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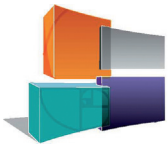

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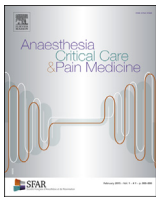

Original Article

Reversal of neuromuscular blockade by sugammadex in laparoscopic bariatric surgery: In support of dose reduction

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ABSTRACT

Introduction: Sugammadex is the first molecule able to antagonize steroidal muscle relaxants with few adverse effects. Doses are adjusted to body weight and the level of neuromuscular blockade. Sleeve gastrectomy is becoming a very popular form of bariatric surgery. It requires deep muscle relaxation followed by complete and rapid reversal to decrease postoperative and especially post-anaesthetic morbidity. Sugammadex is therefore particularly indicated in this setting. The objective of this study was to evaluate the deep neuromuscular blockade reversal time after administration of various doses of sugammadex (based on real weight or at lower doses). Secondary endpoints were the interval between the sugammadex injection and extubation and transfer from the operating room to the recovery room. We then investigated any complications observed in the recovery room.
Materials and methods: This pilot, prospective, observational, clinical practice evaluation study was conducted in the Amiens University Hospital. Neuromuscular blockade was induced by rocuronium. At the end of the operation, deep neuromuscular blockade was reversed by sugammadex at the dose of 4 mg/kg.
Results: Sixty-four patients were included: 31 patients received sugammadex at a dosage based on their real weight (RW) and 33 patients received a lower dose (based on ideal weight [IW]). For identical rocuronium doses calculated based on IBW, sugammadex doses were significantly lower in the IW group: 349 (± 65) mg versus 508 (± 75) mg ($P < 0.0001$). Despite this dose reduction, neuromuscular blockade reversal took 115 (± 69) s in the IW group versus 87 (± 40) s in the RW group, but with no significant difference between the two groups ($P = 0.08$). The intervals between injection of sugammadex and extubation ($P = 0.07$) and transfer from the operating room to the recovery room ($P = 0.68$) were also non-significantly longer in the IW group. The mean dose of sugammadex used by anaesthetists in the IW group was 4 mg/kg of ideal weight increased by 35% to 50% ($n = 20$; 351 ± 34 mg). No sugammadex adverse effects and no residual neuromuscular blockades were observed. Postoperative nausea and vomiting (PONV) was observed in 19.4% of patients in the real weight group versus 27.3% in the ideal weight group (P = NS).
Conclusion: Reversal of deep neuromuscular blockades by sugammadex in obese subjects can be performed at doses of 4 mg/kg of ideal weight plus 35–50% with no clinical consequences and no accentuation of adverse effects.

1. Introduction

Laparoscopic bariatric surgery requires deep muscle relaxation throughout the operation. Pharmacological reversal of the neuromuscular blockade before the patient regains consciousness is highly recommended. Since 2009, many studies have confirmed the rapid efficacy and good safety of sugammadex for reversing moderate and deep neuromuscular blockades induced by steroidal muscle relaxants, but few studies have been conducted in obese populations. In the absence of data, sugammadex is administered at doses calculated as a function of the patient's real weight (RW) or at lower doses based on the patient's ideal weight (IW) [1,2]. The objective of this study was to evaluate the reversal time in morbidly obese subjects after administration of sugammadex based on real weight (RW) or at a lower dose.

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2. Materials and methods

We conducted a pilot, prospective, observational, professional practice evaluation study in the Amiens University Hospital.

After obtaining approval from the Amiens University Hospital non-interventional research ethics committee (CEERNI), adult patients, candidates for laparoscopic bariatric surgery consisting of sleeve gastrectomy, were included, in the absence of a history of allergy to intravenous anaesthetics including muscle relaxants and severe renal failure. The primary objective of this study was to evaluate reversal time (recovery of T4/T1 > 0.90), using a chronometer, as a function of the dose of sugammadex administered by the anaesthetist: 4 mg of sugammadex per kg of real weight or a lower dose (based on ideal weight).

Secondary endpoints were the interval between the injection of sugammadex and extubation and the interval between injection and transfer from the operating room to the recovery room.

All patients were operated under general anaesthesia using 1.5–2 mg/kg propofol, 0.5 μg/kg sufentanil and 0.6 mg/kg rocuronium to facilitate tracheal intubation. All drug doses were calculated based on IBW. Standard monitoring was set up: ECG monitor, noninvasive measurement of mean blood pressure (MBP), heart rate (HR), pulse oximetry (SpO_2) and end-tidal carbon dioxide ($EtCO_2$). Two surface electrodes were placed over the ulnar nerve at the wrist in order to monitor the blockade at the adductor pollicis by acceleromyography (TOF-Watch SX;Organon). TOF Watch® neuromuscular monitoring was calibrated. All neuromuscular monitoring was conducted according to the guidelines established by Good Clinical Research Practice in pharmacodynamic studies of neuromuscular blocking drugs [3]. Anaesthesia was maintained with 4–6% desflurane and 0.1–0.25 μg/kg/min remifentanil. Postoperative nausea and vomiting (PONV) prevention was performed with 8 mg of dexamethasone and 1.25 mg of droperidol. During surgery, rocuronium injections were administered at a dose of 0.15 mg/kg when T2 reappeared in TOF stimulation. The TOF Watch® value at the end of the operation was recorded. An injection of sugammadex was then performed, either at the dose of 4 mg/kg of real weight or at a lower dose based on ideal weight increased by a percentage, as decided by the anaesthetist in charge of the patient. The level of neuromuscular blockade was monitored continuously. A chronometer was started at the time of the sugammadex injection to measure: the T4/T1 response > 90% recovery time, the interval between the sugammadex injection and extubation and the interval between the injection and transfer from the operating room to the recovery room. Tracheal extubation was performed only when the Airway was protected, tidal volumes and minute volumes of more than 10 $ml.kg^{-1}$ IBW, the patients were able to open their eyes and oxygen saturations were acceptable.

An assessment was performed in the recovery room to detect any known complications (pain, drowsiness, muscle weakness, acute respiratory distress, nausea and/or vomiting) and any residual neuromuscular blockade.

Statistical analyses were performed with IBM SPSS 20® software. Calculation of the sample size based on a 60-second reduction of the reversal time indicated that 30 subjects per group were necessary to obtain a power of 95%.

Quantitative variables were expressed as means (± standard deviation) and were compared by Mann-Whitney and Wilcoxon nonparametric tests.

Qualitative variables were described by numbers and percentages and 95% confidence intervals. The various parameters were compared by Pearson's and Fisher's Chi-squared tests.

The primary outcome of this study was reversal time (recovery of a T4/T1 ratio > 0.90) determined by calculating the difference (together with the 95% confidence interval) between the group receiving 4 mg/kg of real weight and the group receiving a lower dose. The type 1 error for the primary outcome was therefore set at 5%.

For all statistical tests, a P value < 0.05 was considered significant.

3. Results

Seventy-five patients were initially included in the study. Eleven were subsequently excluded because of a TOF > 1 of 4 responses at the end of the operation in 10 cases and one patient was excluded because of defective monitoring. The remaining sixty-four patients were divided into two groups:

- the real weight group (RW group): patients received a dose of 4 mg/kg of sugammadex according to their real weight (n = 31);
- the ideal weight group (IW group): patients received a dose of 4 mg/kg of sugammadex based on their ideal weight, increased by a certain percentage (n = 33).

3.1. Epidemiological data

Demographic characteristics were comparable in the two groups (Table 1). Patients in the IW group nevertheless tended to be younger than those of the RW group, with no statistically significant difference (P = 0.08).

3.2. Intraoperative data

Doses of propofol and rocuronium were similar in both groups. Propofol was administered at a dose of 3 ± 0.7 mg/kg in the RW group versus 2.9 ± 0.65 mg/kg in the IW group (P = 0.86) and rocuronium was administered at a dose of 0.88 ± 0.2 mg/kg in the RW group versus 0.85 ± 0.2 mg/kg in the IW group (P = 0.67). No allergic reaction to rocuronium was observed. A halogenated anaesthetic, desflurane, was used for maintenance in every case.

The anaesthetic protocol was therefore similar in both groups, apart from the dose of remifentanil, which was lower in the IW group than in the RW group (P = 0.04).

At the end of the operation, the level of neuromuscular blockade and the reversal time were evaluated by means of a TOF Watch® monitor and a chronometer (Table 2). Deep muscle relaxation was observed in every case (TOF = 0 or 1 response) with a mean post-tetanic count of 3.7 ± 3.6 in both groups.

The reversal time (recovery of a TOF > 0.90) was 28 seconds longer in the IW group. The mean operating time was 82 ± 26 minutes and an anaesthesia time of about 2 hours. No allergic reaction to sugammadex was observed.

Extubation was possible at a mean of 11.6 ± 7.7 min after the sugammadex injection in the IW group versus 9.3 ± 7.2 min in the RW group (P = 0.07). Transfer to the recovery room was possible after 18.5 ± 7.4 min (RW) versus 17.6 ± 7.3 min (IW) (P = 0.68).

Table 1
Patient demographic characteristics.

	RW group (n = 31)	IW group (n = 33)	P value*
Sex ratio M (%)/F (%)	8 (29%)/23 (71%)	8 (24%)/25 (76%)	0.78
Age (years)	43 (±11)	38 (±11)	0.08
BMI (kg/m^2)	44.3 (±5.1)	45.1 (±7.2)	0.99
Weight (kg)	123 (±17)	128 (±24)	0.57
Height (m)	1.67(±0.09)	1.68 (±0.07)	0.68
ASA II score (%)/III (%)	27 (87%)/4 (13%)	29 (88%)/4 (12%)	1.00

M: male; F: female; BMI: Body Mass Index; ASA: American Society of Anesthesiologists.

* Qualitative variables are expressed as numbers (percentage), quantitative variables are expressed as means (± standard deviation), P < 0.05 is considered as significant.