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Original Article

A Comparison of Intravenous Sugammadex and Neostigmine + Atropine Reversal on Time to Consciousness During Wake-Up Tests in Spinal Surgery

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ABSTRACT

Objective: The effect of sugammadex on consciousness is not yet fully understood. This prospective, randomized, double-blind, multicenter study was performed to compare the effects of intravenous (IV) sugammadex and neostigmine + atropine reversals on time-to-consciousness during intraoperative wake-up tests in patients undergoing spinal surgery. **Subjects and Methods:** A total of 66 American Society of Anesthesiologists I–II patients aged 10–25 years undergoing spinal surgery were recruited. In all patients, bispectral index (BIS), motor-evoked potential (MEP), somatosensory-evoked potentials (SSEP), and train-of-four (TOF) scores were monitored. Patients received the same total IV anesthesia protocol with a propofol–remifentanil mixture. Patients were randomly allocated into two groups. During wake-up test, when the TOF count reached 2 (T_2), either sugammadex 2 mg.kg^{-1} in group S or neostigmine 0.04 mg.kg^{-1} + atropine 0.01 mg.kg^{-1} in group N were administered. BIS_{90}, $SSEP_{90}$, MEP_{90} was recorded when TOF ratio reached 90, whereas time-to-consciousness ($Time_{cons}$) was recorded when the patient responded to verbal commands. **Results:** BIS_{90} (77.4 ± 4.7, 74.8 ± 3.7), $SSEP_{90}$ (36 ± 9.9, 29.7 ± 8.5), and MEP_{90} (465.3 ± 34.8, 431.3 ± 28.2) values were significantly greater in group S than in group N ($P < 0.05$ for each variables). $Time_{cons}$ was significantly shorter with sugammadex than with the neostigmine + atropine combination ($P < 0.05$). **Conclusion:** Using IV sugammadex 2 mg.kg^{-1} reversal provides faster responses to verbal commands than neostigmine–atropine combination during the intraoperative wake-up test in patients undergoing spinal surgery because the time to consciousness was significantly shorter. This difference was thought to be related with faster return of neuromuscular transmission because the TOF ratio was >0.9 well before return of consciousness in both groups.

KEYWORDS: *Consciousness, neurophysiological monitoring, propofol, spinal surgery, sugammadex, wake-up test*

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INTRODUCTION

Intraoperative neurophysiologic monitoring (IONM) is essential to reduce the incidence of postoperative neurologic complications during spinal surgery. Although motor-evoked potential (MEP) and somatosensory-evoked potentials (SSEPs) are very popular neurophysiologic methods in monitoring signal conduction in the sensory columns of the spinal cord, an injury in the spinal cord may be missed with these techniques. Therefore, the intraoperative wake-up test has been proposed to be considered as a gold standard for patients with possible spinal injury or motor function test, especially when a signal change occurs during surgery, to check the specificity of this change and to confirm that a neurologic deficit is indeed present, the wake-up test is more likely to be performed.[1,2]

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An optimal anesthesia regimen is crucial during IONM. Anesthetic drugs chosen for general anesthesia in spinal surgery should not affect the motor function of muscles.[3-6] It should allow for a rapid wake-up test whenever neurological injury is suspected, but prevent any deterioration in the quality of evoked potentials. All halogenated inhalational agents reduce the SSEP amplitude and increase SSEP latency. Intravenous (IV) anesthetics have the same effect but to a lesser degree on IONM.[7]

Studies have demonstrated that electroencephalography (EEG), bispectral index (BIS), MEP, and SSEPs provide valuable information on the consciousness of patients after anesthesia is turned off. These electrophysiologic parameters are mostly influenced by withdrawal of the anesthetic effect, except for MEPs which are largely influenced by neuromuscular blockade and its reversal.[7,8] BIS monitoring also affords further insights as to the level of anesthesia, awareness, and consciousness.[9-11] Furthermore, during the wake-up period, acceleromygraphy-guided neuromuscular reversal can provide better neuromuscular function and earlier recovery times.[3]

Sugammadex is a modified ɣ-cyclodextrin that is widely used for the reversal of steroidal neuromuscular-blocking agents (NMBAs) and accelerates recovery.[12,13] However, studies on the effects of sugammadex on consciousness are still lacking.

In this study, we tested the hypothesis that sugammadex administration during intraoperative wake-up test would provide a faster time-to-consciousness than neostigmine + atropine reversal in patients undergoing spinal surgery.

The aim of the present study was to compare the effects of IV sugammadex and neostigmine + atropine reversals on time-to-consciousness (described as the time to obeying verbal commands after reversal of NMBAs), during the intraoperative wake-up test in subjects undergoing spinal surgery. The primary endpoint was the time-to-consciousness and the secondary endpoints were BIS, SSEPs, MEP functions, and train-of-four (TOF) scores during the wake-up test.

Subjects and Methods

Patients

This study was registered at Clinical.Trials.gov (principal author's name: EB and identification number: NCT02390817) and approved by our faculty ethics committee of Cukurova University (decision number: 35/6 and date: November 20, 2014). This randomized, double-blind, prospective, multicenter trial was performed between December 15th, 2015, and August 15th, 2017, at Çukurova University and Ortopedia Hospital. After obtaining written informed parental and personal consent, 66 patients with American Society of Anesthesiologists (ASA) physical status I to II, between the ages of 10 and 25 years, who were undergoing spinal surgery for scoliosis, were recruited. Unconscious patients, those with ASA physical statuses III and IV, and patients with a history of preoperative neurologic disorders were excluded from the study. All patients were instructed and consented on this purely research-oriented-wake-up procedure, preoperatively.

The primary outcome of the study was the time-to-consciousness during the intraoperative wake-up test. The sample size calculation was determined by a pilot study; time-to-consciousness after reversal of NMB was found as 9 ± 1 min after neostigmine + atropine reversal. What was the time to consciousness in the sugammadex group? There was at least a 1 min difference in the time to consciousness for the sugammadex group; accordingly, 27 patients were needed in each group to demonstrate a statistically significant difference with 95% power and 5% significance.

Randomization and blinding

Subjects were randomly allocated into two groups using a personal computer-generated random table. First, two syringes were prepared by a pharmacist who was not one of the investigators. They were assigned a classified label to maintain the double-blind feature of the trial. The syringes were identical and contained sugammadex (MSD) 2 $mg.kg^{-1}$ or the neostigmine 0.04 $mg.kg^{-1}$ + atropine 0.01 $mg.kg^{-1}$ combination in a total volume of 10 mL. The anesthesia provider and data collector did not know which medication was in the syringe.

Study protocol

No premedication was used in patients because of the study protocol. Patients were transferred to the operating room following IV cannulation. Anesthesia induction was achieved with propofol 2 $mg.kg^{-1}$ and maintained by total intravenous anesthesia (TIVA) (propofol 3–4 $mg.kg.h^{-1}$ and remifentanil 10-20 $\mu g.kg.h^{-1}$ mixture) infusion with a 50–50% oxygen-air mixture for all patients.

The depth of anesthesia was assessed based on the patient's clinical status and BIS monitoring of IV anesthetics. BIS values between 40 and 60 were achieved by increasing or decreasing the rate of IV anesthetic agents.

Neuromuscular block was performed using rocuronium 0.6 $mg.kg^{-1}$. Whenever the single twitch height was <5%

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of baseline after the administration of rocuronium, patients were intubated. No routine neuromuscular blocker was used for maintenance. However, it was planned that if the TOF count was greater than 2, rocuronium 0.2 $mg.kg^{-1}$ would be administered for maintenance.

Intraoperative monitoring

Non-invasive blood pressure, electrocardiogram, oxygen saturation (SpO_2) and end-tidal carbon dioxide ($EtCO_2$) (Draeger-Primus Anesthesia Device Monitor, Draeger Medical Systems, Denver, MA) monitoring was applied routinely. BIS monitoring (BISTM Brain Monitoring System, Covidien, San Jose, USA) were also adjusted routinely in all patients. IONM was performed using an EndeavorTM System (Natus Neurology Incorporated; USA). Neuromuscular blockade was monitored using a TOF-Watch® S (Organon Ireland Ltd., Dublin, Ireland) acceleromyograph. A neuromuscular transducer was attached over the thumb and calibrated after propofol induction.

Initial baseline SSEP and MEP samples were taken after anesthesia induction and intubation, before the surgery began. A second baseline was then performed after spine exposure. SSEP-stimulating electrodes were bilaterally placed over the posterior tibial nerves behind the medial malleolus. Stimulation intensity was a maximum (Max) of 32 mA at a duration of 100–500 s. Cortical SSEPs were recorded using sterile subdermal needles and recording electrodes were placed on the scalp at the following locations: Cz' (center of the motor cortex) and PZ (center of the parietal cortex). Consecutive stimulations from the posterior tibial nerve were collected using recording electrodes. The value should range between positive 35 and negative 45 for a healthy person. The sensitivity of amplitude was set to 20–50 μv. The cortical amplitudes of SSEPs from the posterior tibial nerve stimulations were recorded and the mean of the data was calculated on a per-patient basis. For MEP monitoring, needle stimulating electrodes were placed at C3 (right motor cortex) and C4 (left motor cortex). Max 400-1000 V (4000 Ma) electrical stimuli were given by the stimulating electrodes. MEP amplitudes (μV) of the left and right adductor pollicis brevis and tibialis anterior muscles were recorded and a mean of four data points was calculated per patient. Following endotracheal intubation, SSEP and MEP monitoring were applied and then the radial arteries of the patients were cannulated using a 20-gauge peripheral artery catheter.

Data collection

Demographic data (age, sex, weight) and the wake-up durations of the patients were recorded. Hemodynamic data [heart rate (HR), systolic, diastolic, and mean arterial blood pressure (SBP, DBP, and MABP)] were followed continuously, but recorded only at 0, 2, 5, and 10 min during the wake-up test.

BIS_2, $SSEP_2$, and MEP_2 values were recorded when the TOF count reached 2 (T_2) [time to administration of the study drugs], whereas BIS_{90}, $SSEP_{90}$, and MEP_{90} values were recorded when TOF ratio reached 90% [TOF = 90 (T_{90})], during the wake-up period. Additionally, BIS values (BIS_{cons}) and time-to-consciousness ($Time_{cons}$) were also recorded at the time of obeying verbal commands after reversal and these data are presented as BIS_{cons} and $Time_{cons}$, respectively. The TOF repeated every 10 s (train frequency of 0.1 Hz) during wake-up period.

Wake-up test

The surgeons were requested to inform the anesthetist at least a 1/2 hour before the anticipated wake-up test. No neuromuscular blocker was used during this time period. During the wake-up test, TIVA was ceased in all patients. When the TOF count reached 2 in both groups, study drugs [either sugammadex 2 mg/kg (in group S) or neostigmine 0.04 $mg.kg^{-1}$ + atropine 0.01 $mg.kg^{-1}$ combination (in group N)] were given intravenously. When the TOF ratio reached 90 (T_{90}) in both groups, the time between T_2 and T_{90} was also calculated and recorded.

During the wake-up test, verbal commands such as 'move your legs and squeeze my hand' were given for each patient and their responses to these commands were evaluated at 10 s intervals as present or absent. Following the wake-up test, anesthesia was restarted with the same protocol used for TIVA and then rocuronium 1 $mg.kg^{-1}$ was given to all patients. When surgery was completed, the reversal of the neuromuscular block was performed with the same code of syringe drug, which was prepared by the same pharmacist. Subjects were taken to the Post anesthesia care unit (PACU) for postoperative care. The discharge criteria for the ward were normal hemodynamic and respiratory signs and satisfactory analgesia Verbal rating scale (VRS <4).

Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics software package (Version 20.0). Categorical data were presented as numbers and percentages, whereas continuous data were expressed as mean and standard deviation. To compare categorical data between the two groups, the Chi-square test was used. The Kolmogorov–Smirnov test was used to confirm the normality of distribution for continuous variables. To

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compare continuous variables between the two groups, Student's *t* test or the Mann–Whitney U test was used, accordingly. To analyze the change in measurements recorded during the operation, repeated measurements analysis was applied. The level of statistical significance for tests was considered as 0.05.

Results

We evaluated 66 patients, 4 of whom did not meet the inclusion criteria and 2 did not give consent [Figure 1]. A total of 60 patients were randomized. All patients received the allocated intervention and no patients were lost to follow-up. The demographic data of the groups are shown in Table 1. There was no statistically significant difference in the demographic data between the two groups. However, the intraoperative wake-up test duration of the patients was significantly shorter in group S than in group N (8.5 ± 0.73 min and 14.95 ± 0.72 min in group S and N, respectively; $P = 0.001$). No significant difference in hemodynamic variables was found between the two groups. Hemodynamic variables (HR, SBP, DBP, and MABP) during the wake-up test are presented in Table 2.

Comparing BIS data, BIS_2 values were similar and no statistically significant difference was found between the two groups. However, BIS_{90} and BIS_{cons} data were significantly greater in group S than in group N ($P = 0.023$), ($P = 0.007$), [Table 3].

In the comparison of evoked potentials, $SSEP_2$ and MEP_2 values were similar and there was no statistically significant difference between the two groups. However, $SSEP_{90}$ and MEP_{90} values were significantly higher in group S than in group N ($P = 0.011$, $P = 0.001$, for $SSEP_{90}$ and MEP_{90}, respectively) [Table 3].

After reversal of NMB with the study drugs, the TOF count increased in both groups. The time required from T_2 to reach T_{90} (T_2–$T_{90\ time}$) was significantly shorter in

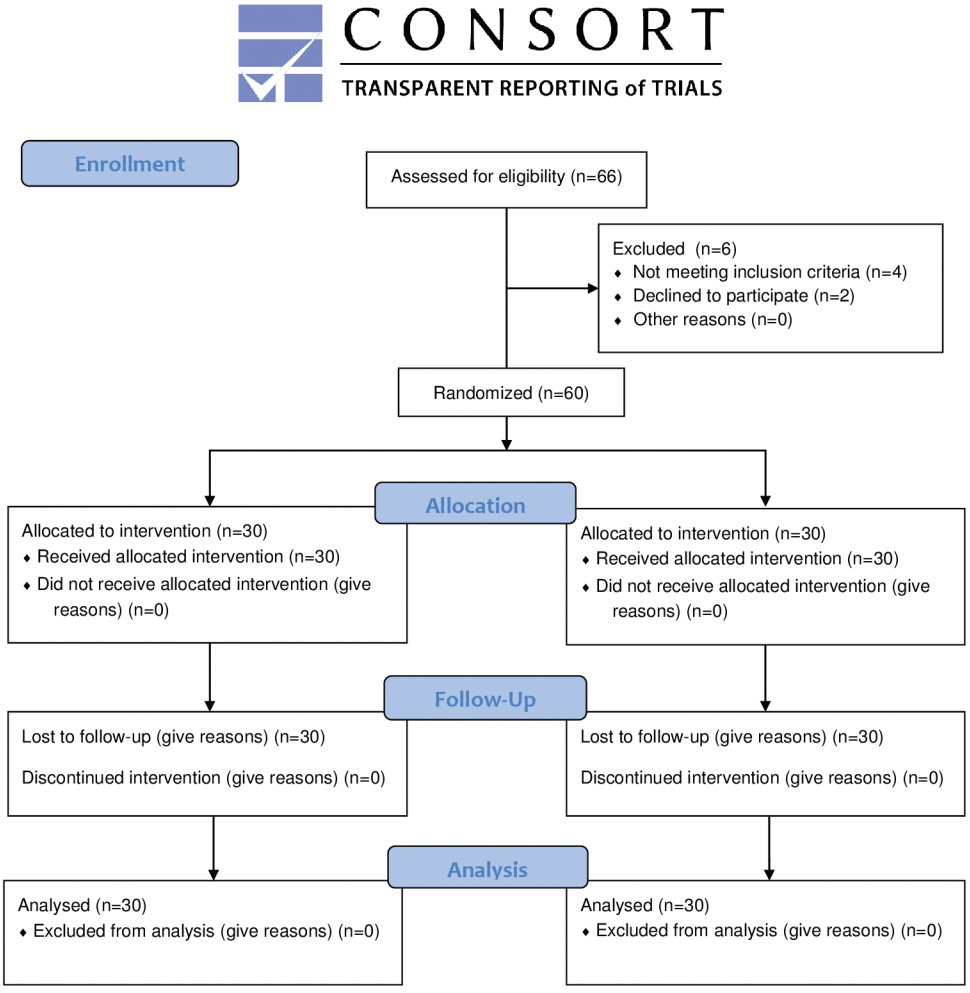


Figure 1: Consort Flow Diagram

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Table 1: Demographic data and duration of wake-up

	Group S (*n*=30)	Group N (*n*=30)	*P*
Age (yr)	16.6±4.29	16.1±4.97	0.629[a]
Gender, *n* (%)			0.12[b]
Male	12 (40)	18 (60)	
Female	18 (60)	12 (40)	
Weight (kg)	53.06±14.39	53.33±9.67	0.93[a]

Percentages are presented as % within group. The values presented as mean±standard deviation (SD), [a]Independent samples *t* test was used., [b]Chi-square test was used.*$P<0.05$ compared with group N

Table 2: Hemodynamic data during wake-up test

	Time	Group S	Group N	*P*
HR (bpm)	$T_{0\ min}$	71.1±12.75	72.36±9.26	0.662
	$T_{2\ min}$	77.9±13.24	80.43±8.5	0.383
	$T_{5\ min}$	85.1±11.54	84.16±11.02	0.750
	$T_{10\ min}$	85.06±12.73	82.13±11.78	0.358
SBP (mmHg)	$T_{0\ min}$	102.76±10.75	98.43±8.9	0.061
	$T_{2\ min}$	112.33±9.93	114.0±11.5	0.552
	$T_{5\ min}$	120.53±14.36	115.63±9.98	0.130
	$T_{10\ min}$	115.94±11.7	112.66±9.5	0.246
DBP (mmHg)	$T_{0\ min}$	60.93±11.88	55.83±9.18	0.068
	$T_{2\ min}$	66.10±8.79	64.36±8.26	0.435
	$T_{5\ min}$	68.96±11.10	67.96±8.35	0.695
	$T_{10\ min}$	66.63±7.75	65,53±7.65	0.583
MABP (mmHg)	$T_{0\ min}$	79.50±9.63	78.03±10.61	0.099
	$T_{2\ min}$	83.9±11.00	82.83±9.47	0.689
	$T_{5\ min}$	90.63±14.43	86.23±11.97	0.204
	$T_{10\ min}$	88.46±12.42	86.03±9.35	0.072

The differences between groups were not statistically significant ($P>0.05$). HR=Heart rate; bpm=Beats per minute; DBP=Diastolic blood pressure; SBP=Systolic blood pressure; MABP=Mean arterial blood pressure. T_0=Time to administration of neostigmine or sugammadex; $T_{2\ min}$=2 minutes after neostigmine or sugammadex administration; $T_{5\ min}$=5 minutes after neostigmine or sugammadex administration; $T_{10\ min}$=10 minutes after neostigmine or sugammadex administration

group S than in group N (3.1 ± 1.3 min and 4.9 ± 1 min in groups S and N, respectively; $P = 0.001$) [Table 3].

Time-to-consciousness ($Time_{cons}$) at the time of obeying verbal commands after reversal of NMB drugs was significantly shorter with sugammadex than with the neostigmine–atropine combination (5.33 ± 0.88 min and 8.9 ± 0.64 min in groups S and N, respectively; $P = 0.001$) [Table 3 and Figure 2].

A total of 17 patients noted that they had postoperative pain at the surgical site. No neurologic deficit was detected. Overall, most patients successfully responded to verbal commands except for two in group N, who struggled to follow verbal commands. No other complications were reported in the groups with respect to anesthesia, the wake-up test, and study drugs.

Table 3: BIS, SSEP, MEP values, T2-T90 time and time to consciousness in groups

	Group S	Group N	*P*
BIS_2	58.03±5.5	57.6±4.1	0.752[a]
BIS_{90}	77.4±4.7*	74.8±3.7	0.023[a]
BIS_{cons}	84.3±2.9*	82.5±1.88	0.007[a]
$SSEP_2$ (μV)	26.7±8.3	24.4±8.3	0.297[a]
$SSEP_{90}$ (μV)	36±9.9*	29.7±8.5	0.011[a]
MEP_2 (μV)	369.9±29.9	354±33.28	0.056[a]
MEP_{90} (μV)	465.3±34.8*	431.3±28.2	0.001[a]
T_2-T_{90} time (min)	3.1±1.3*	4.9±1	0.001[a]
$Time_{cons}$ (min)	5.33±0.88*	8.9±0.64	0.001[a]
Wake-up duration (min)	8.5±0.73*	14.95±0.72	0.00[a]

Data present as mean±SD, *$P<0.05$ compared with group N, when analyzed with [a]T Test. BIS=Bispectral index, SSEP=Somatosensory evoked potential, MEP=Motor evoked potential.BIS_2=BIS value at the time to T_2 which drug administered; BIS_{90}=BIS value at the time to T_{90}, BIScons=value at the time to obey the verbal commands.$SSEP_2$=SSEP value at the time to T_2 which drug administered; $SSEP_{90}$=SSEP value at the time to T_{90}, MEP_2=MEP value at the time to T_2 which drug administered; MEP_{90}=MEP value at the time to T_{90}, T_2-T_{90} time=Time between T_2 and T_{90}, Timecons=time to consciousness (described as the time to obey the verbal commands after reversal of NMB drugs and anesthetics ceased), μV=μv

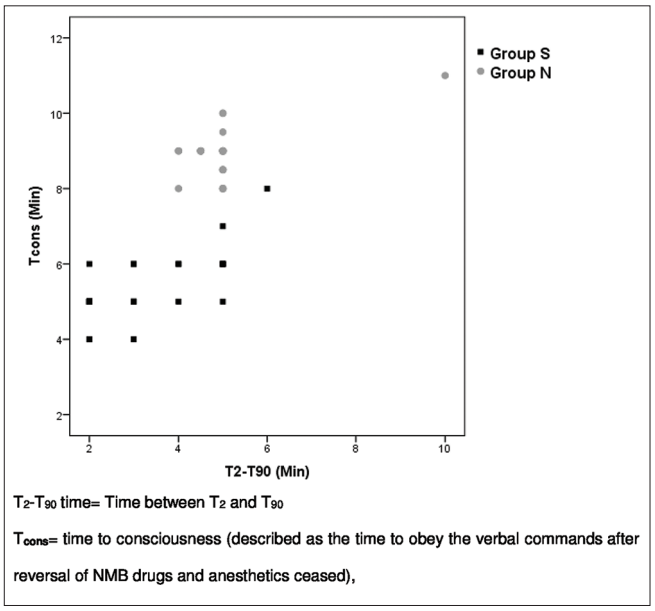


Figure 2: Comparison of the T2–T90 and Tcons

Discussion

The main result of this study is that, in the comparison of reversal with neostigmine and atropine, return of consciousness was several (3.6) minutes faster after reversal with sugammadex; this difference cannot be exclusively explained by a faster return of neuromuscular transmission because the TOF ratio was >0.9 well before return of consciousness in both groups.

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Several studies demonstrated that anesthetic agents might affect BIS, MEP, and SSEP results. Potent inhalation anesthetics produce a dose-dependent decrease in the amplitude of evoked potentials and increased latency in SSEPs.[14-16] Therefore, they are not advocated for use in the monitoring of SSEP and MEP during spinal surgery. However, several authors claimed that TIVA was a better option during IONM because of the unwanted effects of volatile anesthetics.[7,17] Neuromuscular blocking agents may worsen the quality of MEP and therefore we generally avoid the use of neuromuscular blocking agents to prevent any deterioration in the quality of MEPs. However, partial neuromuscular blockade, in a relatively narrow range, has been advocated for spine surgery in order to reduce the potential for movement during the procedure.[18,19]

Furthermore, neuromuscular blocking agents may augment the depth of anesthesia. It has been hypothesized that signals generated in muscle stretch receptors may cause arousal by passing to the brain through afferent nerve pathways. A more profound reversal of rocuronium could possibly lead to more rapid arousal due to effects on muscle stretch receptors, a hypothesis that has been called the 'afferentation' theory of cerebral arousal.[20] Consequently, reversal of neuromuscular blockade leads to the restarting of muscle stretch signals, accelerates recovery, decreases the depth of anesthesia, and increases EEG activity and consciousness state. Aho *et al.*[21] compared the effects of sugammadex and neostigmine reversals on BIS and entropy levels and they found both agents provided a significant rise in the numeric values of electromyogram (EMG), BIS, and entropy, but only had a minimal effect on EEG. This phenomenon was mostly provided by increased EMG activity.[22] The higher values in MEP responses in group S than in group N at the time when the TOF ratio was >0.9 supports this hypothesis.

In the present study, the difference in times to return of consciousness seems to be a separate phenomenon to the difference in times to reversal of paralysis. That is, in both groups, the average time to consciousness was several minutes longer than the time for the TOF ratio to reach 90% (average 2.2 minutes longer in group S and 4 minutes in group N). Therefore, neuromuscular function was not thought to be the limiting factor determining responsiveness, particularly considering that patients could move their limbs when the TOF ratio was significantly less than 90%. Our findings indicate that responsiveness was mainly limited by recovery from the IV anesthetic drugs, not by paralysis. Nevertheless, it is plausible that the faster reversal kinetics and more complete reversal of neuromuscular blockade by sugammadex may have facilitated a more rapid return of consciousness based on the brain afferentation theory described earlier.

BIS and SSEPs have been reported to be correlated with cognition during anesthesia, but there is a paucity of evidence regarding the relationship between BIS and SSEP during the intraoperative wake-up test in subjects undergoing spinal surgery.[23] Besides SSEPs, BIS is also known to be responsive to changes in EMG activity in anesthetized patients and its reliability has been reported to be correlated with EMG activity.[21] Dhaba *et al.*[23] investigated BIS values before and after IV sugammadex or neostigmine administration in patients with or without high EMG activity and found that both study drugs augmented BIS values dependent on the presence of EMG activity. Contrary to the results of Dhaba *et al.*, Schuller *et al.*[24] evaluated the relationship between EMG activity and BIS values in awake subjects and found that BIS monitoring needed muscle activity in order to create values to indicate that the patients were awake. The findings of Dhaba *et al.* have a positive correlation with our results. In the present study, reversal drugs were administered when muscle activity appeared (T_2). We found similar acceleration in BIS values with both drugs when muscle activity was present. However, BIS_{90} and BIS_{cons} values were significantly greater in the sugammadex group than in the neostigmine group. Higher BIS_{90} and BIS_{cons} values in group S were attributed to being correlated with the rapid pharmacokinetic profile of sugammadex and increased EEG activity.

Conflicting data have been reported in the literature regarding the effect and dose of sugammadex on the depth of anesthesia and BIS. Sparr *et al.*[25] investigated the effect of sugammadex on the reversal of rocuronium-induced NMB at doses of 1, 2, 4, 6, or 8 mg/kg on the depth of anesthesia and found that it decreased in about one-fifth of anesthetized patients compared with the control group. We used sugammadex 2 mg/kg for the reversal of NMB in group S and found higher BIS_{90} and BIS_{cons} values at the time to T_{90} and T_{cons}, respectively, compared with the neostigmine group. Additionally, the time between T_2 and T_{90} was statistically significantly shorter with sugammadex (3.1 min) compared with neostigmine (4.9 min). Faster wake-up and time-to-consciousness was achieved in group S than in group N, as profound reversal of rocuronium with sugammadex could possibly lead to more rapid arousal.

This study has three limitations. The first limitation is that the lack of EEGs, because BIS values may be an unreliable indicator of consciousness in patients who received anesthetic or neuromuscular blocking

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agents because BIS varies in sensitivity and specificity between anesthetic agents and individual patients and it is also subject to EMG contamination. The second, we used neostigmine and atropine sulphate for the reversal of rocuronium block because we do not have glycopyrrolate in our clinic. However, atropine can pass the central nervous system and may affect the time to consciousness. The third, as far as we know, there is no equipotency of neostigmine with sugammadex in the literature. We did not consider choosing equipotency of neostigmine for the reversal

In conclusion, using IV sugammadex 2 mg/kg reversal provides faster responses to verbal commands than the neostigmine–atropine combination during the intraoperative wake-up test in patients undergoing spinal surgery. Faster times to consciousness after reversal with sugammadex cannot be explained by a faster return of neuromuscular transmission because the TOF ratio was >0.9 well before the return of consciousness in both groups. One plausible explanation for this phenomenon is that the faster and more complete reversal kinetics afforded by sugammadex may increase the afferentation to the brain at a faster rate, which may lead to a more rapid arousal. Further large-series studies are needed to confirm this relationship between sugammadex reversal and consciousness.

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Conflicts of interest

There are no conflicts of interest.

References

1. Strike SA, Hassanzadeh H, Jain A, Kebaish KM, Njoku DB, Becker D, *et al.* Intraoperative neuromonitoring in pediatric and adult deformity surgery. Clin Spine Surg 2017;30:E1174-81.
2. Chen B, Chen Y, Yang J, Xie D, Su H, Li F, *et al.* Comparison of wake-up test and combined TES-MEP and CSEP monitoring in spinal surgery. J Spinal Disord Tech 2015;28:335-40.
3. Adamus M, Hrabalek L, Wanek T, Gabrhelik T, Zapletalova J. Intraoperative reversal of neuromuscular block with sugammadex or neostigmine lateral interbody fusion, a novel technique for spine surgery. J Anesth 2011;25:716-20.
4. Canbay O, Altıparmak B, Celebi N, Karagoz H, Sarıcaoğlu F. Comparison of propofol and midazolam on patients undergoing spinal surgery with intraoperative wake-up test: Randomized clinical trial. Braz J Anesthesiol 2015;65:470-5.
5. Martin DP, Bhalla T, Thung A, Rice J, Beebe A, Samora W, *et al.* A preliminary study of volatile agents or total intravenous anesthesia for neurophysiological monitoring during posterior spinal fusion in adolescents with idiopathic scoliosis. Spine. 2014;39:1318-24.
6. Yang J, Huang Z, Shu H, Chen Y, Sun X, Liu W, *et al.* Improving successful rate of transcranial motor-evoked potentials monitoring during spinal surgery in young children. Eur Spine J 2012;21:980-4.
7. Sloan TB, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. J Clin Neurophysiol 2002;19:430-43.
8. Pavoni V, Gianesello L, De Scisciolo G, Provvedi E, Horton D, Barbagli R, *et al.* Reversal of profound and "deep" residual rocuronium-induced neuromuscular blockade by sugammadex: A neurophysiological study. Minerva Anestesiol 2012;78:542-9.
9. Kissin I. Depth of anesthesia and bispectral index monitoring. Anesth Analg 2000;90:1114-7.
10. Burrow B, McKenzie B, Case C. Do anaesthetized patients recover better after bispectral index monitoring? Anesth Intensive Care 2001;29:239-45.
11. Ekman A, Lindholm ML, Lennmarken C, Sandin R. Reduction in the incidence of awareness using BIS monitoring. Acta Anaesthesiol Scand 2004;48:20-6.
12. Meretoja OA. Neuromuscular block and current treatment strategies for its reversal in children. Paediatr Anaesth 2010;20:591-604.
13. Keating GM. Sugammadex: A review of neuromuscular blockade reversal. Drugs 2016;76:1041-52.
14. Sloan T. Evoked potentials. In: Albin MS, ed. A Textbook of Neuroanesthesia with Neurosurgical and Neuroscience Perspectives. New York: McGraw-Hill; 1997. p. 221-76.
15. Fung NY, Hu Y, Irwin MG, Chow BE, Yuen MY. Comparison between sevoflurane/remifentanil and propofol/remifentanil anaesthesia in providing conditions for somatosensory evoked potential monitoring during scoliosis corrective surgery. Anaesth Intensive Care 2008;36:779-85.
16. Sloan T, Sloan H, Rogers J. Nitrous oxide and isoflurane are synergistic with respect to amplitude and latency effects on sensory evoked potentials. J Clin Monit Comput 2010;24:113-23.
17. Anschel DJ, Aherne A, Soto RG, Carrion W, Hoegerl C, Nori P, *et al.* Successful intraoperative spinal cord monitoring during scoliosis surgery using a total intravenous anesthetic regimen including dexmedetomidine. J Clin Neurophysiol 2008;25:56-61.
18. Pajewski TN, Arlet V, Phillips LH. Current approach on spinal cord monitoring: The point of view of the neurologist, the anesthesiologist and the spine surgeon. Eur Spine J 2007;16(Suppl 2):115-29.
19. Adams DC, Emerson RG, Heyer EJ, McCormick PC, Carmel PW, Stein BM, *et al.* Monitoring of intraoperative motor-evoked potentials under conditions of controlled neuromuscular blockade. Anesth Analg 1993;77:913-8.
20. Lanier WL. The afferentation theory of cerebral arousal. Neuroanesthesia book 1997;32;27-38.
21. Aho AJ, Kamata K, Yli-Hankala A, Lyytikainen LP, Kulkas A, Jantti V. Elevated BIS and entropy values after sugammadex or neostigmine: An electroencephalographic or electromyographic phenomenon? Acta Anaesthesiol Scand 2012;56:465-73.
22. Rundshagen I, Mast J, Mueller N, Pragst F, Spies C, Cortina K. Nervus medianus evoked potentials and bispectral index during repeated transitions from consciousness to unconsciousness. Br J Anaesth 2008;101:366-73.
23. Dhaba AA, Bornemann H, Hopfgartner E, Ohran M, Kocher K, Liebmann, *et al.* Effect of sugammadex or neostigmine neuromuscular block reversal on bispectral index monitoring of propofol/remifentanil anaesthesia. Br J Anaesth 2012;108:602-6.
24. Schuller PJ, Newell S, Strickland PA, Barry JJ. Response of bispectral index to neuromuscular block in awake volunteers. Br J Anaesth 2015;115(Suppl 1):i95-i103.
25. Sparr HJ, Vermeyen KM, Beaufort AM, Rietbergen H, Prooost JH, Pharm D, *et al.* Early reversal of profound rocuronium-induced neuromuscular blockade by sugammadex in a randomized multicenter study efficacy, safety, and pharmacokinetics. Anesthesiology 2007;106:935-43.