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ORIGINAL ARTICLE

Onset of rocuronium-induced neuromuscular block evaluated subjectively and accerelomyographically at the masseter muscle

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Abstract
Purpose The main aim of this study was to compare the onset times of rocuronium evaluated subjectively and by acceleromyography at the masseter muscle (MM).
Methods Forty female patients were sequentially enrolled in this study. In the first 20 patients, neuromuscular block was evaluated subjectively. After induction of anesthesia with fentanyl and propofol, both the left masseter and ulnar nerves were stimulated in 2-Hz train-of-four (TOF) mode using peripheral nerve stimulators. Contractions of the MM were felt with an anesthesiologist's left hand holding an anesthesia facemask; those of the adductor pollicis (APM) were visually observed. All the patients received a bolus of rocuronium, 0.6 mg/kg. Onset times after rocuronium were defined as the duration until the contractions became impalpable at the MM or invisible at the APM. At the time contraction of the MM had not been felt, intubating conditions were assessed. In the next 20 patients, contractions of the MM and the APM were concurrently quantified using acceleromyography after induction of anesthesia and laryngeal mask insertion. Following 0.6 mg/kg rocuronium, onset of the action was recorded.
Results Onset of the action of rocuronium at the MM evaluated subjectively [mean (SD), 70.3 (17.7) s] was similar to that monitored acceleromyographically [73.3 (27.6) s, $P > 0.05$], and significantly shorter than that at the APM acceleromyographically [111.0 (34.8) s, $P = 0.016$]. Intubating conditions of 20 patients were graded either excellent or good.
Conclusion Subjective evaluation of contractions of the MM by an anesthesiologist's hand may be reliable to determine faster timing for safe tracheal intubation.

Keywords Masseter muscle · Rocuronium · Neuromuscular block · Tracheal intubation

Introduction

The time course of neuromuscular block is generally evaluated at the adductor pollicis muscle (APM). However, the onset of neuromuscular block is much slower at the APM than at the larynx [1], diaphragm [2], and masseter muscle (MM) [3–5]. It is therefore suggested that neuromuscular block at the APM cannot ensure faster timing of tracheal intubation during rapid sequence induction. Intubating conditions should be evaluated by relaxation of the respiratory muscles, specifically by ease of laryngoscopy, vocal cord position, and patient's reaction to intubation [6]. However, direct measurements of neuromuscular block in the larynx and diaphragm are not easy in clinical anesthesia. We previously reported that disappearance of contractions of the MM could be felt subjectively and easily with an anesthesiologist's hand following an injection of vecuronium and could ensure safe and faster timing of tracheal intubation [5]. However, because the MM contractions were only sensed by an anesthesiologist's hand, it was undeniable that the results of the previous study might include some evaluator bias. A further objective study was warranted to establish reliability of the previous results. The main purpose of this study was to compare onset times

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Table 1 Evaluation of intubating conditions [7]

Variable assessed	Excellent	Good	Poor
Laryngoscopy	Easy	Fair	Difficult
Vocal cord position	Abducted	Intermediate/moving	Closed
Diaphragmatic movement or cough after tracheal intubation	None	Slight	Vigorous/sustained

Excellent all qualities are excellent, *good* all qualities are either excellent or good, *poor* the presence of a single quality listed under poor

of rocuronium at the MM evaluated by tactile means and acceleromyography and to determine whether subjective monitoring was useful to determine onset of rocuronium-induced neuromuscular block and allow faster tracheal intubation.

Materials and methods

After approval of the protocol by the Hospital Ethics Committee on Human Rights in Research, 40 adult female patients consented to participate in this study. Patients were ASA physical status I or II, 23–47 years of age, undergoing elective gynecological surgery. None of the patients had neuromuscular, hepatic, or renal disorders or were taking any drug known to interact with neuromuscular blocking agents. Patients whose body mass index (BMI) was $\geq$25 or $<$18.5 were also excluded from the study. Premedication consisted of orally administered ranitidine 150 mg before going to bed on the day before surgery and in the morning of the day of surgery. On arrival at the operating room, all patients were monitored with ECG, noninvasive blood pressure, and pulse oximetry. The first 20 patients were assigned to evaluate the onset of rocuronium-induced neuromuscular block at the MM and APM subjectively using peripheral nerve stimulators. Surface-stimulating electrodes were attached percutaneously on the left ulnar nerve at the wrist and the left masseter nerve at the space formed by the zygomatic arch superiorly the mandibular notch inferiorly, and two peripheral nerve stimulators (Innervator NS-252; Fisher & Paykel Electronics, Auckland, New Zealand) were used to separately stimulate the ulnar and masseter nerves [5]. General anesthesia was induced with fentanyl 2 μg/kg and propofol 2 mg/kg while patients received 100% oxygen through an anesthesia facemask. After loss of consciousness, the nerves were concurrently stimulated with square-wave stimuli of 0.2-ms duration, delivered in a train-of-four (TOF) mode at 2 Hz every 12 s. For the ulnar nerve, output current of 50 mA was applied; however, 30 mA was used to stimulate the masseter nerve to avoid stimulation of other facial muscles and direct stimulation of the MM [6]. Contractions of the MM were palpated with an anesthesiologist's left palm lifting the patient's jaw and holding an anesthesia facemask [5], and contractions of the APM was visually observed by another evaluator. Then, the patients received an i.v. bolus dose of rocuronium, 0.6 mg/kg. The onset time at the MM was defined as the duration until the contracting response of the MM was become impalpable, and that at the APM was defined as the duration until adduction of the thumb could not be visually observed. Immediately after the onset at the MM was confirmed, the patient's trachea was intubated with a 7.0-mm-ID endotracheal tube (Portex Tracheal Tube; Smiths Medical International, Kent, UK) and the intubating conditions (Table 1) [7] were assessed.

The next 20 patients were allocated to monitor rocuronium-induced neuromuscular block acceleromyographically. Anesthesia was induced with fentanyl 2 μg/kg and propofol 2 mg/kg, and laryngeal mask insertion was accomplished without aid of neuromuscular blocking agents. Anesthesia was maintained by a continuous infusion of propofol 4–5 mg/kg/h and intermittent administrations of fentanyl as required. After a stable depth of anesthesia was obtained, the left ulnar and masseter nerves were stimulated with square-wave stimuli of 0.2-ms duration, which was delivered in a TOF mode at 2 Hz every 15 s. The left ulnar nerve was stimulated at the supramaximal current (range, 40–50 mA); the unilateral facial nerve was stimulated at a current of 30 mA. Contraction of the ipsilateral MM (Fig. 1) or APM was measured using an acceleromyograph (TOF-Watch SX; Organon, Dublin, Ireland). A transducer was attached percutaneously on the masseter adherent to the mandible and the volar aspect of the thumb at the interpharyngeal joint. After the control TOF stimuli were administered for a minimum of 10 min to stabilize the TOF responses [8], all the patients received rocuronium 0.6 mg/kg i.v., and onset of the action was recorded. Onset time was defined from the administration of rocuronium to maximum depression of the first twitch (T_1) of the TOF. Times from administration of rocuronium to spontaneous recovery of T_1 to 10% of the control value were observed.

The sample size was calculated based on the preliminary data on an averaged onset time of rocuronium 0.6 mg/kg observed at the MM (75 $\pm$ 12 s). We considered a 20% difference (>15 s) in the onset times measured by tactile and acceleromyographical means at the MM to be clinically different. To obtain statistically significant results with $\alpha = 0.05$ and a power of 0.9, it was necessary that

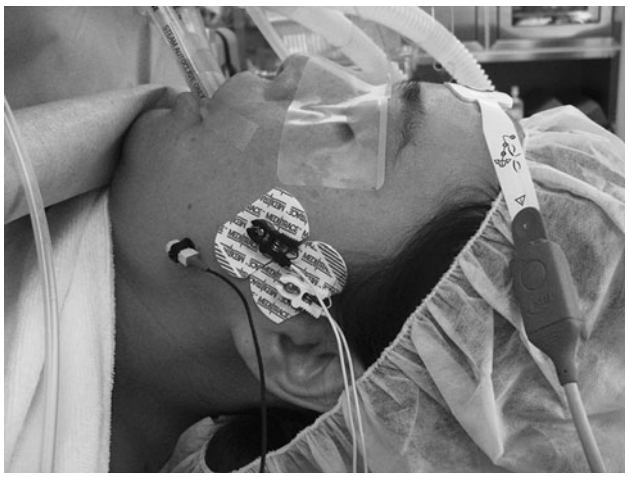

Fig. 1 Placement of surface electrodes stimulating the masseter nerve and an acceleration transducer measuring the contraction of the masseter muscle

15 patients should be included in this study. Allowing for dropouts from the study, we finally enrolled 20 patients. Data are presented as mean (SD). Statistical analysis was performed using StatView software for Windows (SAS Institute, Cary, NC, USA). The unpaired Student *t* test was used for two group comparisons. A P value <0.05 was considered statistically significant.

Results

Data from all 40 patients could be included in the analyses. No differences were found in patient characteristics between the groups (Table 2). There was no difference between the onset times of rocuronium observed subjectively and acceleromyographically at both MM and APM (Table 3). Onset of the action of rocuronium obtained at the MM was significantly faster than those at the APM (Table 3). When evaluating the rocuronium-induced neuromuscular block subjectively, the intubating condition was graded excellent in 12 patients and good in 8 patients; none of the patients had poor intubating condition. In the group AMG, the time from an administration of rocuronium to spontaneously recover to 10% of control of T_1 was significantly shorter in the MM [25.4 (8.2) min, $P = 0.045$] than the APM [34.6 (10.8)].

Table 2 Patient characteristics

Characteristic	Subjective evaluation	Acceleromyography
Age (years)	39.2 (7.1)	41.1 (8.4)
Weight (kg)	51.0 (7.3)	53.4 (6.0)
Height (cm)	156.0 (4.7)	156.9 (5.4)

Data are presented as mean (SD); no significant differences were seen between the groups

Table 3 Onset of the action of rocuronium 0.6 mg/kg

Location	Subjective evaluation	Acceleromyography
Masseter	70.3 (17.7)*	73.3 (27.6)#
Adductor pollicis	143.3 (29.5)	111.0 (34.8)

Data are presented as mean (SD); no significant differences were seen between the groups

* $P < 0.0001$ when compared between the muscles

$P = 0.016$ when compared between the muscles

Discussion

This study demonstrated that the onset time of rocuronium-induced neuromuscular block evaluated subjectively did not differ from that monitored acceleromyographically at the MM. Intubating conditions when contractions of the MM had not been felt by an evaluator's hand were all graded as clinically acceptable conditions. Based on the results of this study, it is likely that subjective evaluation of contractions of the MM during the masseter nerve stimulation is a reliable method to know the onset of rocuronium-induced neuromuscular block and enable faster and safe tracheal intubation. Particularly in a patient with a full stomach, monitoring of the MM contraction during rapid sequence induction may be useful to hasten the timing of tracheal intubation and decrease the risk of pulmonary aspiration.

Previous studies [3, 4] revealed that the onset of rocuronium-induced neuromuscular block occurred significantly faster at the MM than at the APM. Unfortunately, the acceleromyographic monitoring was performed in such studies during a steady state of general anesthesia after laryngeal mask insertion [3] or tracheal intubation [4]. It was true that the results of the previous studies could provide some meaningful information about pharmacodynamic differences of rocuronium between the MM and APM. However, the studies were not really sufficient to apply the acceleromyography at the MM in the clinical setting. The important characteristic of rapid onset of paralysis at the MM should be utilized during induction of general anesthesia to assess the optimal timing for tracheal intubation; however, it is hard to monitor the MM objectively because an acceleration transducer cannot correctly assess the jaw movement during mask-to-face ventilation. Consequently, to perform MM monitoring in the clinical setting, we palpated contractions of the MM evoked by a simple peripheral nerve stimulator during mask ventilation, and subjectively assessed the onset of paralysis based on the disappearance of contractions [5]. Concern was greatest

for some bias of the evaluator in the previous study, but it is deniable because the onset times of rocuronium evaluated subjectively and acceleromyographically were similar. This procedure was proven to be of clinical use for determining the earliest suitable time at which laryngoscopy and tracheal intubation could be performed.

Our study has a limitation that must be acknowledged. Ideally, the TOF stimuli should be delivered in the same stimulation frequency when the onset times of neuromuscular block would be compared because a faster stimulation frequency greatly increases blood flow to the monitored muscle and should produce a shorter equilibration of rocuronium [9]. Therefore, the onset of the action of rocuronium observed subjectively might cause minor delays if the nerves were stimulated every 15 s.

Paralysis of the MM was significantly faster than that of the APM. The faster onset of the action of rocuronium at the MM may be caused by the large volume of blood flow to the centrally located muscles [3] and the faster transfer rate of neuromuscular blocking drugs between the plasma and the neuromuscular junction [10]. The shorter duration of action of rocuronium measured at the MM may also result from greater perfusion and more rapid washout of rocuronium, when compared to the APM [11].

In the present study, we did not assign the patients randomly, and at first evaluated the onset time of rocuronium subjectively. If the acceleromyographical study were to be done first, it is likely that the results might be prejudicial for an evaluator and influence the onset time subjectively evaluated from diminishing contractions of the MM.

In conclusion, tactile assessment of muscle paralysis of the MM after administration of rocuronium enables faster tracheal intubation and may improve patient safety.

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References

1. 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;39:665–9.
2. Cantineau JP, Porte F, d'Honneur G, Duvaldestin P. Neuromuscular effects of rocuronium on the diaphragm and adductor pollicis muscles in anesthetized patients. Anesthesiology. 1994;81:585–90.
3. De Mey JC, De Baerdemaeker L, De Latt M, Rolly G. The onset of neuromuscular block at the masseter muscle as a predictor of optimal intubating conditions with rocuronium. Eur J Anaesth. 1999;16:387–9.
4. de Rossi L, Preußler NP, Pühringer FK, Klein U. Onset of neuromuscular block at the masseter and adductor pollicis muscles following rocuronium or succinylcholine. Can J Anaesth. 1999;46:1133–7.
5. Kitajima O, Suzuki T, Watanabe N, Maeda T, Noda Y, Saeki S, Ogawa S. Monitoring masseter muscle evoked responses enables faster tracheal intubation. J Anesth. 2010;24:173–6.
6. Hemmerling TM, Donati F. Neuromuscular blockade at the larynx, the diaphragm and the corrugator supercilli muscle: a review. Can J Anaesth. 2003;50:779–94.
7. Fuchs-Buder T, Claudius C, Skovgaard LT, Eriksson LI, Mirakhur RK, Viby-Mogensen J. Good clinical research practice in pharmacodynamic studies of neuromuscular blocking agents II: the Stockholm revision. Acta Anaesthesiol Scand. 2007;51:789–808.
8. Suzuki T, Fukano N, Kitajima O, Saeki S, Ogawa S. Normalization of acceleromyographic train-of-four ratio by baseline value for detecting residual neuromuscular block. Br J Anaesth. 2006;96:44–7.
9. Meretoja OA, Taivainen T, Brandom BW, Wirtavuori K. Frequency of train-of-four stimulation influences neuromuscular responses. Br J Anaesth. 1994;72:686–7.
10. Plaud B, Proost JH, Wierda MKH, Barre J, Debaene B, Meistelman C. Pharmacokinetics and pharmacodynamics of rocuronium at the vocal cords and the adductor pollicis in humans. Clin Pharmacol Ther. 1995;58:185–91.
11. Bragg P, Fisher DM, Shi J, Donati F, Meistelman C, Lau M, Sheiner LB. Comparison of twitch depression of the adductor pollicis and the respiratory muscles. Pharmacodynamic modeling without plasma concentrations. Anesthesiology. 1994;80:310–9.