Residual Paralysis at the Time of Tracheal Extubation

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Respiratory and pharyngeal muscle function are impaired during minimal neuromuscular blockade. Tracheal extubation in the presence of residual paresis may contribute to adverse respiratory events. In this investigation, we assessed the incidence and severity of residual neuromuscular block at the time of tracheal extubation. One-hundred-twenty patients presenting for gynecologic or general surgical procedures were enrolled. Neuromuscular blockade was maintained with rocuronium (visual train-of-four [TOF] count of 2) and all subjects were reversed with neostigmine at a TOF count of 2–4. TOF ratios were quantified using acceleromyography immediately before tracheal extubation, after clinicians had determined that complete neuromuscular recovery had occurred using standard clinical criteria (5-s head lift or hand grip, eye opening on command, acceptable negative inspiratory force or vital capacity breath values) and peripheral nerve stimulation (no evidence of fade with TOF or tetanic stimulation). TOF ratios were measured again on arrival to the postanesthesia care unit. Immediately before tracheal extubation, the mean TOF ratio was 0.67 ± 0.2; among the 120 patients, 70 (58%) had a TOF ratio <0.7 and 105 (88%) had a TOF ratio <0.9. Significantly fewer patients had TOF ratios <0.7 (9 subjects, 8%) and <0.9 (38 subjects, 32%) in the postanesthesia care unit compared with the operating room ($P < 0.001$). Our results suggest that complete recovery from neuromuscular blockade is rarely present at the time of tracheal extubation.

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Undetected residual neuromuscular blockade is common in the postanesthesia care unit (PACU). In fact, 16%–42% of patients receiving intermediate-acting muscle relaxants in the operating room (OR) have train-of-four (TOF) ratios <0.7–0.8 in the PACU (1–3). These findings suggest that anesthesia care providers are unable to reliably detect residual neuromuscular block in the OR using standard clinical criteria.

Respiratory and pharyngeal muscle function can be adversely affected during minimal neuromuscular blockade. Studies in awake volunteers and surgical patients have demonstrated that TOF ratios of 0.7–0.9 are associated with impaired airway protective reflexes (4), upper airway obstruction (5), a decreased hypoxic ventilatory response (6), and postoperative hypoxemia (7). On the basis of these findings, several investigators have recommended that full recovery of neuromuscular function (TOF ratio of ≥0.9) should be present at the time of tracheal extubation (3,5,8). Because clinical tests are insensitive in detecting TOF ratios between 0.5–1.0, quantitative neuromuscular monitoring is required to exclude the presence of residual paresis. Debaene et al. (3) recently stated that "quantitative assessment of TOF ratios is mandatory at the end of the surgical procedure" and that "this measurement needs to be performed in the operating room. . .before extubating the trachea." No previous studies have examined the incidence and severity of residual neuromuscular block at the time of tracheal extubation. The aim of the present investigation was to assess TOF ratios immediately before tracheal extubation, when clinicians had determined that full recovery of neuromuscular function had occurred using standard clinical criteria. In addition, all subjects were examined in the PACU to determine whether supramaximal nerve stimulation was recalled as painful when performed in the immediate recovery period.

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Methods

The research protocol was approved by the Evanston Northwestern Healthcare IRB, and informed consent was obtained from all subjects. One-hundred-twenty ASA physical status I or II patients scheduled for

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elective gynecologic or general surgical procedures, between the ages of 18 and 69 yr, were enrolled in the study. Exclusion criteria included: 1) presence of neuromuscular, hepatic, or renal disease, 2) body mass >30% more than ideal body weight, 3) expected procedure duration <60 min, 4) anticipated difficult ventilation or endotracheal intubation, and 5) receiving drugs known to interfere with neuromuscular transmission.

Patients were premedicated with IV midazolam, 1–2 mg. Anesthesia was induced with propofol 1.5–2.5 mg/kg and fentanyl 100 μg/kg and maintained with sevoflurane 0.5%–3.5% in an air/oxygen mixture. Ventilation was controlled to maintain end-tidal carbon dioxide between 30–34 mm Hg. Approximately 1–2 μg/kg fentanyl was administered each hour for the duration of the surgical procedure. All patients received rocuronium 0.6–0.8 mg/kg for tracheal intubation. Anesthesia care providers were instructed to maintain a degree of muscle relaxation using a standard peripheral nerve stimulator such that two responses to TOF stimulation would be visible at the thumb after supramaximal stimulation of the ulnar nerve. Maintenance doses of 5–10 mg of rocuronium were administered to achieve this goal. No muscle relaxants were provided during the last 20–30 min of the surgical procedure. An upper extremity forced-air warming device (Bair Hugger, Eden Prairie, MN) was placed on all study patients to maintain core temperatures >35°C and arm temperature >32°C.

When the surgical procedure was completed, sevoflurane was discontinued and neuromuscular blockade was reversed with neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg. Reversal was not attempted until at least two responses to TOF stimulation were visible. Clinicians were instructed to assess patients for adequacy of neuromuscular reversal using standard clinical criteria recommended in our department (5-s head lift or hand grip, eye opening on command, negative inspiratory force more than −20 cm H_2O, or vital capacity breath >15 cc/kg) and peripheral nerve stimulation (no evidence of fade with TOF or tetanic stimulation [50 Hz]). A 5-s head lift (or hand grip) and the observation of an absence of fade with peripheral nerve stimulation were the minimal requirements; all other tests of residual paresis were at the discretion of the managing clinicians. Other criteria for tracheal extubation included acceptable spontaneous ventilation, evidence of adequate oxygenation and ventilation, and ability to respond to verbal commands. When the anesthesia care providers determined that full recovery of neuromuscular function was present, and that tracheal extubation could be performed, TOF ratios were measured by a research assistant blinded to intraoperative anesthetic management using an acceleromyography device (see below). Clinicians were instructed by the blinded research assistant to delay tracheal extubation for "several minutes" if significant muscle weakness was present (TOF ratio <0.6–0.7).

Immediately before tracheal extubation, TOF ratios were measured using acceleromyography (TOF-Watch; Organon, Inc., Dublin, Ireland). An acceleration transducer was taped to the distal interphalangeal joint of the thumb, and the study arm immobilized with a splint. The study arm was positioned to allow free movement of the thumb; no preload was attached to the thumb. Supramaximal (50 mA) square-wave TOF stimulation was delivered to the ulnar nerve via surface electrodes. Two consecutive TOF measurements (separated by 15 s) were obtained, and the average of the 2 values was recorded. If measurements differed by >10%, additional TOF measurements were obtained (up to 4 TOF values), and the closest 2 ratios were averaged. On arrival to the PACU, a second set of TOF ratios was measured as described above. The time intervals between neostigmine administration, tracheal extubation, and TOF measurements were recorded. Two TOF ratio threshold values were used to define the presence of residual neuromuscular block: <0.7 and <0.9. All TOF measurements were obtained by a research assistant not involved in clinical care.

Patients were instructed in the use of a 100-mm visual analog scale (VAS) score (from 0 mm = no pain to 100 mm = worst pain imaginable) in the preoperative holding area. Before discharge from the PACU, all subjects were asked directly, by a research assistant, about any recall of pain during TOF measurements in either the OR or the PACU. Patients who remembered ulnar nerve stimulation during the immediate recovery period were instructed to quantify discomfort using the VAS.

Data are reported as the number of patients, median and range, or mean ± SD. The proportions of subjects having TOF ratios less than, more than, or equal to the predefined threshold values in the OR and the PACU were analyzed using McNemar's test. Correlations between the presence or absence of severe residual paresis and patient demographic and intraoperative variables were sought using multiple logistic regression analysis. The criterion for rejection of the null hypothesis was $P < 0.05$.

Results

There was an uneven distribution of subjects according to gender, because the majority of patients (84%) enrolled in the study were undergoing gynecologic procedures (Table 1). Intraoperative data, including the total cumulative rocuronium dosage, the number of redoses, and the duration of the surgical procedures, are shown in Table 2. The mean core temperature at the conclusion of the surgical procedure was 36.2° ± 0.7°C.

Table 1. Patient Characteristics

Sample size	120
Sex (male/female)	17/103
Age (yr)	48 ± 8
Weight (kg)	74 ± 14
Height (cm)	165 ± 9
ASA physical status (I/II)	17/103
Smoking history	19
Use of ethanol	72
Preexisting diseases	
Cardiovascular	30
Respiratory	18
Endocrine	21
Other	0
Operative procedures	
Gynecologic	101
General	19

Data are mean ± SD or number of patients.

Table 2. Intraoperative Data

Total rocuronium dose (mg)	76 ± 32
Number of rocuronium redoses	2 (0–9)
Procedure duration (min)	165 ± 69
Blood loss (mL)	356 ± 351
Crystalloid infused (mL)	2750 ± 1258
Temperature (°C) at end of procedure	36.2 ± 0.7

Data are mean ± SD or median (range).

The median TOF count at reversal was 4 (range, 1–4). The average time interval between neostigmine administration and TOF measurements before tracheal extubation was 8 ± 6 min. Immediately before tracheal extubation, the mean TOF ratio was 0.67 ± 0.2. Among the 120 patients, 70 (58%) had a TOF ratio <0.7 and 105 (88%) had a TOF ratio <0.9 at this time (Fig. 1). Overall, the average time interval between neostigmine administration and tracheal extubation was 11 ± 7 min (12 ± 8 min in patients with TOF ratios <0.7 and 8 ± 5 min in patients with TOF ratios ≥0.7).

The mean TOF ratio measured on arrival to the PACU was 0.95 ± 0.15. The average time from neostigmine administration to TOF measurements in the PACU was 19 ± 7 min. Significantly fewer patients had TOF ratios <0.7 (9 subjects, 8%) and <0.9 (38 subjects, 32%) in the PACU compared with the OR (70 and 105 subjects, respectively) ($P < 0.001$) (Fig. 1).

No association was observed between severe residual paresis (TOF ratio <0.7) and any patient demographic or intraoperative variable.

No patients recalled supramaximal nerve stimulation when performed in the OR immediately before tracheal extubation. Only 9 patients (8%) remembered TOF measurements that were recorded in the PACU. The mean VAS score in these 9 subjects was 25 ± 13 mm. No patient reported VAS scores >50 mm on a 100-mm scale.

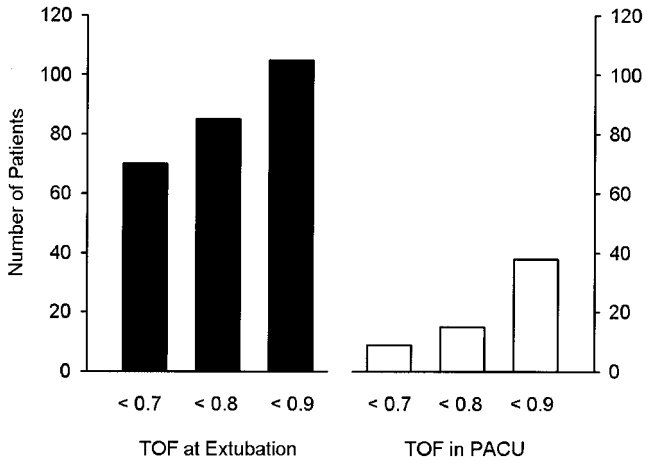

Figure 1. Train-of-four (TOF) ratios measured immediately before tracheal extubation and again on admission to the postanesthesia care unit (PACU). The graphs illustrate the number of patients (of a total of 120) with TOF ratios <0.7, 0.8, and 0.9 at each measurement interval.

Discussion

Residual neuromuscular blockade is a well recognized problem in the PACU. The incidence and severity of residual paresis at the time of tracheal extubation have not been examined. In the present investigation, we observed that acceptable neuromuscular recovery (TOF ratio >0.9) was present in only a small percentage (12%) of patients immediately before removal of the endotracheal tube. Quantitative neuromuscular monitoring is required to detect residual blockade. We also determined that supramaximal stimulating currents can be used in patients emerging from anesthesia; only 8% of patients recalled TOF-Watch monitoring when performed in the OR or PACU using 50-mA stimulation currents.

Complete recovery of neuromuscular function should be present at the time of tracheal extubation to reduce the risk of adverse respiratory events. Recent studies have demonstrated that respiratory and pharyngeal function do not normalize until TOF ratios of 0.8–1.0 are obtained. Eikermann et al. (5) observed that impaired inspiratory flow and upper airway obstruction occurred frequently at a TOF ratio of 0.83. Pharyngeal function and airway protection were impaired at TOF ratios of 0.9 in awake volunteers (4). The hypoxic ventilatory response was reduced by approximately 30% in awake volunteers with TOF ratios of 0.7 (6), and an association between mild residual neuromuscular block and postoperative hypoxemia has been described (7). These findings suggest that removal of an endotracheal tube in the presence of minimal levels of residual block can potentially contribute to adverse pulmonary outcomes. The results from a large, prospective, randomized outcome study support this hypothesis. In a clinical study of 691 patients, residual

block caused by pancuronium was associated with a 3-fold increased risk of postoperative pulmonary complications (9).

There is a growing consensus that the new benchmark for the adequacy of neuromuscular recovery should be a TOF ratio of ≥0.9. Few patients (15 of 120 subjects, or 12%) in our study achieved this benchmark at the time of tracheal extubation. Severe residual paresis (TOF <0.7) was noted in 70 patients (58%) at the time the anesthesia care provider had judged the block to have recovered sufficiently to exclude residual paralysis. The inability of clinicians in our investigation to detect residual block in the OR is not unexpected. A 5-second head lift or hand grip (used by all clinicians in our study) can be maintained in some postoperative patients with TOF ratios as low as 0.25–0.4 (10,11). The use of a peripheral nerve stimulator in the OR may reduce, but does not eliminate, the problem of postoperative paresis (11). Detection of incomplete reversal of neuromuscular blockade is difficult with standard TOF or tetanic stimulation. Experienced observers are unable to detect fade when the TOF ratio is >0.4 (12). Our results demonstrate that few patients had achieved TOF ratios ≥0.9 at the time of tracheal extubation, even when careful clinical examinations were performed and peripheral nerve stimulators were routinely used.

There is a "period of vulnerability" between the time of tracheal extubation and that of complete recovery of neuromuscular function during which a patient may be at risk for adverse respiratory events (13). During this immediate postoperative period, airway obstruction, aspiration of gastric contents, and ventilatory depression are the three most common, severe anesthetic-related complications (14). Previous investigators have examined the incidence of postoperative residual paralysis in the PACU. In these studies, TOF measurements were typically obtained 15–30 minutes after neuromuscular reversal and tracheal extubation (1,9,15). The incidence of incomplete neuromuscular recovery during the immediate recovery period (from tracheal extubation until stabilization in the PACU) has not been previously determined. Our results demonstrate that neuromuscular recovery is seldom complete in the OR and during patient transport to the PACU. A significant reduction in the incidence of residual paresis was noted by the time TOF measurements were obtained in the PACU. Only 9 patients (8%) had TOF ratios <0.7 and 38 patients (32%) had TOF <0.9 at this time. These findings suggest that the "period of vulnerability" is relatively short, and neuromuscular recovery rapid, when intermediate-acting muscle relaxants are used and routinely reversed. However, nearly one-third of patients failed to achieve our clinical benchmark (TOF ≥0.9) in the PACU, approximately 20 minutes after neostigmine administration. The number of patients with residual paralysis in the PACU would likely have been even more if clinicians had not been instructed to delay tracheal extubation in patients with TOF ratios <0.6–0.7.

Kopman et al. (16) have proposed that reports of residual weakness may merely represent an "artifact of improper anesthetic management." In many previous studies, the use of neuromuscular monitoring and reversal drugs was at the discretion of the managing anesthesiologist and inconsistently applied (2,7,15). In other investigations, monitoring (1) and reversal (3) of neuromuscular blockade was avoided in the perioperative setting. Our protocol incorporated several well known methods to reduce the incidence of postoperative paralysis, which included: 1) use of peripheral nerve stimulators in the OR, 2) avoidance of total twitch suppression, 3) use of intermediate-acting muscle relaxants, and 4) administration of anticholinesterases at a TOF count of 2–4 (16). Despite adherence to a rigid protocol designed to limit postoperative paralysis, Kopman et al. (16) noted that 17% of patients had TOF ratios <0.9 in the PACU 30 minutes after reversal of a rocuronium neuromuscular blockade. In the present study, careful intraoperative management of muscle relaxant administration, monitoring, and reversal did not result in clinically acceptable levels of neuromuscular recovery at the time of tracheal extubation in the majority of our patients. Thus, the goal of a TOF ratio >0.9 may be difficult to achieve in all patients in the immediate recovery period.

Small, portable acceleromyography instruments have been developed for routine use in the perioperative setting. These devices can deliver stimulating currents ranging from 1 to 60 mA. Although TOF ratios may remain stable over a wide range of stimulating currents, supramaximal nerve stimulation is required to produce consistently accurate measurements in all subjects (17). Clinicians may be reluctant to use supramaximal stimulating currents in patients emerging from anesthesia, because electrical stimulation of nerves can result in painful muscle contractions. In awake, unmedicated volunteers, TOF stimulating currents of 50 mA resulted in median VAS scores of 5.0–6.0 on a scale of 10 (18). In the postoperative surgical patient, the amnestic and analgesic effects of potent inhaled drugs persist into the immediate recovery period. Therefore, we hypothesized that few patients would recall supramaximal nerve stimulation as painful when performed in the OR or PACU. No subjects recalled TOF stimulation when performed immediately before tracheal extubation. Only 9 patients (8%) remembered TOF measurements that were obtained in the PACU. Mean VAS scores in these 9 patients were low (25 ± 13), and no patients reported pain scores >50 mm on a 100-mm scale. Our findings suggest that 50-mA stimulating currents can

be used during acceleromyography monitoring to detect residual paresis; few patients recall TOF measurements obtained in the early recovery period.

There are limitations to the current investigation. First, acceleromyography was used to quantify residual neuromuscular block. Several studies have noted a close correlation between TOF values obtained by acceleromyography and mechanomyography, a "gold standard" technique (19,20). Recent clinical investigations have demonstrated that acceleromyography may overestimate neuromuscular recovery, and that TOF ratios must recover to 0.95–1.0 to exclude residual paralysis (21,22). Therefore, the true incidence of impaired neuromuscular recovery may have been underestimated in our study. Second, there was a relatively short time interval between neostigmine administration and TOF measurements/tracheal extubation in the OR. The risk of residual block may be reduced if antagonism of rocuronium is initiated 20–30 minutes before tracheal extubation (16,23). Our protocol was designed to reflect standard clinical practices at our institution, however (neostigmine administered at the completion of the surgical procedure). Third, the significant reduction in residual paresis measured in the PACU may have been influenced by our study design, because clinicians were instructed to reverse neuromuscular blockade only at a TOF count of 2–3 and to delay tracheal extubation if the TOF ratio was <0.6–0.7. Fourth, only one set of TOF measurements was obtained in the OR. Complete neuromuscular recovery was not documented with acceleromyography before tracheal extubation. We believe patient safety was not compromised, because clinicians were instructed to delay tracheal extubation if severe residual paresis was noted. Finally, we used a 50-mA stimulating current in all subjects. In a small percentage of patients, a 50-mA stimulus may not represent a supramaximal current.

In conclusion, we determined that significant residual paralysis was present in the majority of patients at the anticipated time of tracheal extubation. Despite the use of a protocol directing strict monitoring and reversal of an intermediate-acting muscle relaxant, and the performance of a careful clinical examination for signs of muscle weakness, clinicians were consistently unable to achieve acceptable levels of neuromuscular recovery in the OR. In order for anesthesiologists to be assured that neuromuscular recovery is complete and that respiratory and pharyngeal muscle function has returned to normal, quantitative neuromuscular monitoring is required.

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