Comparison of Sugammadex versus Neostigmine Costs and Respiratory Complications in Patients with Obstructive Sleep Apnoea

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Objective: To compare sugammadex and neostigmine regarding the efficacy in reversing rocuronium-induced neuromuscular block, the incidence of post-operative respiratory complications and costs in patients undergoing surgery for the treatment of obstructive sleep apnoea (OSA).

Methods: After obtaining ethical approval and patient consent, 74 patients in ASA physical status I or II were randomised into two groups to receive 2-mg kg⁻¹ sugammadex (Group S) or 0.04-mg kg⁻¹ neostigmine+0.5-mg atropine (Group N). Groups were compared regarding time to TOF (train-of-four) 0.9, operating room time, post-anaesthesia care unit (PACU) stay, post-operative respiratory complications, costs related to neuromuscular block reversal, anaesthesia care and complication treatment.

Results: Patient demographics, anaesthesia, surgical data and total rocuronium doses were similar between groups. Time to TOF 0.9 was shorter for group S [Group N: 8 (5–18) min; Group S: 2 (1.5–6) min (p<0.001)]. Operating room time [Group S: 72.4±14.3 min; Group N: 96.6±22.8 min (p<0.001)] and PACU stay [Group S: 22.9±10.1 dk; Group N: 36.3±12.6 dk (p<0.001)] were also shorter in Group S. After extubation, desaturation was observed in 12 (32.4%) patients in group N and in 4 (8%) patients in group S (p=0.048). In group N, three patients were reintubated; there were eight (21.6%) unplanned intensive care unit (ICU) admissions. There was one unplanned ICU admission in group S. Negative pressure pulmonary oedema was observed in one patient in group N. The results regarding costs were as follows. The reversal cost was higher in the sugammadex group (vial cost 98.14 TL) than that in the neostigmine group (ampoule cost 0.27 TL; total 6147.88 TL vs. 3569.5 TL); however, complication treatment cost and total cost were lower in group S than those in group N (199.5 TL vs. 3944.6 TL) (staff anaesthesia doctor cost was 0.392 TL per min and the cost of nurse anaesthetist was 0.244 TL per min).

Conclusion: This study confirmed the efficacy of sugammadex over neostigmine for the reversal of rocuronium-induced neuromuscular block. Sugammadex decreases the incidence of post-operative respiratory complications and related costs in patients with OSA.

Keywords: Complication, cost, neostigmine, rocuronium, sugammadex

Introduction

Complete and rapid reversal of the effects of neuromuscular blocker drugs is a primary element of safety in anaesthesia. Neuromuscular conduction that is not completely improved leads to post-operative residual curarisation and the development of complications that are related to respiration (1, 2).

The use of neostigmine, which is a cholinesterase inhibitor, is a standard procedure for the reversal of the effect of neuromuscular blockers, but some side effects, such as slowed heart rate, increased secretion and bronchospasm, make its use more difficult (3, 4). In contrast, anti-cholinergic drugs, including atropine and glycopyrrolate, which are used for preventing these side effects, increase the frequency of arrhythmia and cause blurred vision and sedation (4). Sugammadex, which is a new agent for the reversal of neuromuscular blockade, is a modified gamma-cyclodextrin. It forms a complex with rocuronium, removes it from the circulation and terminates neuromuscular blockade (5). Sugammadex is a safe agent with a low risk of serious side effects (6). The high cost of sugammadex, which is one of the most expensive drugs in anaesthesia practice, prevents it from being used as a standard neuromuscular reversal drug (7). Although it has been suggested that the cost of sugammadex use in anaesthesia can be reduced by shortening the duration of recovery (8), further clinical studies on sugammadex are required (9).

Obstructive sleep apnoea (OSA) is a common sleep disorder that is characterised by pauses in breathing during sleep because of the obstruction of the upper respiratory tract (10). The OSA frequency among the population who have un-

dergone general anaesthesia is unknown; however, it is estimated that 4% of males and 2% of females in the age range of 30–60 years have OSA and 24% of these are surgically treated patients (10). The risk of developing perioperative complications has increased in patients with OSA. This is true both for patients who are operated for OSA and for patients who are operated for any other reason but have OSA as a co-morbidity (11–15). It has been reported that OSA is an independent risk factor for the development of pulmonary complications and the requirement for post-operative mechanical ventilation (11). It can be suggested that the complete and rapid reversal of neuromuscular blockade will decrease both the frequency of complications and costs in patients with high risk for post-operative respiratory system complications.

This study aims to evaluate the use of sugammadex and neostigmine/atropine in patients who were operated for OSA, the efficiency of sugammadex in antagonising the effect of rocuronium, its effect on the frequency of developing post-operative respiratory system complications and its cost.

Methods

This prospective randomised study was conducted in the Dışkapı Yıldırım Beyazıt Training and Research Hospital after receiving ethical approval from the Erciyes University Clinical Research Ethics Committee and written informed consent from patients. The study included patients who were operated for the treatment of OSA and who were in the ASA physiology classes I and II and in the age group ranging from 19 to 65 years. Patients with known hypersensitivity to the study drugs, those on medications that would interact with muscle relaxants and patients having neuromuscular, respiratory, liver and renal diseases, morbid obese, pregnant and lactating patients were excluded. The patients' age, gender, body mass index and apnoea-hypopnoea index (AHI) were recorded.

Patients were divided into two groups by random selection using numbered envelopes. To reverse the effect of rocuronium at the end of surgery, 2 mg kg⁻¹ sugammadex was administered to the sugammadex group (Group S, n=37) and 0.04 mg kg⁻¹ neostigmine+0.5 mg atropine was administered to the neostigmine group (Group N, n=37).

Patients who were taken to the operating theatre without pre-medication had vascular access established with a 20 G cannula, and a balanced electrolyte solution infusion was initiated at a rate of 5 mL kg⁻¹ h⁻¹. In addition to standard monitoring with electrocardiography, non-invasive blood pressure measurement, peripheral oxygen saturation (SpO₂), end-tidal carbon dioxide pressure (EtCO₂), end-tidal desflurane concentration (EtDes) and body temperature (tympanic), bispectral index (BIS) and neuromuscular function was monitored. An active warming blanket was used, and normo-

thermia was maintained during the intervention. Initial heart rate (HR), systolic arterial pressure, diastolic arterial pressure, mean arterial pressure (MAP) and SpO₂ values were recorded.

The monitorization of neuromuscular activity was performed from the adductor pollicis muscle via an acceleromyography technique (TOF Watch[®] SX, Schering Plough, Dublin, Ireland) according to the Good Clinical Research Practice in Pharmacodynamic Studies of Neuromuscular Blocking Agents guidelines (16). For monitoring neuromuscular activity, the forearm was previously cleaned with alcohol and fixed on an arm board before anaesthesia induction. Electrodes were placed on the ulnar nerve trace and an acceleration transducer was placed on the distal phalanx of the thumb. The other four fingers were fixed in a flat position. Neuromuscular conduction data and skin temperature in the hypothenar region were monitored using a TOF Watch SX.

For anaesthesia induction, 1.5–2.5 mg kg⁻¹ propofol was used and then calibration was performed by acceleromyographic train of four (TOF; 0.2 ms time, 50 mA current, 2 Hz frequency). TOF stimuli, repeated at 15-s intervals, were continued until the end of the intervention. During calibration, patients were administered inhaled oxygen. Endotracheal intubation was performed after providing muscle relaxation with rocuronium and TOF 0.1 was obtained. Cormack–Lehane scores of patients were recorded.

Desflurane in a mixture of oxygen (40%) and nitrous oxide (60%) was used for maintaining anaesthesia. The depth of anaesthesia was titrated in such a way that the BIS value would be 40–60. Controlled positive-pressure ventilation was applied to provide an EtCO₂ value of 30–36 mmHg. EtDes was recorded. When a response to the second TOF stimulus (T2) was obtained from patients, they were administered 0.15 mg kg⁻¹ rocuronium. The total doses of muscle relaxants were recorded. For post-operative pain control, patients were intravenously administered 1 g paracetamol 15 min before the end of the operation.

At the end of surgery, rocuronium was antagonised within 10 s and anaesthesia was terminated. Moreover, the TOF value at this moment was recorded (2). When a TOF 0.9 was obtained, patients were extubated. The time between the administration of a neuromuscular-blockade-reversing agent and obtaining a TOF 0.9 was recorded. The state of consciousness of patients was evaluated just after extubation and then at 5-min intervals (awake and oriented=1, can be awakened with minimal stimulus=2 and can be awakened by touching=3). When patients were alert and oriented, muscle strength was also clinically evaluated (by lifting the head for 5 s and shaking the hands for 5 s), and all measurement times were recorded.

Patients who were alert and oriented and had clinically sufficient muscle strength were transferred to the post-anaesthesia care unit (PACU). The durations of surgery and anaesthesia

and the time spent in the operating theatre were recorded. In PACU, patients were administered 3 L min^{-1} oxygen via a nasal cannula. Their HR values, SpO_2 values, blood pressures and respiratory rates were measured at 5-min intervals. In the PACU the muscle strength was clinically monitored.

Post-operative pain was evaluated using an 11-point visual analog scale (VAS) for pain (0=no pain and 10=the most severe pain ever felt). When the VAS pain score was >3 , dextketoprofen (25 mg i.v.) was administered as an additional analgesic agent.

Patients were monitored both after extubation and in PACU and intensive care unit (ICU) with regard to complications.

Complications associated with respiration were defined as cough, breath holding, increased secretion, desaturation ($\text{SpO}_2 \leq 90$), laryngospasm, bronchospasm, hypoxaemia ($\text{PaO}_2 < 60$), apnoea and pulmonary disorders (atelectasis, pneumonia and others). Complications related to circulation were hypertension (MAP $>20\%$ above initial value), hypotension (MAP $>20\%$ below initial value), tachycardia (HR $>20\%$ above initial value), bradycardia ($\text{HR} \leq 45 \text{ beats min}^{-1}$), rhythm disturbances that were not previously present and cardiac arrest. For treating respiration-related complications, the procedures of administering oxygen with a mask, airway manipulation, airway placement and continuous positive airway pressure (CPAP) mask ventilation were implemented. In case of no improvement in hypoxaemia despite these therapies, re-intubation, admission to the ICU and invasive mechanical ventilation (IMV) were performed. Hypertension that lasted for >1 min was treated with nitroglycerin infusion; a 250-mL fluid bolus or 5 mg ephedrine; tachycardia with esmolol infusion and bradycardia with 0.5 mg atropine. Patients with an Aldrete score of ≥ 9 were referred to the clinic.

Patients whose Aldrete score was <9 despite close monitoring and treatment in PACU for 1 h were transferred to ICU. Unplanned admissions to ICU, pulmonary complications (atelectasis, pneumonia and others), blood gas analyses during follow-up, blood biochemistry evaluation, chest radiography and other unplanned procedures, CPAP, IMV treatments and parenteral antibiotic therapies were recorded.

A static model that included the cost of reversal agents, other administered drugs and therapies anaesthesia doctor and anaesthesia nurse costs, hospitalisation in ICU and the treatment of complications (8, 17). According to this model;

Total cost= Reversal cost+Anaesthesia care cost+ Complication treatment cost,

Reversal cost=treatment price (neostigmine or sugammadex-price) $\times$ frequency of treatment,

Anaesthesia care cost (operation room, PACU, ICU)= duration of care $\times$ price of care per minute (doctor, nurse).

Complication treatment cost=frequency of complications $\times$ cost of 1st day, cost of complication treatment and laboratory test and imaging (blood gases, blood biochemistry, chest radiography and other unplanned procedures, mechanical ventilation, parenteral antibiotic therapy)+cost of ICU on other days.

Costs per minute were calculated using information regarding the monthly incomes of anaesthesia doctor and nurse their pension contributions and their weekly working hours. The Healthcare Application Regulation (HAR) was taken as a basis for the cost of arterial blood gas (ABG) analysis, examination of whole blood, blood biochemistry analysis, mechanical ventilation, hospitalisation in ICU/day and parenteral antibiotic therapy, and public cost was calculated.

The primary outcome measure of the study is the time to obtain a TOF 0.9 after the administration of the reversal agent. The secondary outcome measures are the operation room time, PACU time, frequency of respiratory and circulatory complications and cost (reversal, anaesthesia care, complication treatment).

Statistical analysis

Data were statistically analysed using IBM Statistical Package for the Social Sciences for Windows version 21.0 software (IBM SPSS Statics, New York, USA). Numerical variables were summarised as mean $\pm$ standard deviation and median [minimum–maximum] values. Categorical variables were shown as numbers and percentage values. The normality of numerical variables was determined by the Shapiro–Wilk test, and the homogeneity of variances was determined by Levene's test. The presence of a difference between two groups in terms of numerical variables was investigated with a t-test in independent groups when parametric test conditions were provided. In contrast, when these conditions could not be provided, the difference was investigated using the Mann–Whitney U test. The chi-square test was used for determining the presence of a difference between the groups in terms of categorical variables. The significance level was accepted to be a p value of <0.05 . The size of the sample was determined to be 37 patients in each group (power 0.95 and type 1 error 0.05) on the basis of the difference in durations in PACU that was found in a preliminary investigation (group 1, mean 24.1 ± 3.2 min and group 2, mean 40.7 ± 29.9 min).

Results

The study was completed with 74 patients. All patients were investigated for the primary and secondary criteria for the results.

Characteristics of patient, anaesthesia and surgery

The characteristics of the patient and surgery, dose of rocuronium that was used and duration of surgery were found to be similar in both the groups. The mean BIS was 52.1 ± 3.7 in Group N and 52.4 ± 4.2 in Group S. TOF responses at the

Table 1. Distribution of patients' demographic features, AHI scores and surgical procedures, anaesthesia and surgical characteristics of groups, comparison of TOF 0.9 times, duration of operating theatre use and recovery periods

Variable	Group S	Group N	p
Age (year) [‡]	44.81±9.7	46.62±11.3	0.464 [†]
Weight (kg) [‡]	80.14±11.9	82.38±12.1	0.425 [†]
BMI (kg/m ²) [‡]	28.1±3.2	28.2±3.2	0.892 [†]
ASA I/II (n)	21/16	23/14	0.813 [†]
Cormack–Lehane score (n)	1/2/3/4	34/3/-/-	0.452 [†]
AHI (n)	Mild	14	1.0 [†]
	Moderate	18	
	Severe	5	
AHI score	17.9±10.3	18.2±11.8	0.922 [†]
Surgical procedures (n)	Anterior palatoplasty	31	<0.05 [†]
	Uvulopalatopharyngoplasty	3	
	Tonsillectomy+uvulopalatopharyngoplasty	0	
	Septoplasty	1	
	Tonsillectomy+Lateral pharyngoplasty	2	
EtDes [†]	3.0 (2.9–3.2)	3.1 (3.0–3.2)	0.056 ^{MW}
BIS [‡]	52.1±4.3	52.3±4.2	0.827 [†]
Total rocuronium dose (mg) [‡]	82.6±16.7	85.0±14.7	0.501 [†]
Sugammadex (mg) [‡]	160.2±23.8		
Neostigmine (mg) [‡]		3.29±0.48	
TOF [†] at the application of reversal agent	0.2 (0.0–0.4)	0.2 (0.0–0.4)	0.293 ^{MW}
Time to TOF 0.9 (min) [†]	2 (1.5–6)	8 (5–18)	<0.001 ^{MW}
Duration of surgery (min) [‡]	57.84±12.0	57.73±14.1	0.972 [†]
Duration of anaesthesia (min) [‡]	70.54±11.4	71.49±14.6	0.758 [†]
Duration of operating room (min) [‡]	72.4±14.3	96.6±22.8	<0.001 [†]
PACU time (min) [‡]	22.9±10.1	36.3±12.6	<0.001 ^{MW}

Values are: [‡]mean±standard deviation, [†]median (minimum–maximum) and (n) number. BMI: body mass index; AHI: apnoea–hypopnoea index (mild: 0–15, moderate: 15–30, severe: >30); TOF: acceleromyographic train of four; EtDes: end-tidal desflurane concentration; BIS: bispectral index; PACU: post-anaesthesia care unit. Statistics: [†]t-test, MW: Mann–Whitney U test

time of administering the reversing agent were similar in both the groups. T2 was obtained in 24 patients, T3 in six and T4 in four before sugammadex administration and T2 was observed in 23, T3 in three and T4 in seven before neostigmine administration. The TOF value was 0 before the administration of the reversing agent in three patients in the sugammadex group and in four patients in the neostigmine group.

The median time to reach a TOF 0.9 was 2 (1.5–6) min in Group S and 8 (5–18) min in Group N. The difference between the groups was statistically significant ($p<0.001$). There was also a significant difference between the groups with regard to the operation room and PACU times [mean duration of operating theatre use, Group S: 72.4±14.3 min, Group N: 96.6±22.8 min, $p<0.001$; mean duration of care in PACU, Group S: 22.9±10.1 min, Group N: 36.3±12.6 min, $p<0.001$] (Table 1). The median values of VAS pain scores were found

to be similar in Group S [2 (2–3)] and Group N [2 (2/3)] ($p=0.762$).

Complications and treatments

After extubation, desaturation was observed in 12 patients (32.4%) the neostigmine group and in four patients (10.8%) the sugammadex group and the difference between the groups was statistically significant ($p=0.048$). Three patients in the neostigmine group whose hypoxaemia and airway obstructions did not improve despite the application of oxygen through a mask and airway manoeuvres, were re-intubated. In total, there were eight (21.6%) unplanned admissions and transferred to the ICU in the neostigmine group, including five patients whose hypoxaemia did not improve in spite of 1 hour close monitoring, and the application of CPAP in PACU. In the sugammadex group CPAP was applied in 2 patients in the PACU and one patient (2.7%) with unim-

Table 2. Comparison of post-operative complications and therapies between the groups

Variables		Group S n (%)	Group N n (%)	P
Respiration-related complications	Total	5 (13.5)	12 (32.4)	0.048 ^{ki2}
	Cough	5 (13.5)	8 (21.6)	0.541 ^t
	Desaturation	4 (10.8)	12 (32.4)	0.048 ^t
	Hypoxaemia	3 (8.1)	11 (29.7)	0.035 ^t
	Breath holding	4 (10.8)	8 (21.6)	0.344 ^t
	Increased secretion	3 (8.1)	6 (16.2)	0.479 ^t
	Airway obstruction	3 (8.1)	6 (16.2)	0.479 ^t
	Apnoea	-	6 (16.2)	0.025 ^t
Circulation-related complications	Total	2 (5.4)	14 (37.8)	0.04 ^{ki2}
	Bradycardia	1 (2.7)	8 (21.6)	0.028 ^t
	Tachycardia	1 (2.7)	5 (13.5)	0.199 ^t
	Hypotension	1 (2.7)	1 (2.7)	1.0 ^t
	Hypertension	1 (2.7)	9 (24.3)	0.017 ^t
	Arrhythmia	1 (2.7)	5 (13.5)	0.199 ^t
	Heart failure	-	1	-
Therapies	Atropine	0	6 (16.2)	0.025 ^t
	Dopamine	-	1	-
	Nitroglycerin	-	1	-
	Airway manipulation	3 (8.1)	12 (32.4)	0.021 ^t
	Airway usage	3 (8.1)	11 (29.7)	0.019 ^t
	Need for second anaesthesia	3 (8.1)	12 (32.4)	0.038 ^t
	Re-intubation	-	3 (8.1)	0.021 ^t
	Admission to the intensive care unit	1 (2.7)	8 (21.6)	0.24 ^t
	CPAP	1 (2.7)	8 (21.6)	0.028 ^t
	IMV	-	2 (5.4)	0.028 ^t
	Specialist consultation	-	1	-
	Total number of days in the intensive care unit	1	12	0.493 ^t

Values are the number of occurrences (n) and percentages (%). CPAP: positive-pressure non-invasive mechanical ventilation; IMV: invasive mechanical ventilation. Statistics: ^tt-test, ^{ki2}chi-squared test

proved hypoxaemia was admitted to the ICU. In one patient who was included in the neostigmine group and hospitalised in ICU, negative-pressure pulmonary oedema (NPPO) was detected. The patient who developed NPPO was followed up in ICU for 4 days. IMV was applied for 3 days and CPAP was applied for 1 day. The duration of hospitalisation was 1 day for other patients in ICU and CPAP was implemented in these patients (Table 2). No patient had laryngeal spasm, bronchospasm, atelectasia, aspiration or pneumonia. Antibiotherapy was not performed.

The frequency of complications related to circulation was higher in Group N. Group N included nine patients with hypertension (24.3%), eight patients with bradycardia (21.6%), five patients with tachycardia (13.5%) and five patients with arrhythmia (13.5%) (Table 2). In the neostigmine group, six patients were given an additional dose of atropine due to

bradycardia. Nitroglycerin was administered to one patient with hypertension. Esmolol was not used. Inotropic therapy (dopamine 5–10 µg kg⁻¹ min⁻¹) was administered to a patient who developed heart failure due to NPPO. The frequencies of desaturation ($p < 0.001$), cough ($p = 0.012$) and hypertension ($p = 0.004$) were higher in patients with high AHI scores (moderate and severe).

ABG analysis was performed for all patients who experienced desaturation in the operating theatre and whose desaturation did not improve despite the application of oxygen through a mask, insertion of an airway or airway manipulations. Patients who were treated in ICU underwent ABG analysis twice a day and the patient who was diagnosed with NPPO underwent ABG analysis four times a day. Moreover, PA chest radiography was performed for all patients who were hospitalised in ICU. The patient who was treated due to a

Table 3. Cost analyses of reversal and treatment of complications in the sugammadex and neostigmine groups

Variable	Amount of currency TL	Group S (n=37)	Group N (n=37)
Reversal and anaesthesia care cost	1 flk sugammadex 98.14		
	1 ampoule neostigmine 0.27		
	1 ampoule atropine 0.15	6147.88 TL	3569.5 TL
	Injector 0.5		
	Anaesthesiologist 0.392 TL min ⁻¹		
	Anaesthesia technician 0.244 TL min ⁻¹		
Complication treatment cost	CPAP 11.900		
	IMV 44.5		
	Hospitalisation fee in the intensive care unit 104		
	Package service fee in the intensive care unit 800.55		
	Analysis of blood gases 12.800	199.5 TL	3944.6 TL
	Chest radiography 6.80		
	Haemogram 3		
	Routine biochemistry 10		
	ECO 20		
	Specialist consultation 10		
Total		6347.38 TL	7514.15 TL

CPAP: continuous positive airway pressure mask ventilation; IMV: invasive mechanical ventilation; ECO: echocardiography.

diagnosis of NPPO also underwent complete blood analysis, routine biochemistry analysis, echocardiographic imaging and consultation with a cardiologist.

Cost analysis

The cost of an anaesthesiologist was found to be 0.392 TL min⁻¹ (annual income 53,456 TL/40 hours per week) and the cost of an anaesthesia technician was found to be 0.244 TL min⁻¹ (annual income 33,255 TL/40 hours per week). The reversal and anaesthesia care cost of the sugammadex group was higher than that of the neostigmine group (3569.5 TL in Group N vs. 6147.88 TL in Group S). On the other hand, the cost of complication treatment was found to be higher in Group N (Group N 3944.6 TL, Group S 199.5 TL). The total cost was 7514.15 TL in Group N and 6347.38 TL in Group S. The costs of blood gas analysis, blood biochemistry analysis, IMV, CPAP, complete blood analysis and a hospital bed per day are shown in Table 3.

Discussion

The complete reversal of a non-depolarising neuromuscular blockade effect at the end of the administration of general anaesthesia shortens the recovery period and can prevent the development of respiratory system complications in the early post-operative period (18). Post-operative respiratory system complications are associated with morbidity, mortality and increased hospital costs (19).

The superiority of sugammadex over neostigmine in terms of the reversal of neuromuscular blockade activity is known. The use of sugammadex is recommended at a dose of 16 mg

kg⁻¹ in the event of deep neuromuscular blockade, 4 mg kg⁻¹ in the event of superficial neuromuscular blockade and 2 mg kg⁻¹ when at least two responses are obtained to TOF stimulation, for accelerating the reversal of neuromuscular function (1). The application of a neuromuscular-blockade-reversing agent when a T2 response is received to TOF stimulation is accepted as being safe for the non-occurrence of residual neuromuscular blockade and extubation (20). On the other hand, the period to reach a TOF value of 0.9 can be prolonged with the standard dose of neostigmine used in the case of two responses to TOF stimulation (21) and cholinesterase inhibitors are ineffective when they are used during deep neuromuscular blockade (22). In a wide observational study conducted by Della Roca et al. (23), the time to reach a TOF 0.9 was found to be 2.2 min with sugammadex and 6.9 min with neostigmine in the event of superficial blockade, whereas in the event of deep neuromuscular blockade it was 2.7 and 16.2 min with sugammadex and neostigmine, respectively. In our study, muscle relaxant-reversing agents were given without any prerequisite TOF value at the end of intervention and the time to obtain a TOF 0.9 was found to be 2 min in patients who were given sugammadex and 8 min in patients who were given neostigmine. Considering that giving a volatile anaesthetic agent to patients despite the fact that the operation was ended would not be ethical, a reversing agent was administered without waiting for the occurrence of T2 response. Considering that the TOF responses of the groups at the time of the administration of the reversal agents were similar, we assume that this method did not affect the results.

In our study, the operation room time and PACU timewere found to be shorter in the sugammadex group, which was attributed to rapid reversal of neuromuscular blockade with sugammadex. Poor neuromuscular conduction during the recovery period prevents maximum air flow in inspiration, airway patency cannot be preserved and life-threatening problems such as an inability to swallow, desaturation, aspiration and acute respiratory failure can develop (4, 20, 24). In our study, we think that the higher number of post-operative respiration-related and, accordingly, circulation-related complications in patients who were given neostigmine might be associated with a later improvement in neuromuscular conduction. In our study, the frequency of respiration-related complications was 32% in the neostigmine group and 13% in the sugammadex group. The most common complication related to respiration was observed to be desaturation. Desaturation was found in 12 (32%) patients in the neostigmine group. On the other hand, in the sugammadex group desaturation was detected in 4 (10%) patients. In the neostigmine group, 11 patients with desaturation had hypoxaemia. The most common respiration-related complication after desaturation and hypoxaemia was cough. Although cough is not a complication in itself, it is important because it can cause hypertension, tachycardia, intracranial and intraocular hypertension, laryngospasm and desaturation (25).

There are various studies reporting that the frequency of post-operative complications increases in patients with OSA. In a retrospective study performed on a population who had undergone non-cardiac surgery, the frequency of respiratory system complications was found to be 44% in patients with OSA and 28% in patients without OSA. In the same study, the frequency of desaturation, which is the most common respiratory system complication, was reported to be 17% in patients with OSA and 8% in patients without OSA. Similarly, in another retrospective cohort study conducted on 51,509 general surgery and 65,774 orthopaedic surgery patients, the frequency of respiratory system complications such as aspiration pneumonia and acute respiratory failure requiring intubation and mechanical ventilation was observed to be higher in patients with a diagnosis of OSA (9). Moreover, respiratory depression and recurrent apnoea are frequently seen in patients who are operated on for the treatment of OSA (27). No information about the muscle relaxant-reversing agents that were used is available in these studies. The frequency of post-operative respiration-related complications that was found in our study is consistent with the results of previous studies. Our study shows that the use of sugammadex decreases the incidence of these complications. In patients who were given neostigmine, the frequency of circulation-related complications was 34% and hypertension was the most common complication.

Post-operative complications can develop due to factors related to the patient, surgery and anaesthesia (28). The main risk factors include the administration of general anaesthesia and opioids, the use of muscle relaxants, urgent surgical

interventions, long operation periods, advanced age, male gender, pulmonary disease, obesity and diabetes (28). In our study, the anaesthesia that was administered to the groups was standardised and opioids were not given to patients in order to avoid respiratory depression. The comparison of the frequency of respiratory and circulatory complications and patient, surgery and anaesthesia characteristics revealed only a correlation between a high AHI score and desaturation, cough and hypertension.

There are few data on the analysis of the cost-effectiveness of sugammadex (29). In a retrospective study, which examined the costs of anaesthesia one year after providing unlimited access to sugammadex, it was reported that the cost increased to 147 dollars from 42 dollars per patient, compared to the period in which neostigmine was used (7). In the same study, although no difference was found with regard to the duration of anaesthesia and the durations of operating theatre and recovery unit use, the duration of hospitalisation was found to be shorter. Baumgart et al. (30) suggested that the use of sugammadex could shorten the duration of recovery by 5–10 min and the number of surgical procedures could be increased by 2.4%, provided that a new team was established to spend this time on new operations. On the other hand, Paton et al. (8) stated that it was economically more valuable to shorten the time spent in the operating theatre rather than in the recovery room. According to our results, the use of sugammadex in OSA operations helps neuromuscular function to improve earlier and shortens the time spent in the operating theatre and PACU. Although a reduction in periods of operating theatre use and PACU monitoring does not directly mean that more patients could be operated, showing more attention to patients during the remaining time is important because this increases patient safety (31). In this study, the cost of patient care was calculated by considering that an anaesthesiologist and an anaesthesia nurse provided care to the patient during the period in the recovery room (8). The addition of the costs of the surgical team, which cannot perform another operation while waiting, and other possible surgical procedures can increase the cost of this period much more. The method and findings of our study did not demonstrate that a shortened recovery period decreased the cost. However, it was found that the use of sugammadex provided a remarkable cost advantage by reducing the frequency of complications and the costs of complication treatment. The clinical implication of our study is that in contrast to previous cost analysis of sugammadex which were based on complication probabilities, we investigated the cost of sugammadex prospectively and our cost analysis was based on actual complication rates. According to the HAR, ICU therapy can be invoiced by a daily package fee or by setting prices for the hospital bed, and interventional procedures and therapies separately. In our study, ICU therapy was invoiced on the first day of ICU admission by hospital bed, interventional procedure and treatment fees, and on the following days, the cost was calculated based on the price of the inten-

sive care package fee. When all hospitalisation days in ICU are invoiced according to the package fee, the cost increases between the neostigmine group even more. Total costs may vary between hospitals that use different billing even more.

This study has some limitations. The population in the study includes patients in ASA classes I and II. Based on our results, an interpretation cannot be made for patients with more severe physiological conditions. Another limitation is a lack of data on the rate of residual neuromuscular blockade, because monitoring of neuromuscular conduction was not performed in PACU. In addition, the costs incurred may not be exactly the same as those in other hospitals because of differences in billing techniques. In future studies, investigating the effect of sugammadex use on the vital indicators, such as time passing until normal daily activity is regained and duration of hospitalisation, would be beneficial.

Conclusion

This study verified that sugammadex reverses the action of rocuronium more efficiently than neostigmine. When compared with the use of neostigmine after OSA operations, the use of sugammadex decreases the frequency of respiratory system complications and despite the increased reversal cost the cost of complication treatment and thus total costs are decreased.

Ethics Committee Approval: Ethics committee approval was received for this study from Erciyes University Clinical Research Ethics Committee (2012324/08.05.2012).

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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