR of 0.9 or more in 60% and 77% of patients who had deep and moderate neuromuscular blockades, respectively. However, the requirement of a second IBW-based dose in large percentages of the remaining patients in both groups indicates that high percentages of slow responders should be expected and that there is potential risk of reoccurrence of blockade.

Moderate neuromuscular blockades were successfully reversed with IBW-based doses of sugammadex in 103 laparoscopic bariatric surgery patients studied by Van Lackner et al., although the authors reported longer and great interindividual variability of times to recovery of a TOFR of 0.9 than have been observed for lean patients. Increasing the IBW-based dose by 40% achieved significant reductions in time to a TOFR of 0.9 in the study of Van Lackner et al., but
### Table 1. Patient Characteristics, Comorbidity, and Surgical and Perioperative Variables

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Deep Blockade (n = 43)</th>
<th>Moderate Blockade (n = 77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 (20–68)</td>
<td>46 (26–64)</td>
</tr>
<tr>
<td>RBW (kg)</td>
<td>113 (84–64)</td>
<td>114 (87–165)</td>
</tr>
<tr>
<td>IBW (kg)</td>
<td>63 (51–85)</td>
<td>63 (50–86)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>42 (35–62)</td>
<td>43 (34–71)</td>
</tr>
<tr>
<td>Male/female (%)</td>
<td>33/67</td>
<td>36/64</td>
</tr>
<tr>
<td>ASA risk I/II/III (%)</td>
<td>2/65/33</td>
<td>3/57/40</td>
</tr>
<tr>
<td>AHT, n (%)</td>
<td>24 (56)</td>
<td>31 (40)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>8 (19)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>MI or CHF, n (%)</td>
<td>3 (7)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>OSAS, n (%)</td>
<td>25 (58)</td>
<td>30 (39)</td>
</tr>
<tr>
<td>NIVS, n (%)</td>
<td>23 (53)</td>
<td>29 (38)</td>
</tr>
<tr>
<td>PVT, n (%)</td>
<td>1 (2)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Hemoglobine (g/l)</td>
<td>14 (10–17)</td>
<td>14 (9–17)</td>
</tr>
<tr>
<td>Creatinine (mg/ml)</td>
<td>70.5 (40–129)</td>
<td>67 (47–134)</td>
</tr>
<tr>
<td>Antiplatelets therapy, n (%)</td>
<td>4 (9.3)</td>
<td>7 (9.1)</td>
</tr>
<tr>
<td>Antihypertensive therapy, n (%)</td>
<td>19 (42)</td>
<td>26 (35)</td>
</tr>
<tr>
<td>Surgical technique* (%)</td>
<td>13/20/10/0</td>
<td>23/39/12/3</td>
</tr>
<tr>
<td>Surgical time (minutes)</td>
<td>130 (60–330)</td>
<td>120 (60–260)</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>3 (3–15)</td>
<td>2 (3–30)</td>
</tr>
</tbody>
</table>

Data are expressed as median (range), or absolute number (%).

* Surgical technique: (1/2/3/4/) = 1: tubular gastroplasty; 2: gastroscopic bypass; 3: duodenal switch; 4: others.

AHT = arterial hypertension; ASA = American Society of Anesthesiology; BMI = body mass index; CHF = congestive heart failure; IBW = ideal body weight; MI = myocardial ischemia; NIVS = noninvasive ventilation support; OSAS = obstructive sleep apnea syndrome; PVT = profound venous thrombosis; RBW = real body weight.

Table 2. Rocuronium and Sugammadex Doses, Reversal, and Extubation Times

<table>
<thead>
<tr>
<th></th>
<th>Deep Blockade (n = 43)</th>
<th>Percentile 10–90</th>
<th>Moderate Blockade (n = 77)</th>
<th>Percentile 10–90</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dose of rocuronium (mg)</td>
<td>100 (20–290)</td>
<td>82–144.8</td>
<td>97.5 (30–180)</td>
<td>63.5–151.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Total dose of sugammadex (mg)</td>
<td>280 (120–520)</td>
<td>200–436</td>
<td>150 (100–320)</td>
<td>110–272</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dose of sugammadex per RBW (mg/kg)</td>
<td>2.35 (1.12–4.42)</td>
<td>1.54–3.81</td>
<td>1.23 (0.88–3.37)</td>
<td>1.02–2.354</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to TOFR of 0.9 or more (seconds)</td>
<td>167 (20–460)</td>
<td>83.4–332.8</td>
<td>113 (28–300)</td>
<td>51.6–210</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to tracheal extubation (seconds)</td>
<td>585 (22–1, 320)</td>
<td>127.4–698</td>
<td>220 (30–1, 305)</td>
<td>93–540</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patients requiring a second dose, n (%)</td>
<td>17 (39.5)</td>
<td>—</td>
<td>18 (23.4)</td>
<td>—</td>
<td>0.062†</td>
</tr>
</tbody>
</table>

Data are expressed as median (range). * Mann–Whitney U test. † Chi-square test.

RBW = real body weight; TOFR = train-of-four ratio.
increasing the dose does not hasten recovery, and an effect plateau is seen in most patients around 2 min.24–26 However, outliers and slow responders have been detected when sugammadex is administered after a moderate and deep blockades.27,18,24,25 This issue, the presence of outliers, is of concern because it is related to potentially serious complications. Even after a TOFR of 0.9 or more has been achieved, upper airway weakness and an obstructive pattern have been observed in outlier patients.27 In a recently reported case of inadequate reversal in a morbidly obese patient, repeated doses of rocuronium (total dose of 170 mg) had been given in the course of surgery lasting 170 min.28 Although a TOFR of 0.9 was reached 5 min after sugammadex administration (1.74 mg/kg RBW), recurrence of blockade was detected 15 min later.

The dose of sugammadex must be sufficient to affect the gradient between the peripheral and central compartments, and more is required when repeated doses or continuous infusion of rocuronium has been used. However, overdoses, such as would result from using RBW in morbidly obese patients in the standard calculations, would be costly and ineffective in a high number of patients given the aforementioned ceiling effect. From a clinical point of view, although neuromuscular monitoring is not widely used, it is therefore advisable so that we can identify patients who are likely to exhibit more variability of response.29 Acceleromyography is associated with a reduced incidence of residual blockade,30 and although it overestimates neuromuscular recovery in comparison with mechanomyography,31 it has been validated for clinical research20 and we feel it is viable for this clinical setting.

We did not randomize our patients to moderate or deep blockade during recovery; therefore, even though our two study groups were comparable, lack of randomization remains a formal limitation of our study. A strength, however, is that we reproduced the usual clinical conditions, offering as much rocuronium as the patients needed during surgery and starting reversal just after surgery ended. We also limited the waiting times until a second dose was administered in both groups; therefore, we can assume that more patients might have eventually reached a TOFR of 0.9 or more after a single IBW-based dose. As our aim was to demonstrate an association between underdosing and slower response than has been reported in lean patients, however, we feel the design we applied was both safe and efficient.

We conclude that sugammadex cannot be safely calculated for morbidly obese patients on the basis of IBW. Until a dose regimen that works well in the majority of morbidly obese patients is established, we can expect to see a large number of slow responders and even outliers. The implication seems to be that neuromuscular monitoring of depth is necessary in the morbidly obese so that a second dose of sugammadex can be given as soon as it is clear that response is slow.

References


18. White PF, Tufanogullari B, Sacan O, Pavlin EG, Viegas OJ,


Adjusted Sugammadex Dose in Bariatric Surgery

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