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Comparative Analysis of Monitoring Neuromuscular Block at the Upper Lip, Corrugator Supercilii Muscle, and Thumb

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Purpose: To determine the feasibility and usefulness of monitoring neuromuscular block at the upper lip (UL) in comparison with the corrugator supercilii (CS) muscle and thumb in anesthetized patients. **Methods:** Fifty-four adult patients undergoing total intravenous anesthesia were randomly divided into the UL, CS, and thumb groups (n = 18 per group), and depth of neuromuscular block by rocuronium was assessed acceleromyographically at these sites. **Results:** The supramaximal stimulating current and time to onset of neuromuscular block by rocuronium (0.6 mg/kg) did not differ significantly among the three groups. Minimum value of the first response in train-of-four (T1/control) was significantly higher in the CS group than in the UL and thumb groups ($p < 0.05$). T1/control was significantly higher in the CS group than in the UL and thumb groups 10-20 min after rocuronium, but was significantly lower than in the thumb group 60 min and 80-90 min after rocuronium ($p < 0.05$). The train-of-four ratio was significantly higher in the CS group than in the UL and thumb groups 20 min after rocuronium ($p < 0.05$). **Conclusion:** Depth of neuromuscular block can be monitored at the UL and has similar depth to that assessed at the thumb.

Key Words: buccinator muscle, corrugator supercilii muscle, adductor pollicis muscle, rocuronium, neuromuscular block

Introduction

The depth of neuromuscular block is typically evaluated quantitatively at the thumb. However, neuromuscular monitoring at the thumb can be difficult during surgical procedures as the thumb is often covered with surgical drapes or the upper limbs may lie alongside the trunk. A method for monitoring neuromuscular block at the corrugator supercilii (CS) muscle has been developed as a solution to this. However, monitoring at the CS muscle can also be difficult because monitors placed to assess the depth of anesthesia, such as bispectral index and entropy monitors, cover a large area of the forehead. This can mean the bispectral index or entropy monitor is placed as little as 3 cm from the acceleromyographic transducer which assesses the depth of neuromuscular block at the CS muscle. Because of this, some regard neuromuscular monitoring at the CS muscle to be inadequate for use in clinical settings[1)~3)]. Thus, establishing a method for monitoring the depth of neuromuscular block other than at the thumb or CS muscle would be desirable.

We hypothesized that the depth of neuromuscular block could be properly assessed at the upper lip (UL), which moves mainly by contraction of the buccinator muscle. Therefore, here we investigated the feasibility of monitoring the depth of neuromuscular block at the UL, compared to that of monitoring at the CS or thumb, in anesthetized patients receiving rocuronium.

Materials and Methods

The Ethics Committee of Tokyo Women's Medical University approved the protocol of this open-label, randomized controlled trial, and all patients provided written informed consent. Data were collected between April 3 and December 24, 2012. Eli-

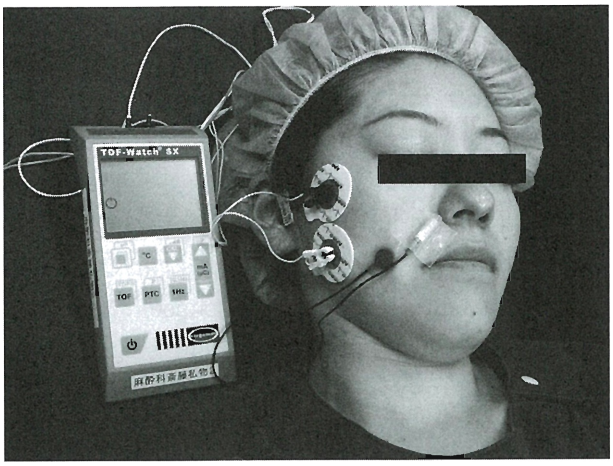

Fig. 1 In the upper lip group, two surface stimulating electrodes were secured over the buccal branch of the facial nerve, and an acceleromyographic transducer was positioned approximately 1 cm lateral to the wing of the nose.

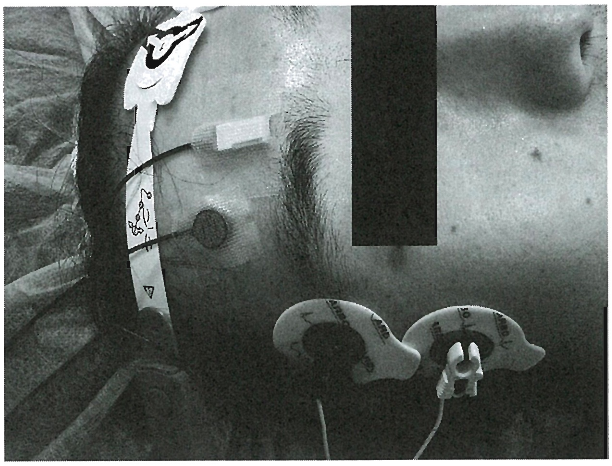

Fig. 2 In the corrugator supercilii group, two surface stimulating electrodes were secured over the external part of the right supercilii arch and an acceleromyographic transducer was placed at the internal half of the supercilii arch.

gibility criteria were as follows: adult patients with an American Society of Anesthesiologists physical status of 1-2 scheduled for elective surgery under general anesthesia or general anesthesia combined with epidural anesthesia; not taking any drug known to affect the action of the neuromuscular relaxant; and no neuromuscular, cardiac, hepatic, renal, or metabolic disorders. Patients were randomly allocated to the UL, CS, and thumb groups by the sealed envelope method (serially numbered, externally generated random numbers). Assuming an α value of 5% and with 90% power, a sample size of 18 patients per group was necessary to detect a difference of $\geqq 0.2$ in the mean T1 [first stimulation in train-of-four (TOF)/control or TOF ratio (T4/T1)], with a standard deviation (SD) of approximately 0.2. According to this power analysis, 54 patients were included in the study.

None of the patients received premedication. After arriving at the operating room, stimulating electrodes and an acceleromyographic transducer were attached. In the UL group, to stimulate the buccal branch of the facial nerve, two surface stimulating electrodes were secured approximately 2 cm anterior to the right ear lobe, the cathode under the zygomatic arch, and the anode superior to the mandible angle. An acceleromyographic transducer was placed approximately 1 cm lateral to the right wing of the nose (Fig. 1). A neuromuscular transmission monitoring device (TOF watch SX, Nihon-Koden Inc., Tokyo, Japan) was connected to the electrodes and transducer. In the CS group, two surface stimulating electrodes were secured over the external part of the right supercilii arch, and an acceleromyographic transducer was positioned at the internal half of the supercilii arch (Fig. 2). In the thumb group, two surface stimulating electrodes were secured over the ulnar nerve at the wrist and an acceleromyographic transducer was attached to the volar aspect of the thumb. A hand adaptor was used to assess the depth of neuromuscular block at the thumb (Fig. 3).

In all three groups, a bispectral index probe (A-2000 BIS Monitor, Nihon-Koden, Inc., Tokyo, Japan) was attached to the forehead and the depth of anesthesia was evaluated. In the CS group, the bispectral index probe was placed over the central or left forehead and left temple, and the acceleromyographic transducer was placed 3 cm from the right edge of the bispectral index probe.

In all patients, general anesthesia was induced by continuous infusion of remifentanil 0.5 μg/kg/min and target-controlled infusion of propofol 3.0 μg/ml. After insertion of a ProSeal laryngeal mask airway (PLMA; LMA ProSeal, LMA North America Inc., San Diego, USA), the lungs were ventilated with air

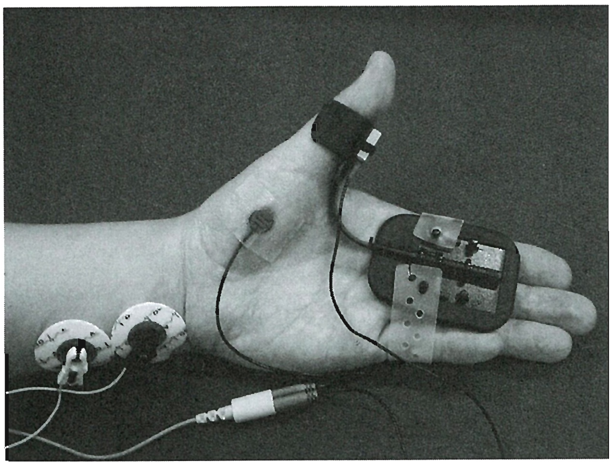

Fig. 3 In the thumb group, two surface stimulating electrodes were placed over the ulnar nerve at the wrist, and an acceleromyographic transducer was attached to the volar aspect of the thumb. A hand adaptor was used to assess depth of neuromuscular block at the thumb.

3 L/min and oxygen 1 L/min. To maintain an appropriate level of general anesthesia, propofol 1.2-2.5 μg/ml and remifentanil 0.2-1.0 μg/kg/min were administered continuously, and bolus doses of fentanyl 2 μg/kg were given as necessary to keep BIS values in the range of 40 and 60. PLMA sizes #4 and #3 were used in male and female patients, respectively. Lungs were ventilated to maintain normocapnia ($P_{ET}CO_2$ 32-37 mmHg) throughout the surgery, with $P_{ET}CO_2$ measured using a multiple gas monitor (IntelliVue MP70 Anesthesia Monitor, Philips Inc., Boeblingen, Germany). Surface skin temperature was maintained above 32.0℃.

Nerve stimulation was started after insertion of the PLMA. The supramaximal stimulating current was determined automatically using the neuromuscular transmission monitor. The monitoring system automatically searched for the stimulus current needed to elicit a maximal response from each muscle. Simulation started with single twitch stimuli (0.2 msec duration, square-wave) delivered at 1 Hz. The stimuli were started at 60 mA, and the stimulating current was decreased in 5 mA increments to 20 mA. When a decrease of 10% or more was detected in response to the single twitch stimuli, the current at which the supramaximal muscular response could be elicited was defined as the stimulation current for the previous stimulation. Thereafter, the current level increased by 10% of the current that could produce the supramaximal response was regarded as the "supramaximal stimulating current". Once the supramaximal stimulating current had been determined in the three groups, TOF stimuli were delivered every 15 sec at this current for 10 min to stabilize the TOF response, as recommended previously[4]. For TOF, four single twitch stimuli of 0.2 msec duration square-wave were delivered every 0.5 sec. T1, T2, T3, and T4 were the 1st, 2nd, 3rd, and 4th responses evaluated acceleromyographically, respectively. Acceleromyography measures acceleration of the stimulated muscle. It is related to the method of Newton's second law: force = mass × acceleration. If mass is constant, the force of muscle contraction can be calculated if acceleration is measured. Based on this mechanism, acceleromyographic T1/control reflects the degree of muscular contraction.

After the stabilization period, the acceleromyographic value of T1 was regarded as the control value, and rocuronium 0.6 mg/kg was administered. TOF stimuli were continuously applied every 15 sec at the supramaximal stimulating current. Time from rocuronium injection to the disappearance of the acceleromyographic response of T1 was defined as time to onset of neuromuscular block. If the response of T1 was not abolished, the time when T1/control reached the minimum level was regarded as the time to onset. Thereafter, T1/control and the TOF ratio (T4/T1) were monitored every 15 sec. Although both of these parameters are indicators of the depth of neuromuscular block, the former represents the level of neuromuscular block in the post-junctional area of the neuromuscular junction and the latter represents that in the pre-junctional area[5].

Peripheral temperature over the UL, CS muscle, or the adductor pollicis muscle was monitored using a surface skin temperature probe connected to the neuromuscular transmission monitor.

Patient characteristics and the duration of anesthesia or surgical procedure were compared among the three groups using analysis of variance

Table 1 Patient characteristics in the three groups

Group	UL (n=18)	CS (n=18)	Thumb (n=18)
Age (years)	50.7±16.0	51.6±13.0	45.1±11.9
Sex (female/male)	13/5	15/3	14/4
Height (cm)	159.8±6.3	159.2±7.6	162.7±6.5
Weight (kg)	57.8±9.2	53.8±9.5	57.3±8.6
ASA PS (1/2)	15/3	16/2	15/3
Duration of anesthesia (min)	170±44	177±51	162±51
Duration of surgery (min)	117±42	126±47	111±42

None of the patient characteristics differed significantly among the three groups.
Values are means±SDs or number.
UL: upper lip, CS: corrugator supercilii, ASA: American Society of Anesthesiologists, PS: physical status.

Table 2 Supramaximal stimulating current, time to onset of neuromuscular block, and minimum value of T1/control in the three groups

Group	UL (n=18)	CS (n=18)	Thumb (n=18)
Supramaximal stimulating current (mA)	50.1±10.4	54.4±11.3	51.7±10.3
Time to onset of neuromuscular block (sec)	100.0±41.8	141.7±75.3	137.7±48.0
Minimum value of T1/control	0.068±0.029	0.151±0.106*	0.037±0.028

Values are means±SD.
*$p<0.05$ compared with the UL and thumb groups.
UL: upper lip, CS: corrugator supercilii.

(ANOVA) and Scheffe's multiple comparisons or the chi-square test. Supramaximal stimulating current, time to onset of neuromuscular block, and minimum value of T1/control were compared among the three groups using ANOVA and Scheffe's multiple comparisons. ANOVA and unpaired t-tests with Bonferroni's adjustment were used to compare T1/control and the TOF ratio during recovery from the neuromuscular block among the three groups. All results are expressed as means ± SD or number. All statistical analysis was performed with the SPSS PASW Statistics 18 software package (IBM Inc., Tokyo, Japan). A p value of <0.05 was regarded as statistically significant.

Results

Among the three groups, patient characteristics and the duration of anesthesia or surgical procedure were comparable (Table 1).

In one, six, and one patient in the UL, CS, and thumb groups, respectively, the control acceleromyographic value could not be determined the first time. However, after repositioning the acceleromyographic transducer or hand adaptor several times, the control value could be determined. The control value could not be obtained the first time in significantly more patients in the CS group than in the UL and thumb groups ($p<0.05$).

As shown in Table 2, the supramaximal stimulating current and time to onset of neuromuscular block did not differ significantly among the three groups. The minimum value of T1/control in the CS group was significantly higher than that in the UL and thumb groups ($p<0.05$).

As shown in Fig. 4, T1/control in the CS group was significantly higher than in the UL and thumb groups 10-20 min after rocuronium ($p<0.05$). For example, 20 min after administration, T1/control values were 0.22±0.16, 0.07±0.03, and 0.04±0.04 in the CS, UL, and thumb groups, respectively. At 60 min and 80-90 min after rocuronium, the T1/control value in the CS group was significantly lower than in the thumb group ($p<0.05$). At 90 min after rocu-

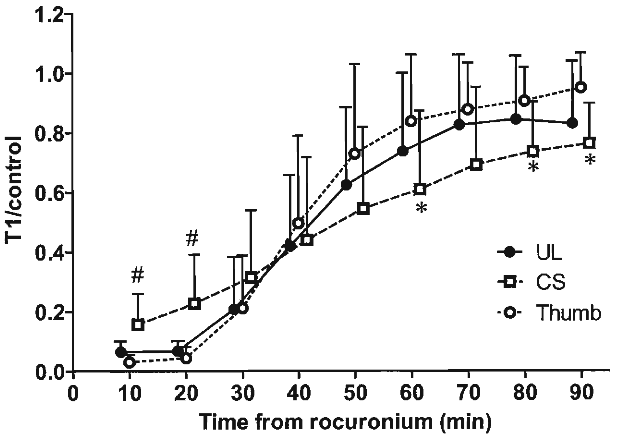

Fig. 4 Recovery of T1/control in the UL (●), CS (□), and thumb (○) groups
UL: upper lip, CS: corrugator supercilii.
# $p<0.05$ compared with the UL and thumb groups.
* $p<0.05$ compared with the thumb group.

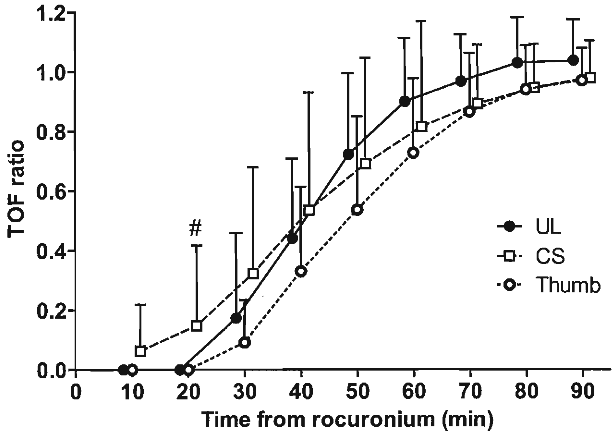

Fig. 5 Recovery of TOF ratio in the UL (●), CS (□), and thumb (○) groups
UL: upper lip, CS: corrugator supercilii, TOF: train-of-four.
# $p<0.05$ compared with the UL and thumb groups.

ronium, T1/control values were 0.76 ± 0.14, 0.83 ± 0.21, and 0.95 ± 0.12 in the CS, UL, and thumb groups, respectively.

As shown in Fig. 5, the TOF ratio was significantly higher in the CS group than in the UL and thumb groups 20 min after rocuronium (0.11 ± 0.19 vs 0.00 ± 0.00 and 0.00 ± 0.00, $p<0.05$).

Surface skin temperature did not decrease to <32.0℃ in any of the patients. The bispectral index was maintained between 40 and 60 during surgery in all patients. Difficult ventilation caused by remifentanil-induced chest wall rigidity or vocal cord closure was not observed in any of the patients.

Discussion

The CS muscle is small and the bispectral index monitor generally needs to be positioned across a large part of the forehead, meaning that the monitor can interfere with the assessment of neuromuscular block over the muscle. In this study, a control value of T1 could not been determined the first time in as many as six of the 18 patients in the CS group. If this value is not determined quickly, general anesthesia may not be induced smoothly. Based on this shortcoming, monitoring the neuromuscular block at the CS muscle does not appear to be clinically relevant.

In this study, the supramaximal stimulating current was above 50 mA in the three groups. It has been shown that this current is more than 50 mA at the facial muscle[6] and sternocleidomastoid muscle[7], but is about 30 mA at the thumb[8]. In a previous study involving monitoring at the thumb[8], when the ulnar nerve was stimulated, the thumb was allowed to move freely. However, in the present study, a hand adaptor was attached to the palm and thumb, and the use of the hand adaptor might have been related to the high stimulating current used in this study.

Time to onset of neuromuscular block by rocuronium 0.6 mg/kg did not significantly differ among the three groups. This result is comparable with that of a previous study examining the monitoring of depth of neuromuscular block at the sternocleidomastoid and adductor pollicis muscles[7]. Hence, the time to onset of neuromuscular block might not differ between the facial, sternocleidomastoid, and adductor pollicis muscles.

In the present study, the minimum value of T1/control after rocuronium was significantly higher in the CS group than in the UL and thumb groups. This may be attributable to the fact that the CS muscle is highly resistant to neuromuscular blocking drugs. Also, T1/control was significantly higher in the CS group than in the UL and thumb groups 10-20 min after rocuronium injection. This is probably because the CS muscle is also resistant to rocuronium. However, 60, 80, and 90 min after rocuronium, T1/control in the CS group was significantly lower than that in the thumb group. We cannot fully explain this result, but assume that recovery of T1/control could not be adequately assessed at the CS muscle as monitoring was difficult at this site. Additionally, we should consider the use of a bispetral index probe in this study. Previously, Plaud et al[2] demonstrated that acceleromyographic values of T1 measured at the CS, orbicularis oculi, and AP muscles returned to their control values determined before rocuronium administration. However, in their study, the bispectral index probe was not attached to the. Hence, in the present study and our previous studies[6)7)] the use of the bispectral index probe at the CS muscle may relate to the insufficient recovery of T1/control at this site.

The monitoring of the degree of neuromuscular block at the UL has not been studied. Therefore, the sensitivity of the UL to rocuronium is not known. The UL is moved by the contraction of the orbicularis oris, buccinator, zygomatic major, and zygomatic minor muscles. The thumb, on the other hand, is moved by the contraction of the adductor pollicis muscle. The present study revealed that the CS muscle was more resistant to rocuronium than the UL (the orbicularis oris, buccinator, zygomatic major, and zygomatic minor muscles) or thumb (adductor pollicis muscle). The results also suggest that the sensitivity of the UL to rocuronium is similar to that of the thumb because the minimum value of T1/control and the recovery of T1/control or the TOF ratio at the UL were comparable to those at the thumb.

The limitation of this study was to wait as long as 10 min between the administrations of propofol and rocuronium during induction of general anesthesia. This "baseline stabilization period" was needed to stabilize the acceleromyographic value of T1[4)]. If the lungs were ventilated with a face mask during this period, the assessment of the acceleromyographic control value of T1 could not be determined properly. This was why we decided, as in our previous studies[6)9)], to ventilate the lungs via a PLMA during the stabilization period.

Conclusion

In conclusion, the depth of neuromuscular block assessed acceleromyographically at the UL is similar to that seen at the thumb. Monitoring neuromuscular block at the UL is not only clinically feasible, it is also easier to perform than at the CS muscle and thus should prove clinically useful.

The authors indicated no conflicts of interest.

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上口唇，皺眉筋，ならびに母指で行う筋弛緩モニターの比較

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〔背景〕全身麻酔中の患者における筋弛緩効果は，通常，手の母指や，前額部にある皺眉筋で筋弛緩モニターを行うことによって定量的に測定される．しかし，手の上には手術用覆布が掛けられたり，前額部には鎮静度を測定するためのプローベが貼付されたりするため，実際には，手の母指や皺眉筋における筋弛緩モニターは困難である．そこで，上口唇における筋弛緩モニター方法について研究を行った．〔方法〕全身麻酔下に手術を施行される成人患者54名を上口唇群，皺眉筋群，母指群の3群に無作為に分けた．上口唇群では筋弛緩モニター機器（TOFウォッチ®SX）に接続されている刺激電極を顔面神経上に，加速度トランスデューサーを鼻翼付近の上口唇上に装着した．皺眉筋群ではそれらを各々顔面神経上，前額部の皺眉筋上に，母指群では尺骨神経上，母指の屈側に装着した．3群間で最大上刺激電流，ロクロニウム0.6 mg/kg投与後の筋弛緩効果発現時間と，T1/controlの最低値，ロクロニウム投与10, 20, 30…90分後のT1/controlとtrain-of-four（TOF）ratio（T4/T1）の回復について比較した．〔結果〕最大上刺激電流と筋弛緩作用発現時間に関しては，3群間で有意差を認めなかった．皺眉筋群では，ロクロニウム投与後のT1/controlの最低値と，ロクロニウム投与10～20分後におけるT1/controlは上口唇群と母指群より高かった．逆に，皺眉筋群におけるT1/controlは，ロクロニウム投与60分後と80～90分後には上口唇群よりも低値となった．TOF ratioに関しては，ロクロニウム投与20分後において，皺眉筋群では，上口唇群と母指群よりも有意に高値であった．〔結論〕顔面神経を刺激し上口唇上に加速度トランスデューサーを装着することによって，母指同様に筋弛緩モニターが可能であった．