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Anesthetic Considerations of Intraoperative Neuromonitoring in Thyroidectomy

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Background: Intraoperative neuromonitoring (IONM) might reduce the incidence of injury to the recurrent laryngeal nerve (RLN) during thyroidectomy. Although dislocation of endotracheal tube surface electrodes can lead to false-positive IONM results (loss of signal), the risk factors for dislocation and the effects of muscle relaxants are unclear. Therefore, to identify factors that affect IONM results, we examined the frequency and risk factors for tube dislocation after cervical extension before surgery, the effect of sugammadex administration, and the correlation between IONM results and postoperative RLN palsy.

Methods: Thirty-nine patients scheduled for thyroidectomy from October 2016 to April 2017 were enrolled. All patients underwent standard IONM and pre- and postoperative laryngoscopy. Differences in patient characteristics in the tube dislocation group and non-dislocation group, and differences in amplitude during vagal stimulation before and after sugammadex administration, were assessed by the Mann-Whitney test or Fisher's exact test.

Results: Tube dislocation occurred in 27 patients (69%). Sterno-cricoid distance was significantly shorter in the dislocation group (n=27) than in the non-dislocation group (n=12) (43.88 [32.2-55.91] mm vs 49.46 [40.66-55.91] mm, respectively; p=0.048). Without sugammadex, amplitude during vagal stimulation was sufficient for monitoring. Nine patients had new-onset RLN palsy, which was transient in all patients. The sensitivity of IONM was 100%, the positive predictive value was 60%, and the negative predictive value was 100%.

Conclusions: The present findings suggest that anesthesiologists should use video laryngoscopy to correct tube dislocation and that a rocuronium dose of 0.6 mg/kg, without sugammadex, is adequate for IONM. (J Nippon Med Sch 2019; 86: 263–268)

Key words: intraoperative nerve monitoring (IONM), thyroid surgery, sevoflurane, neuromuscular blockage, video laryngoscope

Introduction

Postoperative recurrent laryngeal nerve (RLN) palsy is a common complication after thyroidectomy and can worsen patient quality of life. Intraoperative neuromonitoring (IONM) helps in accurately identifying the RLN and ensuring nerve integrity at the end of an operation[1]. International guidelines[2] emphasize the benefit of IONM of the RLN. A recent meta-analysis[3] showed that the mean sensitivity and positive predictive values of IONM for RLN palsy were 66.8% (range: 36.4-93.5%) and 63.4% (range: 35-92.1%), respectively. A common reason for false-positive IONM results is dislocation of surface electrodes used for neural integrity monitor (NIM) electromyography (EMG) of the endotracheal tube. Kim et al.[4] found that EMG amplitudes changed during tube dislocation in a porcine model. However, the risk factors for

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https://doi.org/10.1272/jnms.JNMS.2019_86-408
Journal Website (https://www.nms.ac.jp/sh/jmanms/)

dislocation remain unclear, and no standard method has been established for confirming tube position.

Recent guidelines[5] recommend administration of a low dose of a nondepolarizing muscle relaxant, to limit myogenic response amplitudes in IONM for thyroidectomy. Rocuronium is a short-acting nondepolarizing muscle relaxant, and its antagonist is sugammadex. Unfortunately, there is no direct method of monitoring muscle contractility of vocal folds after induction, which depends on the anesthetic selected and the IONM time point. To abolish any remaining effect of muscle relaxant on IONM results, IONM results before and after sugammadex would need to be compared.

Therefore, the objectives of this study were to (1) examine the frequency of tube dislocation after cervical extension before surgery, (2) identify patient and tumor factors that affect tube dislocation, (3) determine the effect of sugammadex administration on IONM results, and (4) evaluate the accuracy of IONM at our hospital.

Materials and Methods

In the present study, we enrolled 39 patients with thyroid carcinoma scheduled for thyroidectomy and neck dissection during the period from October 2016 through April 2017 at Nippon Medical School Hospital. The extent of thyroidectomy was total thyroidectomy in 15 patients and lobectomy in 24 patients. Preoperative unilateral RLN palsy due to tumor invasion was seen in two patients. Thus, the number of RLNs at risk was 52. Written informed consent was obtained from all patients, and the study was approved by the Institutional Committee of Nippon Medical School (approval number: 28-06-598).

No premedication was used. The vital signs of all patients were checked, including electrocardiography, noninvasive blood pressure measurement, and pulse oximetry. Before induction of anesthesia, anesthesiologists placed graduation lines every 3 mm on the electrode of the endotracheal tube (NIM® EMG Standard Endotracheal Tube; Medtronic Japan, Tokyo, Japan). General anesthesia was induced with propofol 1-2 mg/kg, fentanyl 0.1-0.2 μg/kg, and/or remifentanil 0.1-0.3 μg/kg/min. Intubation was facilitated with rocuronium 0.6 mg/kg. Normal saline was used as the tube lubricant instead of lidocaine jelly. Anesthesia was maintained with 0.7-1 minimum alveolar concentration (MAC) of sevoflurane in an air/O_2 mixture (F_IO_2 0.4, 6 L/min), remifentanil 0.05-0.2 μg/kg/min, bolus fentanyl 1-2 μg/kg/h, and no additional dose of rocuronium.

Using a video laryngoscope, anesthesiologists placed the tube at the point where the middle line of the graduation lines grounded the vocal folds on both sides. The positions of the electrodes for IONM were observed and optimized with a video laryngoscope by anesthesiologists and surgeons at the time of intubation and cervical extension before surgery (McGrath® MAC; Covidien Japan, Tokyo, Japan). We compared tube positions at the time of intubation and cervical extension. If dislocation was greater than 3 mm (i.e., more than one graduation line), the case was recorded as "dislocation positive", and the gap was corrected to the optimal position. After identifying the vagus nerve, "baseline" IONM with vagal stimulation (stimulus intensity: 3 mA) was performed (V1). Then, sugammadex 2 mg/kg was administered, and IONM was performed again 3 minutes later (V1'). IONM stimulation was also performed after tumor removal (V 2). All other thyroidectomy and anesthesia procedures were performed as usual. IONM was recorded with an NIM-Response® 3.0 system (Medtronic Japan). All patients underwent laryngoscopy by an otolaryngologist and a postoperative check by an anesthesiologist on postoperative day 1.

We examined whether tube dislocation was associated with background characteristics, including patient, tumor, and operative characteristics. Patient characteristics included age, sex, height, body mass index, and sternocricoid distance (distance between the cricoid cartilage and suprasternal notch on radiographic images). Tumor characteristics included pathological diagnosis of thyroid tumor, tumor position, tumor size, lymph node metastasis, and preoperative RLN palsy. Operative characteristics included extent of thyroidectomy and lymph node dissection. We also compared the amplitude of vagal stimulation before and after sugammadex administration. Loss of signal (LOS) was defined as a V2 <100 μV or an 80% decrease in nerve amplitude from baseline, as defined by Stopa et al.[6] In addition, LOS was defined as true positive when RLN palsy was observed by laryngoscopy on postoperative day 1 and as false positive when no RLN palsy was observed[7].

Statistical Analysis

All numerical data are expressed as median (range). Differences in patient and tumor characteristics between the tube dislocation and non-dislocation groups, and differences in amplitude during vagal stimulation before and after sugammadex administration, were assessed by the Mann-Whitney test or Fisher's exact test with the Prism software package (ver. 5.0; GraphPad Software, San Diego, CA, USA), unless otherwise specified. A P

Table 1 Preoperative and intraoperative patient characteristics

	Dislocation n=27	Non-dislocation n=12	P value
Dislocation (mm)	(–12-3)	-	
Age	47 (31-78)	46 (30-82)	0.82
Height (cm)	162.5 (140-193)	165 (138-175)	0.68
BMI	23.8 (18.1-34.8)	22.1 (17.4-27.1)	0.22
Sex (male:female)	12:15	7:5	0.33
Sterno-cricoid distance (mm)	43.88 (32.2-55.91)	49.46 (40.66-63.73)	0.048*
Pathological diagnosis			
Papillary carcinoma	26	10	0.22
Medullary carcinoma	1	1	0.53
Undifferentiated carcinoma	0	1	0.31
Multiple tumors	7	0	0.078
Position of tumor			
Upper	14	6	1
Middle	13	8	0.32
Lower	12	8	0.30
Other	2	2	0.57
Maximum tumor size (mm)	15 (0.5-65)	18 (5-44)	0.72
Lymph node metastasis	18	8	0.65
Preoperative RLN palsy	2	0	0.86
Operative procedure			
Total thyroidectomy:lobectomy	13:14	2:10	0.13
Lymph node dissection			
Central	16	8	0.47
Lateral	9	4	0.65
Bilateral	2	0	0.93

Values are numbers or medians (range).
BMI, body mass index; RLN, recurrent laryngeal nerve
*p<0.05

value of 0.05 or less was considered to indicate statistical significance.

Results

Thirty-nine patients (19 men, 20 women) were included in the analysis. All tracheal intubations were successful, without difficulties, on the first attempt.

Patient Background and Tube Dislocation

Among the 39 patients, tube dislocation was observed in 27 (69%), 22 of whom showed caudal movement (a shortening of the distance between the tube electrodes and carina). One showed a 90-degree tube rotation. In another patient, tube dislocation recurred, and the tube position was corrected during surgery. After re-correcting the tube position by using the video laryngoscope, IONM was documented correctly in all cases.

Associations of tube dislocation with the various background characteristics are summarized in **Table 1**. Age, sex, height, and body mass index did not significantly differ between the dislocation group (n=27) and non-dislocation group (n=12), and no significant differences were seen in tumor data (number, size, and position of tumor, pathological diagnosis, or lymph node metastasis). However, sterno-cricoid distance was significantly shorter in the dislocation group than in the non-dislocation group (43.88 [32.2-55.91] mm vs. 49.46 [40.66-55.91] mm, respectively; p=0.048).

Effect of Sugammadex Administration on IONM Results

Figure 1 shows amplitudes during vagal stimulation before and after sugammadex administration. The time between administration of rocuronium and sugammadex was 45 (20-72) min. A significant difference was seen between V1 (292 [114-1283] μV) and V1′ (421 [143-2012] μV) (p=0.001).

Postoperative Symptoms and IONM Accuracy

Nine patients (17.3% of the 52 nerves at risk) had new-onset unilateral vocal fold dysfunction at postoperative day 1. There was no bilateral palsy. All had LOS for V2. All cases of dysfunction were transient, and there were no cases of permanent palsy. All symptoms, such as hoarseness and vocal deterioration, resolved within 3 (1-

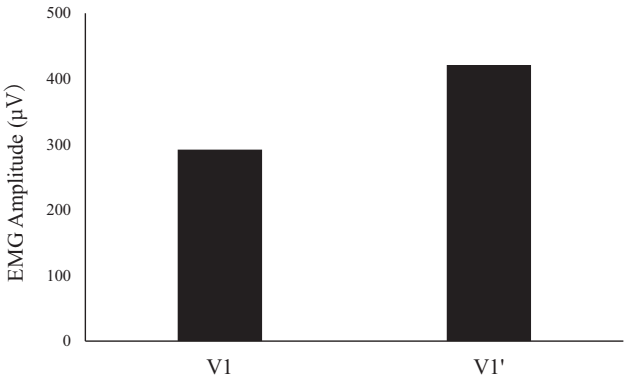

Fig. 1

6) months. The sensitivity of IONM was 100%, the positive predictive value was 60%, and the negative predictive value was 100%, as shown in **Table 2**.

Table 2 The association between presence of RLN palsy and LOS in IONM

	RLN palsy	No RLN palsy	total
LOS	9	6	15
No LOS	0	37	37
Total	9	43	52

Values are expressed as N.
IONM, Intraoperative neuromonitoring; RLN, recurrent laryngeal nerve; LOS, loss of signals

Discussion

In the present study, endotracheal tube use caused no severe adverse events, such as arytenoid subluxation or larynx edema requiring reintubation, which suggests that the NIM® EMG Endotracheal Tube is safe.

Neck extension can change the position of an endotracheal tube[8]. In this study, EMG tube dislocation at the cervical extension position was observed in two-thirds of the patients, and 88% of the dislocations involved caudal movement. In addition, sterno-cricoid distance was shorter in the dislocation group than in the non-dislocation group. Tube dislocation may be the most important factor in successful IONM, so repeatedly monitoring tube position when dislocation is suspected could enhance the quality of IONM, especially for patients with short necks.

In this study, RLN palsy was defined as the presence of (1) postoperative symptoms such as hoarseness or difficulty raising the voice and (2) postoperative vocal fold dysfunction, as determined by laryngoscopy, on postoperative day 1. RLN palsy can result from vagal nerve injury, or from vagal nerve extension during a surgical procedure or tube intubation or extubation[9]. Randolph et al. reported that transient RLN palsy is of short duration, typically several weeks to several months[2]. Another study reported that 6.6% patients developed postoperative unilateral vocal fold paralysis and that 93% completely recovered during a median period of 3 months (range, 1-9 months)[10]. In the present study, nine patients had paralysis postoperatively; however, symptoms resolved within 3 months of the operation (0-6 months). We observed no RLN injuries. However, Echternach et al. reported that 31.3% of patients had an intubation injury to the vocal folds[11]. Therefore, to minimize potential damage to the vocal folds, anesthesiologists should perform intubation carefully. Previous studies reported that glottis views are better with video laryngoscopy than with direct laryngoscopy[12,13]. Among video laryngoscopes, the McGrath® MAC allows surgeons to confirm the position of an inserted tube and has superior maneuverability for correcting the position of a placed tube. This device might have advantages for IONM during thyroid surgery, as proper adhesion of the electrodes and vocal folds has a substantial effect on the results.

There is no direct method of monitoring muscle contractility of vocal folds after induction of anesthesia; thus, all anesthetics that cause neuromuscular blockage, especially muscle relaxants, must be avoided during IONM[14]. The international standard guideline for IONM recommends administration of succinyl choline 2-2.5 mg/kg or a low dose of a nondepolarizing muscle relaxant[2]. Rocuronium is a nondepolarizing muscle relaxant, and its antagonist is sugammadex. Lowry et al.[15] reported that T1 recovered to 25% at 45 min after administration of rocuronium 0.6 mg/kg, the initial dose recommended by the Food and Drug Administration . Sensitivity to rocuronium and the duration of its effect differ in relation to muscle site. A study using muscle-relaxation monitoring found that recovery from muscle relaxant activity occurred earlier in the larynx than in the adductor pollicis[16]. In the present study, V1 recorded at about 46 minutes after administration of rocuronium 0.6 mg/kg was greater than 400 μV, which is sufficient for adequate IONM. Sufficient V1 amplitude for adequate IONM was achieved without sugammadex, which indicates that a rocuronium dose of 0.6 mg/kg is adequate for IONM. In addition, V 1′ amplitude increased after sugammadex administration ($P<0.05$), which suggests a small remaining effect of rocuronium at V1. Sugammadex administration might be useful in abolishing the remaining effects of rocuronium, when IONM is started earlier than 45 minutes after in-

Table 3 The causes of false positivity at IONM

Improper position of NIM tube
Protracted effect of muscle relaxant
Lubricating gel on NIM tube
Equipment malfunction
Improper intensity of stimulation
Anatomic variations of RLN

IONM, Intraoperative neuromonitoring; NIM, neural integrity monitor; RLN, recurrent laryngeal nerve

duction or when V1 amplitude is lower than 100 μV.

The effects of the anesthetic agent used for IONM during thyroid surgery have not been reported, and no current guideline recommends a specific anesthetic agent. For IONM in thyroidectomy, the train of four (TOF) of the adductor pollicis was studied for assessing muscle contractility of vocal folds[14]. A previous study found that TOF did not differ between a 1.0 MAC of sevoflurane and total intravenous anesthesia (TIVA)[17]. In the present study, V1 amplitudes recorded with 0.7-1.0 MAC sevoflurane were greater than 400 μV, sufficiently high for adequate IONM, which suggests that a clinical dose of sevoflurane is adequate for IONM.

Several factors can cause false-positive result in IONM, as shown in **Table 3**. Although tube position was checked after cervical extension and sugammadex administration in all patients, six nerves yielded false-positive results. Tube dislocation or rotation can occur during surgery. When LOS is suspected, anesthetists should evaluate the potential tube dislocation and the possibility of iatrogenic vocal fold palsy. In this study, when LOS was defined after tumor removal, the only remaining surgical procedure was skin closure, which was done quickly. This explains why tube location was not monitored, and no change in surgical procedure occurred, after V2 recording. Frequent direct laryngoscopic exposure can cause temporary vocal fold palsy, as mentioned above. To minimize the risks of iatrogenic hoarseness and vocal fold palsy, we refrained from repeated direct laryngoscopic exposure in this study. Among the six procedures yielding false-positive cases of LOS, three were lobectomies and three were total thyroidectomies. If LOS is observed for low-risk lobectomy cases, anesthesiologists should consider checking tube position after tumor removal, just for the record.

This study had limitations. First, it was an observational study of a small number of cases at a single center. Second, the stimulation points during IONM might have slightly differed, which could have affected the IONM results. Third, neuromuscular monitoring was not conducted; therefore, we could not assess the residual effect of rocuronium 0.6 mg/kg after the start of IONM.

Tube dislocation after neck extension was observed in 69% of the patients. After correcting tube dislocation, no other anesthetic or tumor characteristics were significantly associated with the results of IONM. This suggests the importance of reliable positional correction with the McGrath® MAC video laryngoscope after cervical extension.

Conflict of Interest: The authors declare no conflicts of interest.

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(Received, February 15, 2019)
(Accepted, April 17, 2019)
(J-STAGE Advance Publication, May 17, 2019)