

# Sugammadex is associated with better respiratory recovery than neostigmine following reversal of anaesthesia-associated neuromuscular blockade in the morbidly obese patients following elective laparoscopic surgery

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## ABSTRACT

Complete and reliable neuromuscular reversal is important to successful anaesthetic recovery in the morbidly obese patient undergoing laparoscopic surgery. Our goal was to determine whether sugammadex, a selective reversal agent is associated with better respiratory recovery than neostigmine following the reversal of anaesthesia-associated neuromuscular blockade by rocuronium in the morbidly obese. Peak Expiratory Flow Rate a surrogate marker for respiratory function, was the primary outcome measured and secondary outcome measures included post-operative nausea and vomiting, pain and head lifting. We found that patients reversed with sugammadex had a significantly higher post-operative PEFR as compared to those reversed with neostigmine and glycopyrrolate group.

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## 1. Introduction

Sugammadex is a synthetically modified gamma-cyclodextrin that has recently been identified as a selective reversal agent for rocuronium and vecuronium induced neuromuscular blockade (NMB).<sup>1</sup> It selectively forms one-to-one complexes with steroidal NMB agents such as rocuronium and vecuronium thus reducing the free plasma concentration of these agents, which rapidly terminates NMB. Unlike the commonly used combination of cholinesterase inhibitors and muscarinic receptor blockers, sugammadex acts without interfering with the receptor system.<sup>2</sup>

The clinical safety and efficacy of sugammadex for reversal of rocuronium-induced NMB has been confirmed in several high quality studies.<sup>2–11</sup> There is also evidence that it produces more rapid NMB recovery than neostigmine, however there is relatively limited data pertaining to its physiological effects in morbidly obese patients, who are particularly high risk for adverse respiratory events in the immediate post-operative period.<sup>10,11</sup>

To date there has not been a study comparing the respiratory recovery of morbidly obese patients following NMB reversal with sugammadex or neostigmine. The aim of this cohort comparison study was to compare the immediate physiological effects of reversal of the NMB using sugammadex versus neostigmine in morbidly obese patients.

## 2. Material and methods

Forty consecutive morbidly obese patients (BMI > 35 kg/m<sup>2</sup>) undergoing either elective laparoscopic cholecystectomy or bariatric surgery under general anaesthetic between July 2013 and November 2013 were enrolled into this prospective cohort comparison study auditing two anaesthetists' practices for the same operating upper general surgical consultant.

Anaesthetic drug doses were calculated according to corrected body weight (CBW), according to the formula  $CBW = IBW + 0.4 \times (\text{total body weight} - IBW)$ , where IBW is ideal body weight. Use of CBW for dose calculation is advocated by many bariatric anaesthetists, as it appears to be the measure that best accounts for the altered pharmacokinetics of the morbidly obese.<sup>12</sup>

General anaesthesia was induced identically in both groups with intravenous fentanyl 0.1 µg/kg CBW and propofol 2 mg/kg CBW.

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Muscle relaxation was induced with rocuronium (Esmeron, Organon, USA) 0.6 mg/kg to a maximum of 1.1 mg/kg CBW prior to intubation and with maintenance doses of 0.1–0.2 mg/kg CBW to maintain normocapnia, up to a maximum of 2 further doses. For maintenance of anaesthesia, the patients were ventilated with a mixture of air, oxygen and sevoflurane in vol% depending upon the age of the patient and the clinical response. All patients received standardised intra-operatively intravenous pain relief of 1 g paracetamol, 50 mg diclofenac and 100 micrograms further of fentanyl.

Standard anaesthesia monitoring consisted of non-invasive arterial blood pressure, pulse oximetry, temperature monitoring, ECG and monitoring of neuromuscular function. The body temperature was controlled and maintained over 35°C with a minimum of 35.9°C at time of reversal. Neuromuscular function was monitored using accelerometry (TOF-Watch Device, Organon, Oss, The Netherlands). The electrodes were placed on the patient's skin over the facial nerve on the Orbicularis oculi and Corrugator supercilii muscles after careful preparation at 1–2 cm apart. Before tracheal intubation, supramaximal stimulation was performed followed by single-twitch stimulation (1 Hz). After intubation, the stimulation was changed to train-of-four (TOF) and measurements were recorded every 15 seconds. At the end of surgery, operative time was noted and when two responses were achieved on the train-of-four (TOF) stimulation, a NMB reversal agent was administered; either sugammadex 2.0 mg/kg CBW or neostigmine 50 µg/kg CBW with glycopyrrolate 10 µg/kg CBW. Neuromuscular function measurements were continued every 15 seconds after reversal until a TOF ratio of 0.9 was achieved.

Peak Expiratory Flow Rate (PEFR), a surrogate marker for respiratory function, was the primary outcome measure. This was recorded prior to induction and at 5, 10 and 20 minutes after reversal. Secondary outcome measures included pain (as measured by a visual analogue scale), post-operative nausea and vomiting (PONV) requiring use of rescue anti-emetic ondansetron, and head lifting score. These outcome measures were also recorded 5, 10 and 20 minutes after administering reversal agent to assess global clinical outcomes.

Patients reversed with sugammadex were compared with those reversed with neostigmine and glycopyrrolate. The following software packages were utilised: Statistical Package for the Social Science (SPSS), version 21.0 (SPSS, IBM, Armonk, NY, USA) and Excel 2010 (Microsoft, Redmond, WA, USA). Data was assessed for normal distribution using the Shapiro–Wilk method of analysis. Parametric continuous variables are referred to as the mean (SD); comparisons use a two-tailed *t*-test. Categorical variables are compared using a two-tailed Fisher's exact test. The non-parametric continuous variables are referred to as median, alongside their interquartile range (IQR). Statistical significance is considered if  $p < 0.05$ .

### 3. Results

Of the 40 patients who underwent elective laparoscopic bariatric surgery or laparoscopic cholecystectomy, 20 were reversed with sugammadex and 20 with neostigmine and glycopyrrolate. There was no significant difference between patient characteristics, co-morbidity prevalence or duration of surgery in the two groups (see Table 1).

The pre-operative PEFR were comparable between the two groups (see Table 2). As shown, the recovery in PEFR was significantly better in the Sugammadex group at 5, 10 and 20 minutes post-reversal time.

Secondary outcome measures of time to TOF 0.9 and time to head lift were significantly shorter in patients receiving sugammadex as compared to those patients receiving neostigmine and glycopyrrolate (see Table 3). Post-operative pain scores were significantly better in the sugammadex group, and proportion of patients requiring rescue anti-emetics trended to less in the sugammadex group.

### 4. Discussion

Morbidly obese patients undergoing anaesthesia for general surgery are at high risk for respiratory complications following reversal of NMB.<sup>13</sup> There is considerable interest in assessing the efficacy of anaesthetic reversal agents on respiratory function. PEFR has been shown to be a good surrogate measure of respiratory muscle strength, with low PEFR associated with ineffective swallowing and coughing and inadequate protective reflexes from the larynx and pharynx, as well as respiratory muscle weakness which can result in hypoventilation and hypercapnia.<sup>14,15</sup>

Postoperative residual curarization (PORC) is defined as residual paresis after emergence from general anaesthesia with neuromuscular blocking drug.<sup>11</sup> The presence of PORC attenuates the normal ventilatory response to hypoxia by impairing adequate function of the carotid body. PORC may impair coughing, as well as increasing the likelihood of atelectasis. It has been shown that even a small degree of PORC increases the incidence of critical respiratory events.<sup>11</sup> Reliance on clinical signs and symptoms to determine degree of reversal of neuromuscular function is not effective and only careful monitoring of neuromuscular function (in this study through assessment of TOF) can accurately detect PORC.

Sugammadex can also be used to treat the symptoms of PORC.<sup>11</sup> The recommended dose of sugammadex depends on the depth of neuromuscular block: 16 mg/kg for a deep block, 4 mg/kg for a shallow block and 2 mg/kg to speed up recovery of neuromuscular function, when at least two responses on TOF stimulation are achieved.

**Table 1**  
Demographics of patients

Parameter	Sub-parameter	Neostigmine and glycopyrrolate (n=20)	Sugammadex (n=20)	P value
Surgery Undertaken	Bariatric Procedure	7	9	
	Cholecystectomy	13	11	
Mean age (years)		42.0 (±8.0)	44.0 (±10.7)	0.51
Gender (% female)		16 (80%)	17 (85%)	1.00
Mean BMI in kg/m <sup>2</sup>		42.5 (±6.4)	42.9 (±6.7)	0.85
Number with ASA 3 or above (%)		6 (30%)	8 (40%)	0.74
Co-morbidities	Number with hypertension (%)	12 (60%)	11 (55%)	1.00
	Number with COPD (%)	7 (35%)	8 (40%)	1.00
	Number with diabetes mellitus (%)	6 (30%)	4 (20%)	0.72
	Number with sleep apnoea (%)	3 (15%)	3 (15%)	1.00
Duration of surgery (minutes)		70.1	76.9	

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