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Research Article

Improved recovery profiles in sinonasal surgery Sugammadex: Does it have a role?

Nevan Mekawy, Eman A. Fouad Ali *

Department of Anesthesia, Faculty of Medicine, Cairo University, Egypt

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KEYWORDS

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Abstract *Objective:* Sinonasal surgery is one of the shared airway surgeries that are not uncommonly complicated intra or postoperatively. The proper anesthetic management of these cases plays a crucial role creating a bloodless field. Sugammadex is a new selective relaxant binding drug as it provides a rapid decrease in free rocuronium in the plasma and at nicotinic receptor that help proper awakening of these patients which is extremely important for minimizing the postoperative respiratory complications. The aim of this study is to compare recovery profile in sinonasal surgery in patients reversed by conventional anticholine esterase (Neostigmine) versus those reversed by Sugammadex.

Methods: This study included 40 patients ASA physical status I and II aged 20–45 years with chronic sinusitis undergoing endoscopic sinus surgery with or without septoplasty, hypotensive anesthesia to maintain MAP (50–60 mm Hg), muscle relaxation throughout the procedure at 1–2 posttetanic count (PTCs) by rocuronium infusion, and anesthetic depth maintained using BIS (50–60). Patients were allocated randomly into two equal groups to receive either Sugammadex 4 mg/kg (group I) or Neostigmine 0.05 mg/kg and atropine 0.02 mg/kg (group II) as a reversal agent, and assessment of postoperative respiratory complications was performed using the Postoperative Respiratory System Evaluation Score (PRSES) at 1st and 5th minutes after extubation.

Results: The reversal time showed highly significant difference between the two groups. Patients in the Sugammadex group could reach a TOF of 0.9 in a mean time 2.47 (0.51) min versus 24.21 (4.7) min for the Neostigmine group; postoperative respiratory complications, the Sugammadex group and the Neostigmine group did not differ statistically; however, more patients in Neostigmine

* Corresponding author.
E-mail address: Mhz_home@hotmail.com (E.A. Fouad Ali).
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group showed respiratory complications at 1st and 5th minutes after extubation as shown by PRSES Scoring System.

Conclusion: This study showed that the use of Sugammadex in reversing rocuronium induced neuromuscular block in patients undergoing functional endoscopic surgery is superior to Neostigmine. Further studies are required to weigh the cost benefit relationship of the use of Sugammadex in routine clinical practice.

1. Introduction

Sinonasal surgery is one of the shared airway surgeries that are not uncommonly complicated intra or postoperatively due to factors related either to the surgeon or to the type of surgery itself [1]. The spread of endoscopic sinus surgery is aiming for minimizing surgical invasiveness, blood loss, and pain than the open method for all mild and moderate cases [2].

The proper anesthetic management of these cases plays a crucial role to minimize the intra-operative conditions by creating a bloodless field by using peripheral vasodilator, beta blockers, and ensuring deep muscle relaxation, thus facilitating the endoscopic surgical intervention [3,4].

As for postoperatively, proper awakening of these patients is extremely important for minimizing the postoperative respiratory complications as laryngo-spasm, stridor, and difficulty in breathing, so that adequate reversal of the residual of non-depolarizing neuromuscular blocking drugs at the end of the surgery is of critical importance for avoiding these complications in the early postoperative period [5], as it involves the muscles that maintain the patency of the airway or attenuate the ventilatory response to hypoxia especially with the patients who had postoperative nasal obstructions [6].

Sugammadex is a new selective relaxant binding drug that is designed to encapsulate steroidal non-depolarizing neuromuscular blocking agents (NDBAs) and that will allow an effective reverse of any degree of block of both rocuronium and vecuronium [7], as it provides a rapid decrease in free rocuronium in the plasma and subsequently at nicotinic receptor at motor end plate; this promotes the liberation of acetylcholine in which its deficiency may prolong the action of neuromuscular blocking agent [8]. It is a modified –γ– cyclodextrin compound (Organon USA Inc., Roseland NJ). Therefore, its mechanism of action does not result in stimulation of the cholinergic nervous-system [9], thereby avoiding undesirable side effects of routinely used anticholinesterases that need addition of muscarinic antagonist [10].

Aim of the study: Is to compare recovery profile in sinonasal surgery in patients reversed by conventional anticholine esterase (Neostigmine) versus those reversed by Sugammadex.

2. Methods

The study was performed in Kasr el- Ainy hospital in ENT department, 40 patients ASA physical status I and II aged 20–45 years with chronic sinusitis undergoing endoscopic sinus surgery with or without septoplasty were included in the study. Patients enrolled in the study were allocated randomly into two equal group – using a computer generated system – to receive either Sugammadex 4 mg/kg (group I) or Neostigmine 0.05 mg/kg and atropine 0.02 mg/kg (group II) as a reversal agent.

The study excluded patients with cardiovascular system pathology, coagulation defects, bronchial asthma, COPD, or who have muscle disease or neuromuscular disorder. Patients with renal, hepatic diseases and those who are taking any drugs that affect renal function or blood coagulation were also excluded from the study. Patients with history of difficult intubation or suspected to be difficult were also excluded from the study.

Premedication was omitted in all patients. Upon arrival to the operating room, monitors were applied for heart rate reading, mean arterial blood pressure (non-invasively), and pulse oximeter for O2 saturation values. Also, the silver chloride electrodes of nerve stimulator were applied over the ulner nerve, and neuromuscular data were monitored using accelromyography (TOF guard, shering plough-Ireland).

Standard BIS monitor strip (BIS X, Aspect medical system, Norwood, MA, USA) was placed on the patient forehead of the dominant hemisphere according to the guidelines of the manufacturer.

A 20 gauge venous cannula was inserted on the dorsum of the hand. Preoxygenation with 100% oxygen was performed for 5 min while asking the patient to perform mouth breathing during this time calibration of the TOF guard was performed. Induction of anesthesia with propofol 2–2.5 mg/kg, fentanyl 1 μq/kg, and then rocuronium 0.6 mg/kg was administered to facilitate tracheal intubation and was performed when complete blockade occurs as shown by the TOF guard. Ventilator was controlled to maintain end tidal CO_2 at 30–35 mm Hg.

Another IV cannula 20 gauge that was introduced for hypotensive agent infusion Nitroglycerine at a dose of 0.5–5 μq/kg/min was used and titrated to maintained mean arterial pressure between 50 and 60 mm Hg, and propranolol (B-blocker) was given at dose 0.01–0.015 mg/kg to maintain HR and controlling tachycardic reflex of Nitroglycerine. Muscle relaxant infusion at 10–15 μq/kg/min was used to maintain muscle relaxation throughout the procedure at 1–2 posttetanic count (PTCs). Anesthesia was maintained with 50% oxygen in air and 1.5 MAC isoflurane; before patient positioning, an oro-pharyngeal pack was introduced; and then, the patient positioned with head up 30° before surgery started. By the end of the surgical procedure, the surgeon introduced a nasal pack. We stopped the relaxant infusion, the hypotensive agents, and isoflurane was minimized to 0.4%, and the naso-pharyngeal pack was then removed followed by proper inspection for postnasal bleeding and through suctioning.

Upon the appearance of the T2, discontinuation of isoflurane was performed, and either Sugammadex 4 mg/kg or Neostigmine 0.05 mg/kg and atropine 0.02 mg/kg were given to the patients (both prepared in identical 10 ml syringe) by a resident who was blind to the drug injected. Adequate return of neuromuscular function was assessed by the TOF guard. Extubation

Table 1 Postoperative Respiratory System Evaluation Scoring (PRSES) [11].

PRSES-1	Normal respiratory pattern, respiratory rate < 16 and deep enough
PRSES-2	Cough reflex, at least three times without pause times/minute (with retching sound, strain, or short duration of apnea)
PRSES-3	Spasmodic respiratory pattern, extension of exprium
PRSES-4	Partial laryngospasm, severe inspiratory stridor (which can be treated by positive ventilation with oxygen)
PRSES-5	Complete laryngospasm, no air exchange (which needs muscle relaxation with succinylcholine for ventilation)

was performed at TOF ratio of 0.9 and after performing clinical signs of recovery and after full awakening and ability of the patient to follow verbal commands. The time from administration of the study drug till TOF ratio of 0.9 is considered the reversal time immediately after extubation all patients were asked to perform 5 s head lift and hand squeeze for 5 s.

A scoring system of postoperative respiratory complication was performed using the Postoperative Respiratory System Evaluation Score (PRSES) at 1st and 5th minutes after extubation [11] Table 1.

3. Statistical analysis

Data were presented as mean (SD) or number (%) as appropriate. Comparison between the two groups was performed using unpaired Student's *t* test. Categorical variable were compared using Chi-squared or Fisher's exact tests as appropriate. A *p* value less than 0.05 was considered statistically significant.

4. Results

A total of 54 patients consented to participate in this study, and all were ASA I and II. Nine patients were excluded because they did not meet the inclusion criteria, and five patients were withdrawn from the study due to inability to apply the study protocol; these five patients had BIS reading higher than 60 before the reversal drug injection that mandates reopening of inhalational agents which violates the study protocol.

There was no significant demographic difference among the two groups (Table 2). The duration of surgery, isoflurane consumption, Nitroglycerine requirements, rocuronium supplemented, and intraoperative blood loss were comparable and showed no differences between the two groups (Table 3).

Table 2 Demographic data of both groups [mean (SD) or ratio].

	Group I (n = 20)	Group II (n = 20)	P value
Age (years)	28.2 (5.7)	31.4 (6.8)	0.115
Weight (kg)	74.9 (9.8)	76.8 (11.2)	0.248
Sex (male/female)	17/3	11/9	0.082
ASA (I/II)	14/6	16/4	0.711

Table 4 Incidence of postoperative respiratory complication using (PRSES score) in both groups [number (%)].

	Sugammadex group (n = 20)	Neostigmine group (n = 20)	P value
1 min			
Press 1	13 (65%)	10 (50%)	0.50
Press 2	6 (30%)	8 (40%)	0.74
Press 3–5	1 (5%)	2 (10%)	0.99
5 min			
Press 1	16 (80%)	12 (35%)	0.30
Press 2	4 (20%)	7 (35%)	0.48
Press 3–5	0 (0%)	1 (5%)	0.99

As for the reversal time, it showed highly significant difference between the two groups; patients in the Sugammadex group could reach a TOF of 0.9 in a mean time 2.47 (0.51) min versus 24.21 (4.7) min for the Neostigmine group Table 3.

As for the clinical signs of recovery, 17 of 20 patients in the Sugammadex group and 15 of the 20 patients in the Neostigmine group were awake and oriented before transfer to the PACU $p = 694$.

After extubation, one patient only in the Sugammadex group and four patients in the Neostigmine group were unable to perform sustained head left for 5 s $p = 0.341$.

As for postoperative respiratory complications, the Sugammadex group and the Neostigmine group did not differ statistically; however, more patients in Neostigmine group showed respiratory complications at 1st and 5th minutes after extubation as shown by PRSES Scoring System (Table 4).

5. Discussion

The current study showed that – compared to Neostigmine – the use of the novel reversal agent Sugammadex to reverse a steady state of relaxation provided by rocuronium infusion

Table 3 Intra- and postprocedure data in both groups [mean (SD)].

	Group I (n = 20)	Group II (n = 20)	P value
Duration of the surgery (min)	102.3 (12.4)	106.7 (15.1)	0.32
Isoflurane consumption (ml)	54.3 (11.9)	52.9 (10.7)	0.693
Nitroglycerine requirement (mg)	11.6 (2.4)	12.3 (1.8)	0.303
Rocuronium supplemented (mg)	67.2 (8.3)	70.1 (9.4)	0.307
Intraoperative blood loss (ml)	104.6 (13.2)	111.2 (9.8)	0.060
Recovery time (min)	2.47 (0.51)	24.21 (4.7)	< 0.0001

was associated with more rapid and complete reversal with less postoperative respiratory complications.

The study also focused on benefits of ensuring a rapid and complete reversal after a procedure that shares the airway and mandates proper and full recovery of the airway reflexes after awakening.

The study demonstrated that Sugammadex was associated with much faster reversal time 2.47 (0.51) min versus 24.21 (4.7) min for Neostigmine resulting in a reversal time, which is almost 10 time faster than Neostigmine, and this rapid reversal after functional endoscopic surgery is highly desirable since these patients have obstructed nose with nasal pack and the prompt and complete return of the airway reflexes and neuromuscular function will help them to maintain a patent airway.

The recovery to a TOF ratio of 0.9 is considered the standard for neuromuscular recovery after neuromuscular blockers [12]. This is the rational behind choosing the time from injection of the reversal until a TOF of 0.9 as the reversal time in the current study.

The use of Neostigmine for the reversal of residual neuromuscular block is only permitted once recovery has already started; therefore, the appearance of the second twitch T2 of the train of four responses should be detected before the injection of Neostigmine [13].

Therefore, the appearance of T2 was chosen as a prerequisite prior to injection of any reversal agents to permit proper comparison of the study drugs.

The results of the present study were concomitant with those found in previous studies that compared the reversal using either Sugammadex or Neostigmine or Edrophonium [14] and concluded that Sugammadex was way faster in reversing rocuronium and vecuronium induced neuromuscular block than other reversal agents.

Also, previous studies have shown that Sugammadex at doses of 4 mg/kg and 8 mg/kg was able to reverse profound neuromuscular block induced by rocuronium in a mean time 1.7 min [15].

In the current study, the reversal agent was administered as the volatile agent was discontinued which is the usual clinical practice in anesthesia to allow the assessment of the reversal time without being influenced by the volatile agent, and this is contradictory to the study of Bradely et al. in which the volatile agent continued until the TOF ratio of reached 0.9 [12].

Many studies have shown that residual neuromuscular blockade is associated with various complications in the recovery room with subsequent morbidity and mortality [16]. In our study, none of the patients showed residual neuromuscular blockade, and all patients were able to reach a TOF of 0.9. Unlike the study of White et al. [14] which administered the Sugammadex in the presence of the volatile anesthetic, the current study administered the drug while the anesthetic has been discontinued since volatile anesthetic can potentiate the neuromuscular junction and this can potentially slow the reversal process. However, to exclude the risk of awareness in the patients of the current study, the BIS monitor was used and patients were excluded if the BIS was 60 or more before the reversal agent injection and reopening of the isoflurane was performed.

In conclusion, this study showed that the use of Sugammadex in reversing rocuronium induced neuromuscular block in patients undergoing functional endoscopic surgery is superior to Neostigmine. Further studies are required to weigh the cost benefit relationship of the use of Sugammadex in routine clinical practice.

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