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Comparison of Sugammadex Dose for Intraoperative Neuromonitoring in Thyroid Surgery: A Randomized Controlled Trial

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Objectives/Hypothesis: To compare effect of 1 and 2 mg/kg of sugammadex on the incidence of intraoperative bucking and intraoperative neuromonitoring (IONM) quality in thyroid surgery.

Study Design: Randomized controlled trial.

Methods: Patients qualified for thyroid surgery with IONM were eligible for this double-blind, randomized, controlled trial. After tracheal intubation with 0.6 mg/kg rocuronium, 1 or 2 mg/kg of sugammadex was administered to patients in group I or II, respectively. The quality of the IONM for the external branch of the superior laryngeal nerve (EBSLN) was evaluated (strong/intermediate/weak). The initial amplitude of electromyography for the vagus nerve (V1) and the recurrent laryngeal nerve (R1) were recorded. Intraoperative bucking movements was recorded.

Results: A total of 102 patients (51 in each group) completed the study. Time from sugammadex administration to initial checking for the EBSLN was not different between group I and II (25.0 ± 7.9 vs. 25.5 ± 9.0 minutes, $P = .788$). There was no difference in the neuromonitoring quality for the EBSLN between group I and II (strong/intermediate/weak: 46/5/0 vs. 50/1/0, $P = .205$). The amplitudes of V1 (1,086.3 ± 673.3 μV vs. 1,161.8 ± 727.5 μV, $P = .588$) and R1 (1,328.2 ± 934.1 μV vs. 1,410.5- ± 919.6 μV, $P = .655$) were comparable between the groups. Patients who experienced bucking were significantly fewer in the group I than the group II (13.7% vs. 35.3%, $P = .020$).

Conclusion: A dose of 1 mg/kg sugammadex induced less bucking than 2 m/kg while providing comparable IONM quality during thyroid surgery.

Key Words: Neural monitoring, recurrent laryngeal nerve, sugammadex, thyroid surgery, vocal cord paralysis.

Level of Evidence: 2.

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INTRODUCTION

Intraoperative neuromonitoring (IONM) during thyroid surgery has been widely used to identify injury of the recurrent laryngeal nerve (RLN) and to predict functional status of the RLN.[1] For successful IONM, adequate neuromuscular blockade reversal is a prerequisite. Among the various strategies in neuromuscular blockade for qualified IONM, using a sufficient dose of rocuronium followed by sugammadex has been shown to be desirable for both safe tracheal intubation and successful IONM.

However, the optimal dose of sugammadex has not been established. An excessive dose of sugammadex can induce rigorous patient movement during surgery, while vocal cord movement can not recover adequately for qualified IONM when the dose is insufficient. Several studies have suggested 2 mg/kg as an effective dose of sugammadex for qualified IONM,[2–4] however, these studies focused on complete reversal of neuromuscular blockade. The side effects of excessive doses of sugammadex have not been investigated. In fact, a lower dose of less than 2 mg/kg could be more beneficial as long as neuromuscular blockade is revered while not causing unwanted bucking during thyroid surgery because abrupt patient movement during neck manipulation can be dangerous.

We hypothesized that 1 mg/kg sugammadex would also allow sufficient reversal of neuromuscular blockade induced by 0.6 mg/kg rocuronium for effective IONM with less bucking, than conventional 2 mg/kg sugammadex. This study aimed to compare these two doses of sugammadex (1 vs. 2 mg/kg) in both achieving effective IONM and avoiding unwanted bucking during thyroid surgery.

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MATERIALS AND METHODS

American Society of Anesthesiologists physical status I to II patients over 18 years old who were scheduled to undergo thyroid surgery under IONM were recruited between October 2018 and August 2019. Patients who underwent open thyroid surgery were included in the study. Patients with history of thyroid surgery or preoperative vocal cord palsy were excluded from the study. This prospective randomized controlled study was approved by the Institutional Review Board of the Seoul Metropolitan Government Seoul National University Boramae Medical Center (no. 30-2018-45). The trial was registered at the ClinicalTrials.gov (NCT03689413). Written informed consent was obtained from all subjects.

Randomization

The patients were randomly allocated, at a 1:1 ratio, to group I (1 mg/kg sugammadex group) or group II (2 mg/kg sugammadex group). An investigator who did not clinically participate in this study generated the random allocation sequence using computer-generated block randomization (size 6 blocks that included the letters A and B). Each generated letter was concealed in a sequentially numbered opaque envelope. The enrolled patients were allocated to the assigned groups depending on the letter (A or B) inside the concealed envelope, which was opened and revealed to the standing anesthesiologist in the operating theater by an assistant nurse on the day of the operation while blinding the surgeon. All patients were unaware of their group allocation.

Anesthesia

After patients were admitted to the operating theater, standard monitoring including peripheral oxygen saturation, electrocardiographic, noninvasive blood pressure, and bispectral index (BIS) monitoring was performed. Induction of anesthesia was initiated with a continuous infusion of propofol and remifentanil using a target-controlled infusion system with Orchestra™ infusion pumps (Fresenius Vial, France) after the administration of lidocaine 30 mg. After the loss of consciousness, rocuronium at 0.6 mg/kg was administered for muscle relaxation in all patients.

In all patients, tracheal intubation was performed with a NIM™ standard reinforced electromyography (EMG) endotracheal tube (Medtronic, Jacksonville, FL) with a 7.0 mm internal diameter (ID) for men and a 6.0 mm ID for women, by a single anesthesiologist (J.-M.L.). Patient positioning for thyroid surgery was performed by placing a standard pillow beneath the patient's neck prior to tracheal intubation to avoid displacement of the tracheal tube intubated during patient positioning for the surgery.[5] After patient positioning, the anesthesiologist tilted the operating table to the Trendelenburg position to offset the back-up effect by the pillow and raised the table for the unity of his vision with the patient's airway axis while performing laryngoscopy. Next, the anesthesiologist performed tracheal intubation by direct laryngoscopy. The electrode of the EMG tube was placed at the level of the vocal cords. The modified Cormack-Lehane grade was evaluated.

After tube fixation, sugammadex at 1 or 2 mg/kg was administered to the patient according to the assigned group. Acceleromyography was performed by stimulating the facial nerve and observing acceleration measurements at the eyelid over the orbicularis oculi muscle. Anesthesia was maintained with a continuous infusion of propofol and remifentanil. The standing anesthesiologist adjusted the effect-site target concentration (Ce) of remifentanil 5 minutes before the surgical incision to 4 μg/kg/ml and adjusted the Ce of propofol to maintain a BIS value between 40 and 60.

All setups and monitoring processes were performed in compliance with the standards outlined in the International Neural Monitoring Study Group guidelines.[6] The NIM response 3.0 system (Medtronic, Jacksonville, FL) was used for nerve monitoring. The stimulation duration was set at 100 ms, the event threshold was set at 100 mV, and the stimulus current was set at 1 mA with a frequency of 4 Hz.

Operative Techniques and Outcome Evaluation

Pre- and postoperative laryngoscopic vocal cord examinations, and operations were performed by a single surgeon (Y.J.C.) who was blinded to the patient allocation. A conventional low collar skin incision was made along the skin crease at the lower neck. After the isthmus was divided, the avascular plane between the cricothyroid muscle and the upper pole of the thyroid gland was exposed. Then, the external branch of the superior laryngeal nerve (EBSLN) was stimulated using a nerve stimulator (Prass standard monopolar stimulator probe, Medtronic, Jacksonville, FL), and cricothyroid muscle twitching was subjectively evaluated as 'strong/intermediate/weak'. The train-of-four ratio (TOFr) was recorded at the time of EBSLN stimulation. After mobilizing the upper pole, EMG signals were recorded according to standardized IONM procedures. If the patient showed significant bucking, the surgeon suspended the operation and resumed it after one minute. Every bucking event was recorded. The primary endpoints of the study were the quality of IONM, degree of cricothyroid muscle twitching, EMG amplitude of the signal of the vagus nerve before surgical dissection (V1), and signal of the RLN at the initial identification (R1). The secondary endpoint was the number of intraoperative bucking events.

Statistics

Quantitative variables of patient characteristics and outcome measures are presented as the means ± standard deviation (SD). Categorical variables are presented as numbers with percentages. Binary outcomes were compared using χ^2 tests or Fisher's exact tests, depending on the distribution of variables according to the Kolmogorov–Smirnov test. Comparisons between the two groups were performed with Student's *t*-test or the Mann–Whitney test. A *P*-value <.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics 21.0 software (IBM Corporation, Chicago, IL).

Sample Size Calculation

Previous studies have reported that satisfactory nerve monitoring was achieved in 96% of patients when the qualitative evaluation of nerve monitoring was performed after the administration of 2 mg/kg sugammadex.[4] To establish a non-inferiority study in which 1 mg/kg sugammadex would not be less satisfactory, the number of subjects required for the study with a 10% non-inferiority margin, type I error of 0.05, and 80% power was 48 patients per group. Considering a dropout rate of 5%, the sample size was calculated to be 102 patients.

RESULTS

The process of patient screening, enrolment, randomization, and analysis is shown in the CONSORT flow diagram (Fig. 1). A total of 102 patients were enrolled (51 in each group) and completed the trial. The demographic data of the patients are presented in Table I. The

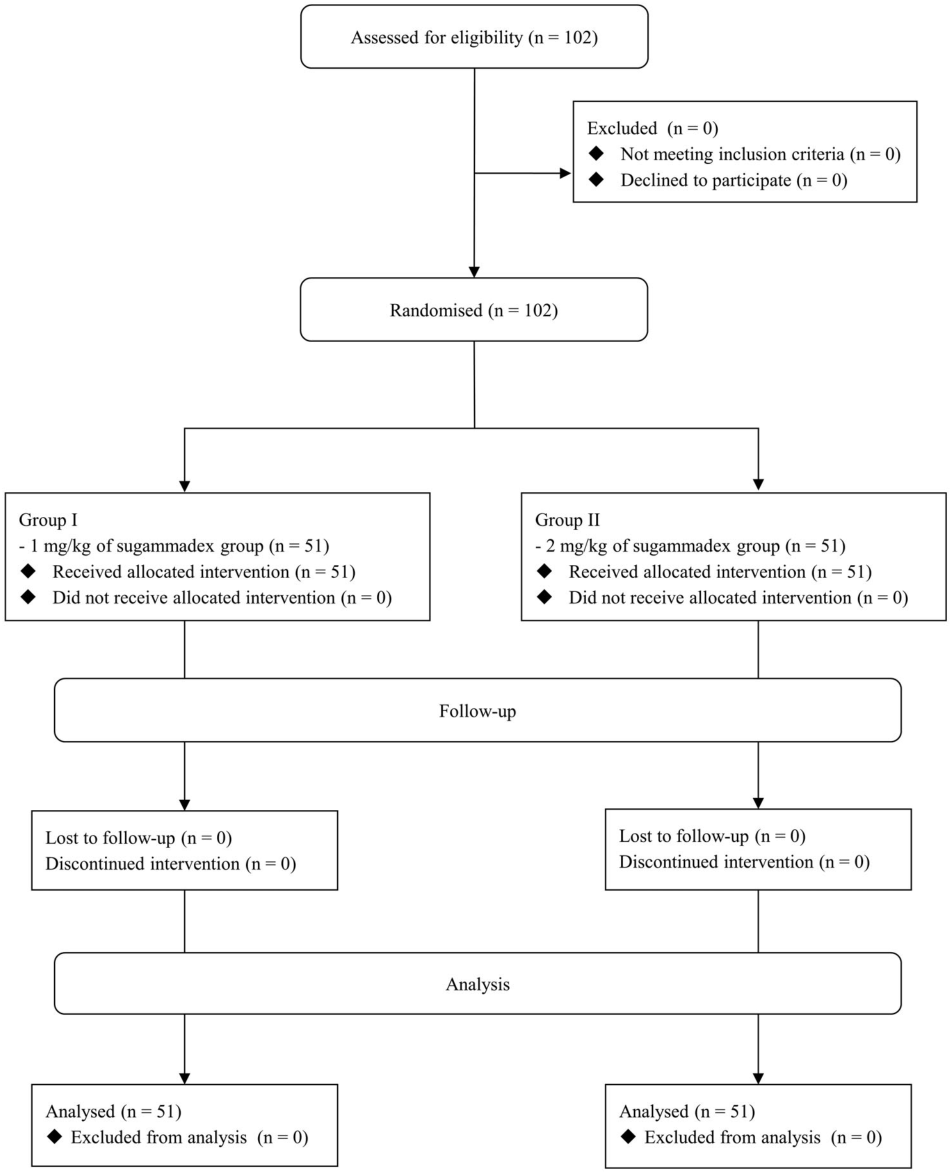

Fig. 1. CONSORT flow diagram.

modified Cormack-Lehane grade was mostly recorded as 2B in both groups. There were no adverse events associated with the study, and tracheal intubation was successfully performed at the first attempt in all patients without any harmful events. There was no difference between the two groups in terms of sex, age, body mass index, tumor size, operative extent, or diagnosis. RLN injury occurred in one patient. The RLN injury occurred during RLN dissection after checking the R1 signal. The patient's vocal cord function recovered in 2 months.

Table II shows the timeline of the anesthetic and operative procedures, which were comparable in the two groups. The mean time from rocuronium injection to sugammadex injection was 9.6 ± 3.3 minutes in group I and 10.1 ± 3.5 minutes in group II (0.526). Mean time taken from sugammadex injection to EBSLN stimulation was 25.0 ± 7.8 in group I and 25.5 ± 9.0 in group II (P = .788).

The quality of IONM is demonstrated in Table III. The TOFr at EBSLN stimulation was not different between the two groups, and the number of patients with TOFr >90% was similar in the two groups. The EBSLN response was strong or intermediate in all patients, and the two groups showed no differences (strong/intermediate/weak: 46/5/0 in group I and 50/1/0 in group II, P = .205). The mean amplitudes of V1 and R1 were comparable in groups I and II (V1: 1,086.3 ± 673.3 vs. 1,161.8 ± 727.5 μV, P = .588; R1: 1,328.2 ± 934.1 vs. 1,410.5 ± 919.6 μV, P = .655). The number of patients who showed bucking was lower in group I than in group II (7/51 [13.7%] vs. 18/51 [37.3%], P = .020).

Patient characteristics	Group I (n = 51)	Group II (n = 51)	*P*-value
Gender (M/F)	20/31	11/40	.084
Age (yr)	55.3 (13.7)	53.2 (14.2)	.960
Height (cm)	160.7 (8.6)	160.2 (7.9)	.766
Weight (kg)	69.5 (13.8)	64.8 (12.2)	.072
Body mass index (kg/m^2)	26.9 (4.8)	25.2 (4.0)	.063
Diagnosis			
Papillary thyroid cancer	39	37	.553
Follicular thyroid carcinoma	4	2	
Benign	8	11	
Operative extent			
Lobectomy	35	32	.532
Total thyroidectomy	16	19	
Tumor size (cm)	1.9 (1.6)	1.5 (1.1)	.231
Modified Cormack-Lehane grade (1/2A/2B/3/4)			
Number of patients	5/16/18/8/4	4/14/27/5/1	.338
%	10/31/35/16/8	8/27/53/10/2	

Table I.
Patient Characteristics.

Data are presented as means (standard deviation) or numbers.

	Group I (n = 51)	Group II (n = 51)	*P*-value
Time (min)			
Rocuronium to sugammadex	9.6 (3.3)	10.1 (3.5)	.526
Sugammadex to skin incision	6.7 (3.5)	6.8 (4.5)	.899
Sugammadex to EBSLN	25.0 (7.8)	25.5 (9.0)	.788
Skin incision to EBSLN	18.7 (6.2)	18.5 (6.9)	.892
Sugammadex to V1	31.9 (9.3)	32.6 (10.0)	.740
Sugammadex to R1	34.1 (10.5)	34.4 (10.6)	.895

Table II.
Timeline of the Procedures.

Data are presented as means (standard deviation) or numbers.
EBSLN = external branch of the superior laryngeal nerve; R1 = signal checking for recurrent laryngeal nerve at initial identification of it; V1 = signal checking for vagus nerve before surgical dissection.

	Group I (n = 51)	Group II (n = 51)	*P*-value
TOFr at EBSLN	88.9 (30.0) %	91.9 (27.1) %	.607
EBSLN response			
Strong	46	50	.205
Intermediate	5	1	
Weak	0	0	
V1 amplitude			
<500 μV	5	2	.436
>500 μV	46	49	
R1 amplitude			
<500 μV	2	1	.205
>500 μV	49	50	1.000
Amplitude of V1 (μV)	1,086.3 (673.3) [274 to 3,043]	1,161.8 (727.5) [447 to 4,263]	.588
Amplitude of R1 (μV)	1,328.2 (934.1) [239 to 4,886]	1,410.5 (919.6) [216 to 5,012]	.655
Bucking	7 (13.7%)	18 (35.3%)	.020

Table III.
Quality of Intraoperative Neuromonitoring.

Data are presented as means (standard deviation), [range of data] or numbers.
EBSLN = external branch of the superior laryngeal nerve; R1 = signal checking for recurrent laryngeal nerve at initial identification of it; TOFr = train-of-four ratio; V1 = signal checking for vagus nerve before surgical dissection.

DISCUSSION

The present study showed that both 1 and 2 mg/kg sugammadex could provide appropriate conditions for IONM during thyroid surgery, while 1 mg/kg was safer in terms of unwanted intraoperative bucking events induced by surgical stimulation.

For nerve sparing, meaningful qualified IONM should be performed during thyroid surgery, as well as the prevention of unwanted intraoperative bucking movement. The signals of V1 and R1 in the patients who received 1 mg/kg sugammadex in the present study were similar to those reported in previous studies in which 2 mg/kg sugammadex was used for reversal of neuromuscular blockade.[2,3] Additionally, the surgeon evaluated the quality of IONM in patients of the group I as good while assessing the EBSLN response in the present study. Therefore, 1 mg/kg sugammadex should be comparable to 2 mg/kg in terms of the quality of IONM.

Unsuccessful IONM has been reported to occur at a rate of 3.8% to 23% in previous studies,[7–10] and one of the common reasons for unsuccessful IONM could be failure of neuromuscular blockade recovery. In general, 0.6 mg/kg rocuronium combined with 2 mg/kg sugammadex has been recommended for optimal conditions for both tracheal intubation and high-quality IONM.[2–4] However, we occasionally observed intraoperative bucking when we used 2 mg/kg sugammadex, and 35.3% of patients in group II had bucking in this study. Considering that prompt bucking movement often occurs during tracheal manipulation, harmful events such as tracheal injury or RLN injury may occur. Our results showed that 1 mg/kg sugammadex decreased the incidence of unwanted bucking during thyroid surgery compared with 2 mg/kg sugammadex (13.7% vs. 35.3%).

The timing of sugammadex administration is another important issue. Skin incision and flap dissection are strong surgical stimuli to patients. In this study, we administered sugammadex immediately after tube fixation, which was approximately 6 to 7 minutes before the skin incision. Therefore, neuromuscular blockade could be reversed at the time of skin incision and flap dissection. Of the 18 patients who had bucking events in group II, 11 (61.1%) patients had bucking during skin incision and flap dissection. Likewise, all seven patients (100%) who had bucking events in group I had bucking during skin incision and flap dissection. Considering that a previous study reported that 20% of patients experienced bucking when sugammadex was given at the time of skin incision,[2] bucking during skin incision and flap dissection may have occurred less often if we had given the sugammadex at the time of skin incision rather than immediately after tube fixation. Sugammadex 1 mg/kg at the time of skin incision combined with 0.6 mg/kg of rocuronium might be the best option for IONM. However, this was not investigated in the present study.

The appropriate timing and dose of sugammadex administration depends on the depth of neuromuscular blockade and can be properly estimated by acceleromyography.[11,12] It is well known that 2 to 4 mg/kg sugammadex is useful for safe extubation in patients receiving general anesthesia with rocuronium.[13–15] However, this knowledge should be strictly applied to the emergence from anesthesia. IONM for thyroid surgery does not necessarily require full recovery from neuromuscular blockade, such as emergence from general anesthesia, in terms of TOFr monitoring. We monitored the TOFr with stimulation of the facial nerve while attaching the sensing probe on the orbicularis oculi muscle because the orbicularis oculi muscle follows the time course of paralysis and recovery of the adductor pollicis muscle.[16] However, the laryngeal muscle shows faster recovery characteristics from neuromuscular blockade than the adductor pollicis muscle.[17,18] In fact, a previous study showed that a sufficient EMG response was achieved with vagal stimulation during thyroid surgery, while the TOFr did not recover >90%.[3] In this study, the EBSLN was checked first among the other nerves, and all patients had a strong or intermediate EBSLN response, and there was no difference in the quality of EBSLN monitoring between the two groups, although seven patients in group I and five patients in group II had TOFr <90% on EBSLN stimulation. This result is consistent with that of a recent study reporting that partial recovery of neuromuscular function using 0.5 or 1 mg/kg sugammadex was sufficient for IONM in animal experiments.[19] The study also reported that 50% recovery of the laryngeal EMG signal was achieved at 6 minutes after the administration of 1 mg of sugammadex.[19] Therefore, we believe that neuromuscular function can sufficiently recover with 1 mg/kg sugammadex for qualified IONM, regardless of the TOFr, and that the routine use of TOFr monitoring only for IONM is unnecessary because surgeons can visually determine whether neuromuscular blockade recovers in terms of saving the target nerves before more invasive surgical manipulation of the area where they suspect there will be the nerves to be saved.

Although the routine use of reversal agents facilitates IONM in all clinical settings, the selective use of reversal agents is also considerable because of spontaneous neuromuscular blockade recovery. A study reported spontaneous recovery in the majority of patients without the use of reversal agents, and 12.5% of the patients who had an inappropriate V1 signal required sugammadex.[20] The proportion of the patients who require reversal agents is dependent on the dose of the neuromuscular blocking agent and the time from neuromuscular blocking agent injection to nerve stimulation. In the present study, the period from neuromuscular blocking agent injection to nerve stimulation was approximately 35 minutes, which is relatively quick compared to times reported in previous studies.[19,20] Whether to use a reversal agent selectively or routinely should be decided based on the surgical teams' experience.

In continuous IONM, a higher V1 signal is required than in intermittent IONM. In continuous IONM, a baseline amplitude higher than 500 μV should be achieved to adequately detect signal decreases. Although it is a limitation of this study that continuous IONM was not used, V1 was higher than 500 μV in most of the patients (93.1%), suggesting that the use of sugammadex might be more beneficial for continuous IONM. Seven patients had a V1 lower than 500 μV in this study, which might be because of EMG tube malpositioning or insufficient exposure of the vagus nerve. The EMG tube should be positioned precisely, and the vagus nerve should be fully exposed to achieve proper amplitude detection even when sugammadex is used.

A previous study showed that the modified Cormack-Lehane grade was 1/2A/2B/3/4 in 73.9%/21.0%/3.3%/1.6%/0.2% of patients when the authors evaluated laryngoscopy in 605 Asian people.[21] In our study, grade 2B was recorded in most patients in both groups. We hypothesized that the difficulty originated from the back pillow that was applied for the surgical position of thyroid surgery in the trial. We believe that the advancement of optical techniques in the era of laryngoscopy, such as video-laryngoscopy, can help to overcome this problem for tracheal intubation in the surgical position for thyroid surgery.

There are several limitations to this study. First, we did not monitor the TOFr continuously or at more time points. However, we believe that TOFr monitoring should not be necessary in situations in which the surgeon checks the signal quality. Second, cricothyroid muscle twitching was evaluated subjectively by the operating surgeon, which limited accurate evaluation of the cricothyroid muscle response. This was because we did not want to add an additional invasive procedure, such as needle electrode insertion into the cricothyroid muscle, for this study. Nonetheless, we believe that this subjective evaluation was sufficient to identify the presence of the EBLSN and to evaluate the effect of sugammadex. Third, all surgeries and postoperative vocal cord evaluations were performed by the same surgeon, which might be a potential source of bias. Last, the outcomes of IONM could be influenced by factors related to the surgeon's and anesthesiologist's levels of experience. Prior to commencing this study, the operating surgeon and anesthesiologist had more than 8 years of experience as attending staff in a large-volume tertiary center. and abundant experience in thyroid surgery. The different backgrounds of the team members must be considered when interpreting the outcomes of IONM in this study. Recently, the use of IONM in thyroid surgery has been increasingly agreed upon by many surgeons. Therefore, we planned to investigate the surgical conditions in thyroid surgery under IONM instead of debating the efficacy of IONM in this trial.

CONCLUSIONS

One mg/kg sugammadex after tracheal intubation is sufficient for IONM, similar to 2 mg/kg sugammadex, and provides safer surgical conditions in terms of unwanted bucking events. We suggest that 1 mg/kg sugammadex is an appropriate dose for IONM during thyroid surgery.

BIBLIOGRAPHY

1. Randolph GW, Kamani D. Intraoperative electrophysiologic monitoring of the recurrent laryngeal nerve during thyroid and parathyroid surgery: experience with 1,381 nerves at risk. *Laryngoscope* 2017;127:280–286.
2. Lu IC, Wu CW, Chang PY, et al. Reversal of rocuronium-induced neuromuscular blockade by sugammadex allows for optimization of neural monitoring of the recurrent laryngeal nerve. *Laryngoscope* 2016;126:1014–1019.
3. Gunes ME, Dural AC, Akarsu C, et al. Effect of intraoperative neuromonitoring on efficacy and safety using sugammadex in thyroid surgery: randomized clinical trial. *Ann Surg Treat Res* 2019;97:282–290.
4. Margarita Kontoudi MG, Loizou C, Kristoloveanou K, Pandazi A. Intraoperative rocuronium reversion by low doses of sugammadex, in thyroid surgery, with monitoring of the recurrent laryngeal nerves. *ARC J Anesthesiol* 2016;1:19–28.
5. Kim J, Moon HJ, Chai YJ, et al. Feasibility of attachable ring stimulator for intraoperative neuromonitoring during thyroid surgery. *Int J Endocrinol* 2020;30:2020.
6. Randolph GW, Dralle H, International Intraoperative Monitoring Study G, et al. Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. *Laryngoscope* 2011;121:S1–S16.
7. Beldi G, Kinsbergen T, Schlumpf R. Evaluation of intraoperative recurrent nerve monitoring in thyroid surgery. *World J Surg* 2004;28:589–591.
8. Snyder SK, Hendricks JC. Intraoperative neurophysiology testing of the recurrent laryngeal nerve: plaudits and pitfalls. *Surgery* 2005;138:1183–1191.discussion 1191-1182.
9. Chan WF, Lo CY. Pitfalls of intraoperative neuromonitoring for predicting postoperative recurrent laryngeal nerve function during thyroidectomy. *World J Surg* 2006;30:806–812.
10. Dionigi G, Bacuzzi A, Boni L, et al. The technique of intraoperative neuromonitoring in thyroid surgery. *Surg Technol Int* 2010;19:25–37.
11. Naguib M. Sugammadex: another milestone in clinical neuromuscular pharmacology. *Anesth Analg* 2007;104:575–581.
12. Duvaldestin P, Kuizenga K, Saldien V, et al. A randomized, dose-response study of sugammadex given for the reversal of deep rocuronium- or vecuronium-induced neuromuscular blockade under sevoflurane anesthesia. *Anesth Analg* 2010;110:74–82.
13. Shields M, Giovannelli M, Mirakhur RK, Moppett I, Adams J, Hermens Y. Org 25969 (sugammadex), a selective relaxant binding agent for antagonism of prolonged rocuronium-induced neuromuscular block. *Br J Anaesth* 2006;96:36–43.
14. Suy K, Morias K, Cammu G, et al. Effective reversal of moderate rocuronium- or vecuronium-induced neuromuscular block with sugammadex, a selective relaxant binding agent. *Anesthesiology* 2007;106: 283–288.
15. Mirakhur RK. Sugammadex in clinical practice. *Anaesthesia* 2009;64:45–54.
16. Ungureanu D, Meistelman C, Frossard J, Donati F. The orbicularis oculi and the adductor pollicis muscles as monitors of atracurium block of laryngeal muscles. *Anesth Analg* 1993;77:775–779.
17. Wierda JMKH, Kleef UW, Lambalk LM, Kloppenburg WD, Agoston S. The pharmacodynamics and pharmacokinetics of Org-9426, a new nondepolarizing neuromuscular blocking-agent, in patients anesthetized with nitrous-oxide, halothane and fentanyl. *Can J Anaesth* 1991;38: 430–435.
18. Meistelman C, Plaud B, Donati F. Rocuronium (Org-9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. *Can J Anaesth* 1992;39:665–669.
19. Lu IC, Wu SH, Chang PY, et al. Precision neuromuscular block management for neural monitoring during thyroid surgery. *J Invest Surg* 2020; 14:1–8.
20. Empis de Vendin O, Schmartz D, Brunaud L, Fuchs-Buder T. Recurrent laryngeal nerve monitoring and rocuronium: a selective sugammadex reversal protocol. *World J Surg* 2017;41:2298–2303.
21. Koh LK, Kong CE, Ip-Yam PC. The modified Cormack-Lehane score for the grading of direct laryngoscopy: evaluation in the Asian population. *Anaesth Intensive Care* 2002;30:48–51.