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ORIGINAL ARTICLE

Assessment of neuromuscular block at the orbicularis oris, corrugator supercilii, and adductor pollicis muscles

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Abstract
Purpose We studied neuromuscular block at the orbicularis oris, corrugator supercilii, and adductor pollicis muscles in anesthetized patients.
Methods Fifty-four adult patients undergoing air–oxygen–sevoflurane–fentanyl and epidural anesthesia were randomly divided into orbicularis oris, corrugator supercilii, and adductor pollicis groups of 18 patients each. In the three groups, the degree of neuromuscular block caused by rocuronium 0.6 mg/kg was monitored at the orbicularis oris, corrugator supercilii, and adductor pollicis muscles acceleromyographically.
Results Onset of neuromuscular block did not significantly differ among the three groups [157 ± 60, 186 ± 73, and 148 ± 45 s; mean ± standard deviation (SD)]. Minimum value of 1st stimulation in train-of-four (T1)/control at the corrugator supercilii group was significantly higher than in the orbicularis oris and adductor pollicis groups (0.108 ± 0.066 vs. 0.021 ± 0.024 and 0.002 ± 0.007; $P < 0.001$). T1/control at the orbicularis oris group was significantly higher than at the adductor pollicis group 30 min after rocuronium ($P < 0.05$). T1/control at the corrugator supercilii group was significantly higher than at the orbicularis oris and adductor pollicis groups 10–30 and 10–40 min, respectively, after rocuronium ($P < 0.05$). Train-of-four ratios at the orbicularis oris and corrugator supercilii groups were significantly higher than at the adductor pollicis group 40–120 min after rocuronium ($P < 0.05$).
Conclusion The corrugator supercilii muscle is more resistant to rocuronium than the orbicularis oris and adductor pollicis muscles. Recovery of neuromuscular block at the orbicularis oris muscle is slower than that at the corrugator supercilii muscle but was faster than that at the adductor pollicis muscle.

Keywords Orbicularis oris muscle · Corrugator supercilii muscle · Adductor pollicis muscle · Rocuronium

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Introduction

The level of neuromuscular block can be evaluated at the corrugator supercilii (CS) muscle. Monitoring neuromuscular block at the CS muscle is useful to detect a profound degree of neuromuscular block [1–4]. However, when the depth of neuromuscular block is assessed at the CS muscle by acceleromyography, concomitant monitoring of the orbicularis oculi and production of a mixed signal cannot be avoided [1–3]. Additionally, a probe for monitoring the degree of hypnosis, i.e., bispectral index or entropy, is

routinely attached to the patient's forehead. As the probe occupies a large part of the forehead, in the clinical settings, neuromuscular block monitoring at the CS muscle may be difficult. We felt there should be a facial muscle other than the CS muscle suitable for neuromuscular block monitoring and subsequently compared acceleromyographic monitoring at the orbicularis oris (OO) muscle and electromyographic evaluation at the adductor pollicis (AP) muscle after administration of vecuronium. We found that neuromuscular block recovery at the OO muscle is faster than at the AP muscle [5]. However, acceleromyographic assessment of neuromuscular block following rocuronium administration at the OO muscle had not yet been compared with that at the CS and AP muscles. Therefore, using acceleromyographic monitoring, we compared the degree of neuromuscular block at the OO, CS, and AP muscles in anesthetized patients receiving rocuronium.

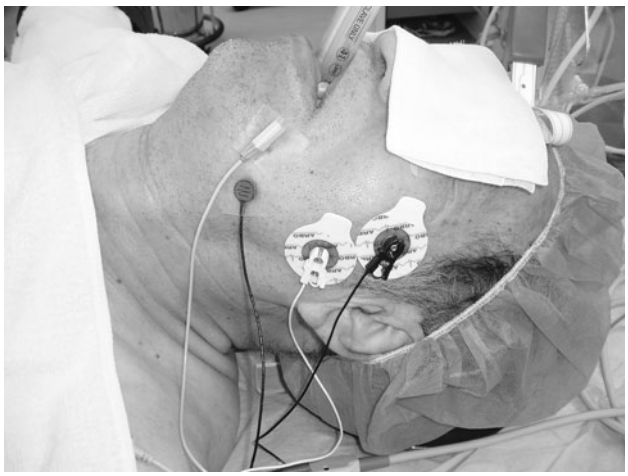

Fig. 1 Two surface-stimulating electrodes attached over the buccal branches and marginal mandibular branch of the facial nerve. An acceleromyographic transducer and a surface thermometer probe were placed over the orbicularis oris muscle

Methods

The ethics committee of Tsujinaka Hospital Kashiwanoha approved the protocol of this open-label, randomized controlled trial, and all patients gave their written informed consent. Study participants consisted of 54 adults, American Society of Anesthesiologists Physical Status (ASA PS) classification 1 or 2 who were scheduled for elective colonic surgery under general combined with epidural anesthesia. The sealed envelope method (serially numbered, externally generated random numbers) was used to randomly allocate 54 patients (18 per group) to the OO, CS, or AP groups. No patient was taking any drug known to affect the action of neuromuscular relaxant or had neuromuscular, cardiac, hepatic, renal, or metabolic disorders. Assuming an α of 5% and with 90% power, a sample size of 18 patients per group was necessary to detect a difference $\geq$0.2 in the mean T1 [1st stimulation in train-of-four (TOF))/control or TOF ratio (T4/T1)], with a standard deviation (SD) of approximately 0.2 [6]. Thus, 54 patients were enrolled. No patient received premedication. Once in the operating theater, patients received an epidural catheter placed through the T10/11 intervertebral space to provide a test dose of 60 mg lidocaine 2% (3 ml) and a continuous infusion of lidocaine 2% at a rate of 6–8 ml/h.

In the OO group, about 2 cm anterior to the left ear lobe, two surface-stimulating electrodes were attached and an acceleromyographic transducer was placed approximately 1.5 cm infero-lateral to the left oral angle (Fig. 1). The cathode was placed under the zygomatic arch, and the anode was placed superiorly to the mandible angle to stimulate the buccal and marginal mandibular branches, respectively, of the facial nerve. This method is in accordance with that in our previous study [5]. A neuromuscular

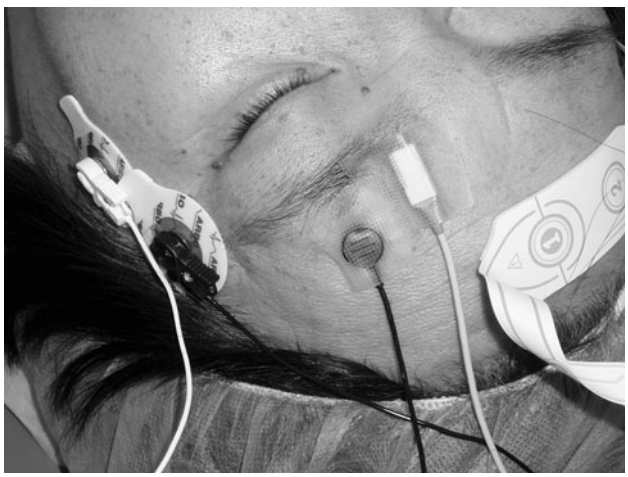

Fig. 2 Two surface-stimulating electrodes placed over the external part of the left supercilii arch, and an acceleromyographic transducer attached at the internal half of the supercilii arch for the corrugator supercilii

transmission monitor (TOF watch SX, Schering–Plough Corporation, Kenilworth, NJ, USA) was connected to the stimulating electrodes and an acceleromyographic transducer. In the CS group, two surface-stimulating electrodes were placed over the external part of the left supercilii arch, and an acceleromyographic transducer was placed at the internal half of the supercilii arch, using adhesive tape, for the corrugator supercilii (Fig. 2). An entropy probe (GE-Healthcare Inc. Tokyo, Japan) was attached to the forehead. In the CS group, the entropy probe was placed over the center or right side of the forehead and right temple. The left part of the entropy probe was at least 3 cm apart from the acceleromyographic transducer. In the AP group, two stimulating electrodes were positioned over the ulnar

nerve at the wrist, and an acceleromyographic transducer was attached to the volar aspect of the thumb.

In all patients, propofol 2.5 mg/kg and fentanyl 2 μg/kg were used to induce anesthesia. After insertion of a laryngeal mask airway (LMA), the lungs were ventilated with air 3 L/min, oxygen 1 L/min, and sevoflurane 1.7% of end-tidal concentration. LMA # 5 and 4 were used in male and female patients, respectively, and the lungs were ventilated to maintain normocapnia [partial pressure of end-tidal carbon dioxide pressure ($P_{ET}CO_2$) 4.4–4.9 kPa). During anesthesia induction, nerve stimulation was started after loss of the eyelash reflex was confirmed. At first, the supramaximal stimulating current was determined. Single-twitch stimuli of 0.2 ms duration square-waves were delivered at 1 Hz, stimuli were started at 60 mA, and the stimulating current was decreased in 5-mA decrements (60, 55, 50, 45,..., 20 mA). In response to the single-twitch stimuli, when a decrease ≥10% or more was detected in the acceleromyographic transducer signal, the current at which the supramaximal muscular response could be elicited was defined as the stimulation current for the previous stimulation. The supramaximal stimulating current was regarded as the level that was a 10% increase above the level that yielded supramaximal response. Thereafter, TOF stimuli at that current level were applied every 15 s.

In the three groups, if movement was too small to obtain sufficient acceleromyographic control values in response to nerve stimuli, the monitoring device (TOF watch SX®) indicated an error message. In such cases, we first removed the acceleromyographic transducer and carefully observed OO muscle, CS muscle, and thumb movements in the OO, CS, and AP groups, respectively, and then reattached the transducer to make the plane of the transducer perpendicular to muscles or thumb movements. Once the supramaximal stimulating current had been established, TOF stimuli were applied every 15 s at that current level. Four single-twitch stimuli consisting of 0.2-ms duration square-waves were delivered at 2 Hz. The corresponding acceleromyographic responses were evaluated. After baseline stabilization for 10 min, the supplied current was recalibrated and adjusted to produce supramaximal stimulation. Acceleromyographic control value was again determined, as recommended previously [7]. Thereafter, rocuronium 0.6 mg/kg was administered intravenously.

After rocuronium, TOF stimuli were continuously applied every 15 s. Times from rocuronium to the onset of neuromuscular block were compared among the three groups. The time when the T1/control decreased to the minimum value was regarded as the neuromuscular block onset. The minimum T1/control values were compared among groups. After neuromuscular block onset was determined, TOF stimuli were continuously applied every 15 s. T1/control and TOF ratio (T4/T1) were recorded every 10 min after rocuronium. In this way, T1/control or TOF ratios were compared every 10 min among groups. Anesthesia was maintained with air 3 L/min, oxygen 1 L/min, sevoflurane 1.7% end-tidal concentration, and continuous administration of 2% lidocaine via the epidural catheter. A bolus dose of fentanyl 2 μg/kg was administered as required. Esophageal and surface skin temperatures over the OO, CS, or AP muscle were measured. After the surgical procedure, if the TOF ratios were <1.0, a bolus dose of sugammadex 2 mg/kg was given intravenously to antagonize the residual neuromuscular block.

Patient data anesthesia or surgical procedure duration were compared among groups using analysis of variance (ANOVA) and Scheffe's multiple comparison or chi-square test. Supramaximal stimulating currents, times to neuromuscular block onset, and minimum T1/control values were compared among the three groups using ANOVA and Scheffe's multiple comparison. ANOVA and unpaired *t* tests with Bonferroni's adjustment were used to compare the T1/control or TOF ratio during recovery from neuromuscular block among groups. All results are expressed as mean ± SD or number. Statistical significance was set $P < 0.05$. A statistical package (SPSS PASW statistics 18, IBM Inc.) was used to perform analyses.

Results

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

In two, four, and zero patients in the OO, CS, and AP groups, respectively, the control acceleromyographic value could not be determined the first time; however, once the

Table 1 Characteristics of the patients in whom the degree of neuromuscular block was assessed at the orbicularis oris, corrugator supercilii, or adductor pollicis muscle

	Orbicularis oris ($n = 18$)	Corrugator supercilii ($n = 18$)	Adductor pollicis ($n = 18$)
Sex (female/male)	6/12	7/11	8/10
Age (years)	69.7 ± 10.9	67.4 ± 10.2	63.1 ± 12.8
Height (cm)	162.1 ± 8.1	159.9 ± 8.0	159.9 ± 11.1
Weight (kg)	56.3 ± 11.9	57.4 ± 9.2	53.5 ± 8.2
ASA PS (1/2)	8/10	9/9	12/6
Duration of anesthesia (min)	267 ± 89	241 ± 84	214 ± 85
Duration of surgery (min)	221 ± 86	176 ± 82	158 ± 77

Sex, age, height, weight, ASA physical status, and operative time did not significantly differ among groups. Values are mean ± standard deviation or number

ASA American Society of Anesthesiologists, *PS* physical status

Table 2 Supramaximal stimulating current, onset of neuromuscular block, and minimum value of T1/control after administration of rocuronium 0.6 mg/kg at the orbicularis oris, corrugator supercilii, or adductor pollicis muscle

	Orbicularis oris ($n = 18$)	Corrugator supercilii ($n = 18$)	Adductor pollicis ($n = 18$)
Supramaximal stimulating current (mA)	55.7 ± 7.8	56.0 ± 6.9	43.7 ± 12.3*
Onset of neuromuscular block (s)	157 ± 60	186 ± 73	148 ± 45
Minimum value of T1/control	0.021 ± 0.024	0.108 ± 0.066**	0.002 ± 0.007

Values are mean ± standard deviation

* $P = 0.001$ compared with orbicularis oris and corrugator supercilii muscles

** $P < 0.001$ compared with orbicularis oris and adductor pollicis muscles

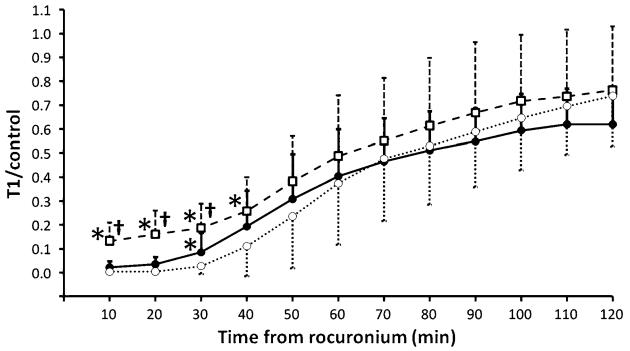

Fig. 3 Recoveries of 1st stimulation in train-of-four (T1)/control after rocuronium 0.6 mg/kg administration in the OO (*filled circles*), CS (*open squares*), and AP (*open circles*) groups. Values are mean ± standard deviation. $^{\dagger}P < 0.05$ compared with OO group. $^{*}P < 0.05$ compared with AP group. *OO* orbicularis oris, *CS* corrugator supercilii, *AP* adductor pollicis

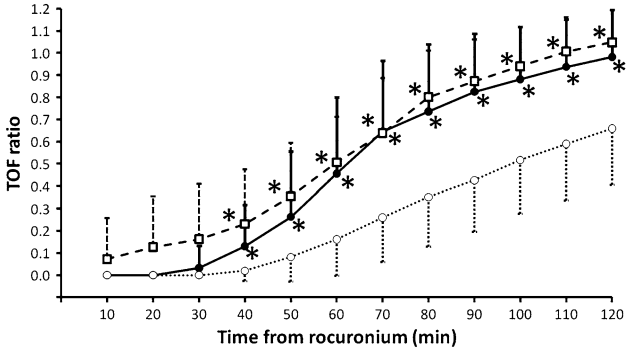

Fig. 4 Recoveries of train-of-four (TOF) ratio after rocuronium 0.6 mg/kg administration in the OO (*filled circles*), CS (*open squares*), and AP (*open circles*) groups. Values are mean ± standard deviation. $^{*}P < 0.05$ compared with AP group. *OO* orbicularis oris, *CS* corrugator supercilii, *AP* adductor pollicis

acceleromyographic transducer was repositioned, the control value was accurately determined. The number of patients in whom the control value could not be obtained the first time did not significantly differ among groups. As shown in Table 2, the supramaximal stimulating current in the OO or CS group was significantly higher than that in the AP group ($P = 0.001$). Onset of rocuronium 0.6 mg/kg-induced neuromuscular block did not significantly differ among groups. The minimum value of T1/control in the CS group was significantly higher than that in the OO or AP group ($P < 0.001$).

T1/control in the OO group was significantly higher than in the AP group 30 min after rocuronium ($P < 0.05$). T1/control in the CS group was significantly higher than in the OO and AP groups 10–30 and 10–40 min, respectively, after rocuronium ($P < 0.05$) (Fig. 3). TOF ratio in the OO or CS group was higher than in the AP group 40–120 min after rocuronium ($P < 0.05$) (Fig. 4).

At surgical procedure termination, TOF ratios were <1.0 in two, one, and ten patients in the OO, CS, and AP groups, respectively. In these patients, sugammadex 2 mg/kg was given. Within 3 min after sugammadex administration, TOF ratio recovered to a value >1.0 in all cases, and the final values of T1/control were 0.60–1.42, 0.63–0.93, and 0.74–1.16 in the OO, CS, and AP groups, respectively.

The esophageal and peripheral temperatures did not decrease to <35.5 and 32.0°C, respectively, in any patient. In seven, eight, and six patients in the OO, CS, and AP groups, respectively, systolic arterial pressure decreased to <90 mmHg more than once, which returned to a value of >100 mmHg immediately after administration of ephedrine 0.1 mg/kg. In no patient did systolic arterial pressure increase >180 mmHg. Response and state entropy were maintained between 40 and 60 during the surgical procedure in all patients.

Discussion

We compared acceleromyographic monitoring of neuromuscular block at the OO, CS, and AP muscles in anesthetized patients receiving rocuronium. The supramaximal stimulating current is higher at the OO or CS muscle than that at the AP muscle. Onset times of rocuronium 0.6 mg/kg-induced neuromuscular block do not differ among the three muscles. The minimum value of T1/control at the CS muscle is higher than that at the OO or AP muscle. T1/control at the OO muscle was higher than at the AP muscle

30 min after rocuronium. T1/control at the CS muscle was higher than at the OO and AP muscles 10–30 and 10–40 min, respectively, after rocuronium. TOF ratio at the OO or CS muscle was higher than at the AP muscle 40–120 min after rocuronium.

It is a gold standard for anesthetists to evaluate the degree of neuromuscular block at the AP muscle or thumb. Nevertheless, the upper limbs of the anesthetized patients are commonly covered by a surgical drape, which prevents movement of the patient's thumb. Moreover, the patient's arms sometimes lie alongside the trunk during a surgical procedure. Therefore, it may also be difficult to measure the depth of neuromuscular block at the AP muscle acceleromyographically. The level of neuromuscular block is often assessed at the CS muscle [1–4]. However, the CS muscle is too small to accurately evaluate the degree of neuromuscular block [1–3]. We propose that monitoring neuromuscular block at the OO muscle is of clinical value. Our study demonstrates that the control acceleromyographic value could not be obtained at the first recording in four patients in the CS and two in the OO group. Thus, not only at the CS muscle but also at the OO muscle, control value determination is thought to be difficult. In the clinical settings, if the control value cannot be determined at the CS muscle at the induction of general anesthesia, it might be of clinical use to switch from neuromuscular block monitoring at the CS muscle to that at the OO muscle.

Kopman et al. [8] reported that when the degree of neuromuscular block is assessed at the AP muscle, a 30 mA current can produce supramaximal nerve stimulation in a majority of patients. In contrast, in this study, the mean supramaximal stimulating current at the AP muscle was as high as 43.7 mA. Kopman et al. [8] studied the supramaximal stimulating current mechanically using a force transducer. However, in our study, the current was determined acceleromyographically. Moreover, as noted in the "Methods" section, once the necessary current strength had been determined, it was increased by 10% automatically, which was regarded as the actual current. Therefore, in this study, the supramaximal stimulating current would have been overestimated. In addition, mean currents at the OO and CS muscles were still higher than at the AP muscle, i.e., 55.7 and 56.0 mA, respectively. Larsen et al. [9] and Gätke et al. [10] showed that a mean current of 55 mA produced supramaximal contraction of the orbicularis oculi muscle and was between 45 mA and >60 mA, respectively. We also show that the current at the OO muscle is as high as 55.3 mA [5]. Thus, a higher current is thought to be necessary to elicit maximal facial muscle contractions.

In this study, onset of rocuronium 0.6 mg/kg-induced neuromuscular block did not differ among the three muscles. Plaud et al. [2] reported onset of the block induced by rocuronium 0.5 mg/kg at the CS or orbicularis oculi muscle was slower than that at the AP muscle. We previously reported that onset using vecuronium 0.1 mg/kg at the OO muscle was significantly faster than that in the AP muscle [5]. Onset times at different muscles have not yet been clarified.

In this study, after rocuronium 0.6 mg/kg administration, the minimum T1/control value at the CS muscle was higher than that at the OO or AP muscle. The mean minimum values were 0.108 and 0.002 at the CS and AP muscles, respectively. Plaud et al. [2] showed similar results. Additionally, this study demonstrated that the mean minimum T1/control values were 0.021 and 0.002 at the OO and AP muscles, respectively. These results were also comparable with those in our previous study, which examined the minimum value of T1/control after vecuronium 0.1 mg/kg [5]. Hence, the difference in sensitivity to neuromuscular blocking agents might be trivial at the OO and AP muscles.

Previous studies show that recovery from neuromuscular block evaluated at the CS is faster than that at the AP muscle [1–4]. Also in this study, T1/control in the CS group was higher than that in the OO and AP groups 10–30 and 10–40 min, respectively, after rocuronium 0.6 mg/kg administration. T1/control in the OO group was higher than in the AP group 30 min after rocuronium. TOF ratio in the OO or CS group was higher than that in the AP group 40–120 min after rocuronium 0.6 mg/kg. Based on these findings, we presume that the recovery of T1/control at the OO muscle is slower than that at the CS muscle, but faster than that at the AP muscle. In contrast, the recoveries of TOF ratio at the OO and CS muscles follow similar time course, and are faster than that at the AP muscle. In other words, this study revealed that significant differences in T1/control among the different muscles were observed 10–40 min after administration of rocuronium, but those in TOF ratio 40–120 min after rocuronium. It has been reported that T1/control represent neuromuscular block at the post-junctional region of the neuromuscular junction, while TOF ratio is related to neuromuscular block at the pre-junctional region [11]. From this viewpoint, the difference in the degree of neuromuscular block at the post-junctional region may be apparent when the level of neuromuscular block is profound, and that at the pre-junctional region is thought to become marked as the level of neuromuscular block subsides.

In the OO group, the acceleromyographic transducer was attached near the oral angle, so it is unlikely that movement was caused by OO muscle contraction only, as the masseter muscle contraction probably would have affected oral angle movement. Strictly speaking, it may be that OO muscle movement was not monitored but that of the mandible.

At the termination of the surgical procedure, TOF ratios were <1.0 in two, one, and ten patients in the OO, CS, and AP groups, respectively. In these patients, sugammadex 2 mg/kg was given. Within 3 min of its administration, TOF ratio had recovered to >1.0 in all cases. Conversely, final T1/control values were 0.60–1.42, 0.63–0.93, and 0.74–1.16 in the OO, CS, and AP groups, respectively. Thus, final T1/control values after sugammadex varied most apparently at the OO muscle. We cannot explain these results clearly. However, it may be difficult to determine precise T1/control values at the OO muscle before rocuronium administration, as rocuronium causes a wide variation in the final T1/control at the OO muscle.

In this study, we used sevoflurane 1.7%, which was almost equal to 1 minimum alveolar concentration (MAC) of sevoflurane, to maintain general anesthesia in all patients. It is well known that the advance of a patient's age decreases sevoflurane MAC [12, 13], and thus, we should have changed sevoflurane dosage according to the patients' age.

In conclusion, assessing neuromuscular block level can be performed at the OO muscle. Compared with the AP muscle, a higher supramaximal stimulating current is needed for TOF monitoring at the OO or CS muscle. Among the OO, CS, and AP muscles, onset times of rocuronium-induced neuromuscular block do not differ. Compared with the value at the OO or AP muscle, the minimum value of T1/control at the CS muscle is higher. In regard to that in the CS muscle, T1/control recovery at the OO muscle is slower, but it is faster than that in the AP muscle. Compared with the TOF ratio at the AP muscle, T1/control recovery at the OO or CS muscle is faster.

Conflict of interest This study was funded by The Japan Society for Clinical Anesthesia.

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