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RESEARCH

Dosage of sugammadex according to the calculated lean body mass in obese female patients: time to reverse moderate neuromuscular blockade induced by rocuronium

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Background: Sugammadex is a selective relaxant binding agent for antagonism of prolonged rocuronium-induced neuromuscular blockade. The recommended dose is 2 mg/kg. Based on the pharmacological characteristics of sugammadex in obese patients, the calculated lean body mass (CLBM) should be used to determine the dose to reverse moderate neuromuscular blockade induced by rocuronium.
Objective: A study was undertaken to prove that sugammadex can be used according to CLBM to reverse moderate neuromuscular blockade in obese female patients.
Methods: This is a prospective, non-randomised, observational study. Sugammadex was used at the end of bariatric surgery on obese patients with a body mass index > 32 kg/m^2. The dose was calculated according to the lean body mass. Muscle blockade was assessed using train-of-four monitoring.
Results: Twenty women were included in this study. All patients were female and ASA 2. The age of patients ranged between 20 and 50 years with a mean age of 35.74 (±10) years. The mean CLBM was 50 kg. The mean time from administration of sugammadex to reverse neuromuscular blockade from two responses of TOF to T4/T1 > 90% was 167.25 seconds (2.8 minutes) (60–285 seconds).
Conclusion: It is concluded that the calculated lean body mass can be used to calculate the dose of sugammadex for obese female patients to reverse moderate neuromuscular blockade induced by rocuronium.

Keywords: calculated lean body mass, neuromuscular blockade, rocuronium, sugammadex

Introduction

Muscle relaxants must be administered according to the calculated lean body mass (CLBM) and not to the real weight of the patient, particularly in the case of morbidly obese patients. Rocuronium used according to the ideal body weight has a shorter duration of action than when the real bodyweight is used.[1] Sugammadex is a molecule that reverses neuromuscular blockade induced by rocuronium and vecuronium.[2] We recruited obese female patients who were monitored during bariatric surgery with a train-of-four (TOF) monitoring and a measure of the single twitch before and after rocuronium administration. At the end of surgery, patients received 2 mg/kg of sugammadex according to the CLBM and we measured the recovery time from two to four responses of TOF, and the time to obtain a ratio T4/T1 equal to or greater than 90%. The aim of this study was to determine whether the CLBM can be used in obese female patients to determine the dose of sugammadex necessary to reverse rocuronium neuromuscular blockade in obese female patients.

Methods

A prospective, non-randomised, observational study was conducted between May 15 and August 3, 2009. Following ethical committee approval, we measured the recovery time (TOF—90%) of patients older than 18 years during bariatric surgery. The procedures included gastric bypasses, gastric sleeves or gastric bandings. The body mass index (BMI) was above 32 kg/m^2. Twenty consecutive patients gave their informed consent to participate in the study. A recommended dose of sugammadex is 2 mg/kg weight.[3,4]

TOF and twitch were measured with a TOF-watch SX monitor 2.2 (Organon (Ireland) Ltd., Swords, Co. Dublin, Ireland) and electronically recorded every 15 seconds. A stimulus of 60 mA current over 200 µs was used.[3]

The anaesthetic technique included propofol (2 mg/kg), sufentanil (0.2 µg/kg), rocuronium (1.2 mg/kg) and desflurane. Although a recommended rocuronium dose is 0.6–1.2 mg/kg weight,[3,4] we used 1.2 mg/kg and used the CLBM as the weight factor. The twitch (100%) was measured before administration of the muscle relaxants but after induction of anaesthesia. At the end of the procedure, sugammadex (2 mg/kg CLBM) was administered when the TOF reached two responses out of four. The time between two and four twitches of TOF with a twitch above 90% of the initial one (T4/T1 ≥ 90%) was noted in seconds.

Lean body mass (LBM) was calculated using the formula of James[5] for females:

$$\text{CLBM} = 1.07 \times \text{weight(kg)} - (148 \times [\text{weight (kg)}/\text{height(cm)}]^2)$$

We measured the mean time to recovery and the range. We determined the relationship between: (i) the BMI and recovery time, (ii) weight and recovery time, (iii) CLBM and recovery time and (iv) body temperature and recovery time. The statistical

analysis included the covariance between each factor and the correlation coefficient of Pearson.

Exclusion criteria were patients with a history of allergic reaction on sugammadex, rocuronium or other neuromuscular blockers, hepatic or renal failure, patients with neuromuscular diseases and patients with any chronic medication having a myorelaxant effect such as benzodiazepines. All patients were older than 18 years.

Results

The study was carried out on 20 ASA 2 female patients. The patients ranged in age from 20 to 50 years with a mean age of 35.74 (±10) years. The patient demographic and surgical data are given in Table 1. For patient 12, we had to replace the accelerometer of the TOF-Watch at the beginning of anaesthesia to ensure calibration of the neuromuscular stimulation prior to neuromuscular relaxation. The automatic record of the TOF was corrected for the baseline twitch.

The characteristics of the neuromuscular blockade and sugammadex reversal are summarised in Table 2. The mean BMI was 41.43 kg/m^2 (37.42–47.25). The weight range was 90 kg to 130 kg, with a height of 154 cm to 182 cm. The mean weight was 110.32 kg. The mean CLBM was 50 kg (42.96 kg–64.24 kg). The mean dose of sugammadex was 100 mg (90 mg–130 mg). In Figure 1, the recovery curves for each patient are shown. Patients 8 and 16, following a recovery to above 90%, showed a lower value during the subsequent minute. All values were above 90% within 360 seconds (6 minutes).

The time to four twitch responses and 90% of the initial twitch is given in Table 2. The mean time was 167.25 seconds (2.8 minutes) (116.25–213.75 [60–285]) and a median time of 150 seconds (2.5 minutes).

The regression curves between weight (Figure 2), BMI (Figure 3), LBM (Figure 4), body temperature (Figure 5) and recovery time showed no direct relationship with recovery. The covariance was low.

Discussion

We obtained only a small sample and during the short period of study we were unable to include men that met the inclusion criteria of the study. These are limitations of our study.

Sugammadex forms very tight 1:1 complexes with aminosteroid-based relaxants.[2] It reverses rocuronium or vecuronium-induced neuromuscular blockade.[2–4] It is a selective relaxant binding agent. The dose of sugammadex is related to the dose of the neuromuscular agent.[3,6–8]

Leykin et al. stated[1] that the dose of rocuronium should be assessed on the basis of the ideal rather the real bodyweight in clinical practice. In obese patients, Meyhoff et al.[9] recommend using the ideal bodyweight (IBW) for dosing of rocuronium. The IBW dosage provides a shorter duration of action, without a difference in onset time or tracheal intubation conditions. Pühringer et al.[10] showed that obesity did not alter pharmacodynamics or pharmacokinetics in female patients.

In our study the dose of rocuronium (1.2 mg/kg) was based on the calculated lean body mass. Intubation of our patients was accomplished with ease. During anaesthesia, we followed the neuromuscular blockade with a TOF-Watch SX, to maintain a full block during the procedure. Murphy et al.[11] and others[12] validated the TOF-Watch SX monitor as a safe quantitative technique to assess the neuromuscular blockade and the residual curarisation. According to Kopman et al.[2,12]: 'there is now general agreement that return to TOF ratio of 90% or greater at the end of surgery should be our goal after the administration of nondepolarizing relaxants'. In our study, a TOF-Watch monitor was used and all the values were electronically registered every 15 seconds.

Table 1: Demographic and surgical patient data

Patients	Weight (kg)	Height (cm)	BMI (kg/m^2)	CLBM (kg)	Surgery
1	110	163	41.40	51.20	Gastric bypass
2	119	169	41.66	54.81	Gastric bypass
3	95	154	40.06	44.76	Gastric banding
4	130	176	41.97	58.00	Gastric banding
5	108	160	42.17	48.10	Gastric banding
6	112.5	168	39.86	53.90	Gastric banding
7	108	162	41.15	49.12	Gastric banding
8	107	162	40.77	50.02	Gastric banding
9	95	154	40.06	44.76	Gastric banding
10	124	162	47.25	47.20	Gastric banding
11	111	160	43.36	48.31	Gastric banding
12	130	176	41.97	58.00	Gastric banding
13	90	155	37.46	46.51	Gastric banding
14	109	166	39.56	52.16	Gastric bypass
15	108	159	42.72	47.12	Gastric bypass
16	106	154	44.69	42.96	Gastric banding
17	124	182	37.43	64.24	Gastric banding
18	108	158	43.26	47.13	Sleeve
19	97	161	37.42	50.51	Gastric banding
20	115	161	44.36	48.44	Gastric banding

Table 2: Study results

Patients	Anaesthesia time in minutes	Body temperature in C°	Dose of rocuronium in mg	Dose of sugammadex in mg	Time to TOF T4 in seconds and (minutes)	Time to 90% recovery in seconds and (minutes)
1	176	31.6	95	100	30 (0.5)	195 (3.2)
2	186	33.5	85	110	30 (0.5)	225 (3.7)
3	92	36.8	65	90	75 (1.2)	255 (4.2)
4	89	34.0	70	115	45 (0.7)	210 (3.5)
5	97	33.5	60	100	30 (0.5)	60 (1)
6	92	35.7	75	108	30 (0.5)	60 (1)
7	84	34.0	70	100	45 (0.7)	150 (2.5)
8	93	35.7	65	100	45 (0.7)	285 (4.7)
9	92	35.1	65	90	75 (1.2)	150 (2.5)
10	101	34.3	75	95	90 (1.5)	150 (2.5)
11	69	33.3	60	95	95 (1.6)	105 (1.7)
12	142	35.4	95	100	60 (1)	120 (2)
13	83	34.9	62.5	95	45 (0.7)	90 (1.5)
14	188	34.1	78.5	105	15 (0.2)	90 (1.5)
15	241	31.1	95	95	45 (0.7)	285 (4.7)
16	82	33.8	55	90	60 (1)	255 (4.2)
17	109	30.2	85	130	75 (1.2)	195 (3.2)
18	104	34.7	65	95	90 (1.5)	210 (3.5)
19	189	35.2	85	100	75 (1.2)	135 (2.2)
20	60	35.2	50	100	60 (1)	120 (2)

Stout et al.[13] and Wulf et al.[14] found that desflurane did not significantly alter the time to recovery from rocuronium. However, desflurane anaesthesia significantly prolonged the duration of action of rocuronium at 0.9 mg/kg single bolus dose, when compared with sevoflurane or propofol anaesthesia maintenance regimens.[15] In our study, all the anaesthesia procedures were

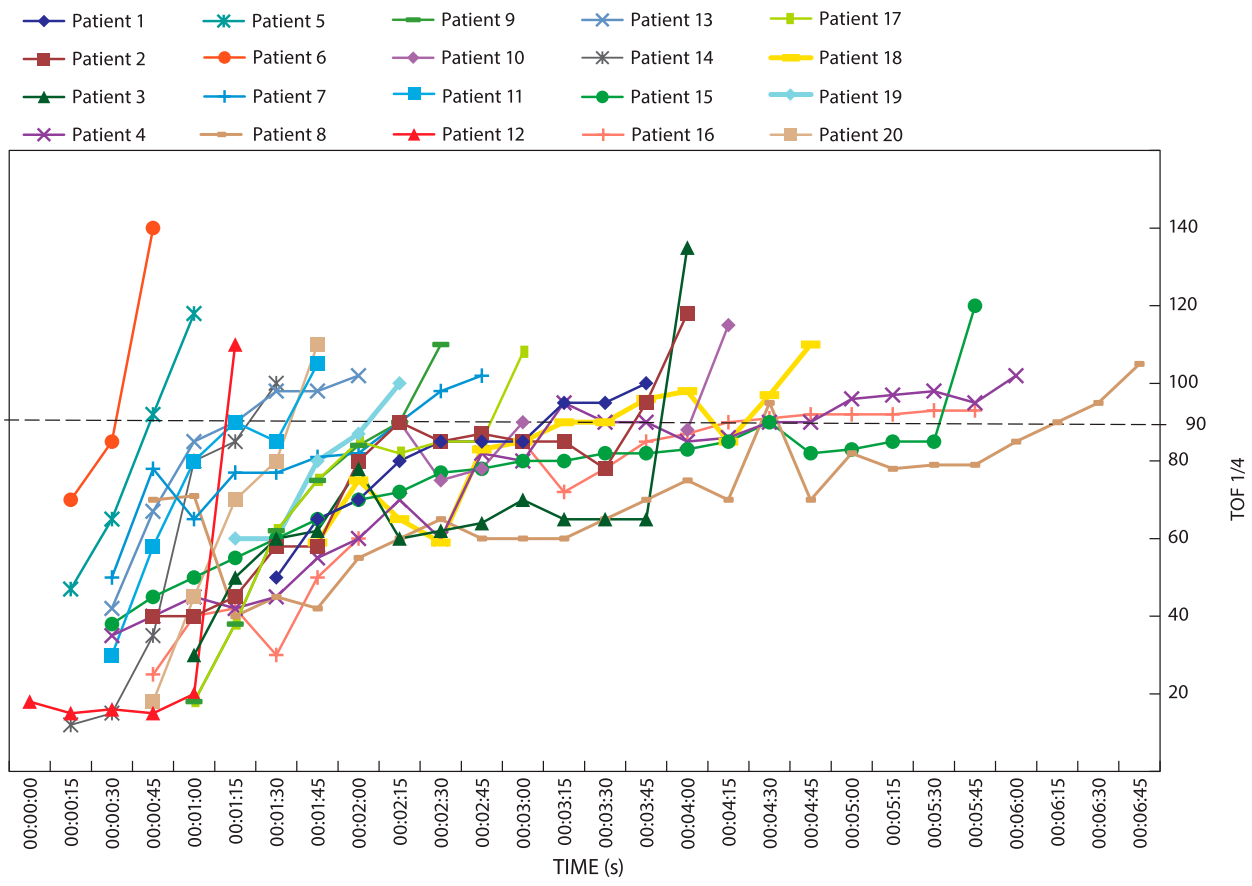

Figure 1. Time to recover 4 on TOF and ratio T4/T1 90%.

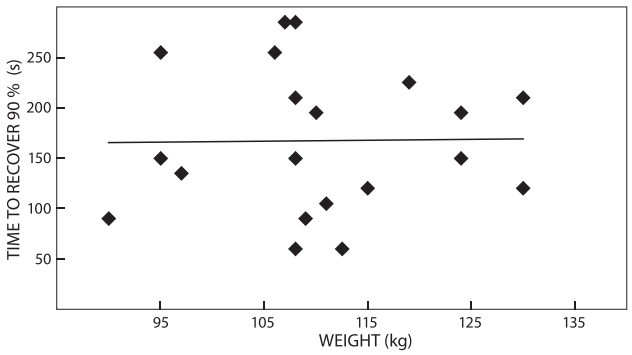

Figure 2: Regression graph between time to recovery 90%, and weight in kg.

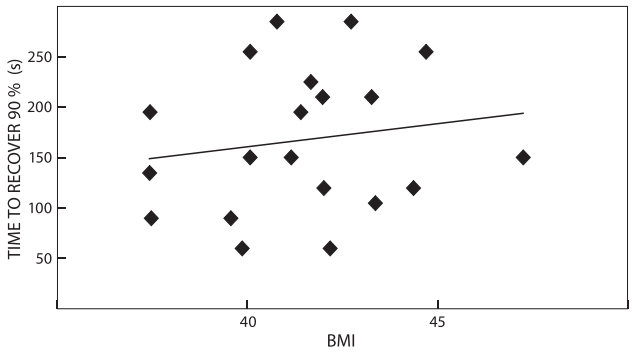

Figure 3: Regression graph between time to recovery 90%, and BMI in kg/m^2.

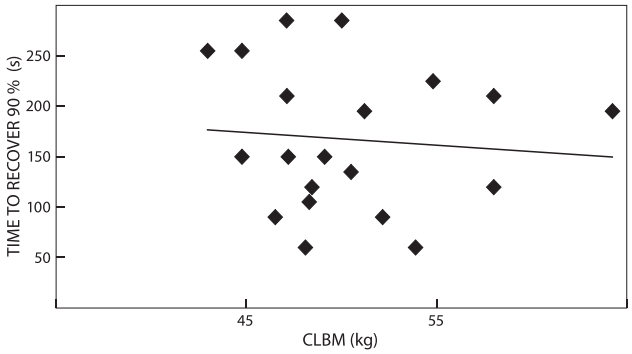

Figure 4: Regression graph between time to recovery 90%, and CLBM in kg.

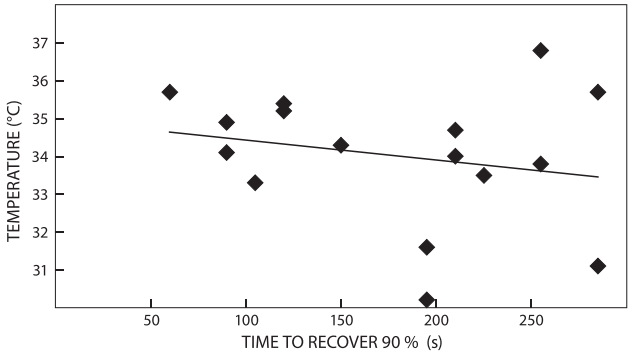

Figure 5: Relation between time to recovery 90% and temperature.

done with desflurane and rocuronium 1.2 mg/kg. Desflurane can change the time to recovery, but should the effect of sugammadex be influenced by the inhalational anaesthetic? Reversal of rocuronium-induced block by sugammadex did not differ between anaesthesia with propofol or sevoflurane.[16]

Most patients (except patient 3) became hypothermic but sugammadex (2 mg/kg), given based on the CLBM, was effective at quickly reversing neuromuscular blockade for all. This was true even though it has been demonstrated that hypothermia prolongs the duration of action of rocuronium.[17] We did not observe inadequate ventilation after extubation of patients and transfer to recovery room where the hypothermia was treated.

Debaene and Meistelman[4] propose using sugammadex at the end of the procedure when the TOF indicates a second twitch of 4, at a dosage of 2 mg/kg in order to obtain recovery in a time period shorter than 5 minutes. Mirakhur[18] recommends 2 mg/kg for a shallow block and 4 mg/kg for a deep block. Groudine et al.[7] showed that with a dosage of 2 mg/kg there was a great variability in recovery time, reported to be between 1.8 and 15.2 minutes, but with higher dosages (8 mg/kg) the mean recovery time narrows to 0.8 to 2.1 minutes. Plaud et al.,[3] in a multicentre randomised dose-finding study with patients aged from 28 days to 65 years, found that the mean time was less than 2 miutes, except in children and adolescents where it was longer. When 0.6 mg/kg rocuronium was used, the neuromuscular blockade was reversed with 2 mg/kg of sugammadex in a time shorter than 3 minutes. This was dose dependent. In our study, the mean time is 167.25 seconds (2.8 minutes) (116.25–213.75 [60–285]) and the median is 150 seconds (2.5 minutes).

These results are comparable to the results of the literature. But in the literature the dosage is calculated according to bodyweight,[19] IBW[20] or IBW + 40%[21] and not the CLBM. The effect of sugammadex is dose dependent. If we use the bodyweight for the dosage, sugammadex would be very effective. The mean weight of our population is more than twice (2.24) the CLBM. For each patient, one ampoule of sugammadex was sufficient to reverse neuromuscular blockade. Conversely, as the drug is expensive, its economically justified use would be good practice.[22,23] If we transfer the ratio to the cost, on average we would overspend by 125%. This is based on the cost and the volume of one ampoule of the drug. It may be better practice to use the CLBM to calculate the dose of sugammadex, instead of the total bodyweight. We recommend a similar study on similarly obese patients which includes a larger sample of both men and women who remain normothermic during surgery.

Conclusion

Our results show that the calculated lean body mass can be used for the dosage of sugammadex to reverse moderate neuromuscular blockade at the end of the procedure. The dosage of 2 mg/kg in a population of obese female patients allows a recovery time comparable to the general population of adults. We recommend the use of 2 mg/kg based on the calculated lean body mass. Monitoring of the neuromuscular blockade is important to detect any residual curarisation.

Disclosure statement – No potential conflict of interest was reported by the authors.

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