Intraoperative Acceleromyography Monitoring Reduces Symptoms of Muscle Weakness and Improves Quality of Recovery in the Early Postoperative Period

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ABSTRACT

Background: The subjective experience of residual neuromuscular blockade after emergence from anesthesia has not been examined systematically during postanesthesia care unit (PACU) stays. The authors hypothesized that acceleromyography monitoring would diminish unpleasant symptoms of residual paresis during recovery from anesthesia by reducing the percentage of patients with train-of-four ratios less than 0.9.

Methods: One hundred fifty-five patients were randomized to receive intraoperative acceleromyography monitoring (acceleromyography group) or conventional qualitative train-of-four monitoring (control group). Neuromuscular management was standardized, and extubation was performed when defined criteria were achieved. Immediately upon a patient's arrival to the PACU, the patient's train-of-four ratios were measured using acceleromyography, and a standardized examination was used to assess 16 symptoms and 11 signs of residual paresis. This examination was repeated 20, 40, and 60 min after PACU admission.

Results: The incidence of residual blockade (train-of-four ratios less than 0.9) was reduced in the acceleromyography group (14.5% *vs.* 50.0% control group, with the 99% confidence interval for this 35.5% difference being 16.4–52.6%, $P < 0.0001$). Generalized linear models revealed the acceleromyography group had less overall weakness (graded on a 0–10 scale) and fewer symptoms of muscle weakness across all time points ($P < 0.0001$ for both analyses), but the number of signs of muscle weakness was small from the time of arrival in the PACU and did not differ between the groups at any time.

Conclusion: Acceleromyography monitoring reduces the incidence of residual blockade and associated unpleasant symptoms of muscle weakness in the PACU and improves the overall quality of recovery.

What We Already Know about This Topic

- Patients monitored with acceleromyography are less likely to demonstrate residual neuromuscular blockade after surgery than are those monitored with train of four (TOF), but whether patient symptoms are affected has not been determined

What This Article Tells Us That Is New

- In 115 patients, residual neuromuscular blockade and patient symptoms of weakness were reduced in patients monitored with acceleromyography compared with those monitored with traditional TOF

RESIDUAL neuromuscular blockade is commonly observed in the postanesthesia care unit (PACU) when neuromuscular blocking agents (NMBAs) are administered intraoperatively. Recent large-scale studies have reported that 38–64% of patients receiving intermediate-acting NMBAs exhibit evidence of incomplete neuromuscular recovery in the early postoperative period (defined as a train-of-four [TOF]) ratio of less than 0.9).[1–5] Although a high incidence of residual blockade in the PACU has been reported using objective neuromuscular monitoring, most

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clinicians in the United States and Europe think clinically significant muscle weakness is a rare event.[6] However, emerging evidence suggests residual blockade may impair clinical recovery. Volunteer studies and clinical investigations have demonstrated that TOF ratios less than 0.9 are associated with adverse respiratory events, including reduced upper airway volumes,[7] airway obstruction,[7–10] hypoxemia events,[10,11] and postoperative pulmonary complications.[12] In addition, significant delays in meeting PACU discharge criteria and achieving PACU discharge have been observed in patients with TOF ratios less than 0.9 after surgery.[13]

Assessment of clinical recovery should include endpoints important to both clinicians (adverse respiratory events, PACU length of stay [LOS]) and patients. In particular, patient-perceived quality of recovery is becoming an increasingly important outcome measure in clinical research.[14] Few studies have investigated the unpleasant symptoms of muscle weakness that may be associated with residual blockade. At a TOF ratio of 0.7–0.75, awake volunteers describe a variety of "uncomfortable" symptoms (visual disturbances, facial weakness, difficulty speaking and swallowing, and generalized fatigue).[15] Some of these symptoms have been observed in postoperative patients with TOF ratios as great as 0.9.[16,17] However, no previous clinical trials have assessed systematically postoperative patients for symptoms and signs of muscle weakness that may result in poor quality of recovery.

Small degrees of residual blockade can be reliably detected only with the use of quantitative neuromuscular monitoring.[18] The use of quantitative acceleromyography monitoring allows clinicians to measure TOF ratios intraoperatively and thereby reduce the incidence of residual blockade in the PACU.[10,19,20] In addition, by decreasing the frequency and severity of postoperative residual blockade, acceleromyography may reduce the occurrence of adverse events associated with incomplete neuromuscular recovery.[10] We hypothesized that acceleromyography monitoring, by reducing the incidence of postoperative residual blockade (defined as a TOF ratio less than 0.9), would diminish overall weakness (graded on a 0–10 scale) and associated symptoms and signs of residual paresis. Early recovery during PACU stay was assessed and quantified using a standardized examination for symptoms and signs of muscle weakness, quality of recovery scoring systems, and standard recovery landmarks.

Materials and Methods

Study Population and Anesthetic Management

This investigation was approved by the NorthShore University HealthSystem Institutional Review Board (Evanston, Illinois), and written informed consent was obtained from all patients. The study was conducted at a single tertiary medical center (Evanston Hospital) affiliated with the University of Chicago Pritzker School of Medicine. Participants were recruited by reviewing operating room schedules and contact by telephone on the day before surgery. The trial type was parallel arm with per-protocol analysis of data. One hundred fifty-five patients (American Society of Anesthesiologists physical status I-III) undergoing elective surgical procedures requiring neuromuscular blockade, with an anticipated duration of at least 60 min, were enrolled (enrollment period: October, 6, 2009 to October 27, 2010). Exclusion criteria included presence of an underlying neuromuscular disease, use of drugs known to interfere with neuromuscular transmission, renal insufficiency (serum creatinine more than 1.8 mg/dl) or renal failure, hepatic disease (liver function test results more than 50% above normal values), age younger than 18 yr, and surgical procedures requiring positioning that prevented access to the ulnar nerve for neuromuscular monitoring.

With the use of a computer-generated randomization code, patients were allocated randomly (simple, 1:1) to one of two groups before entering the operating room. Patients assigned to the acceleromyography group were evaluated intraoperatively with quantitative neuromuscular monitoring (numerical TOF ratio). Patients randomized to the control group had neuromuscular function assessed using conventional qualitative monitoring (presence or absence of fade to a TOF nerve stimulation). The individual randomization assignments were concealed in opaque envelopes until the patients entered the operating room. Anesthetic management was standardized in all subjects. Intravenous midazolam (2 mg) was administered before the patients were transport to the operating room. Monitoring applied in the operating room included electrocardiography, pulse oximetry, automatic blood pressure assessment, capnography, Bispectral Index monitoring (BIS® system; Aspect Medical Systems, Newton, MA), and core temperature *via* an esophageal probe. Anesthesia was induced with 1.5–2.5 mg/kg propofol, 50 mg lidocaine, 100 μg fentanyl, and 0.6–0.8 mg/kg rocuronium. Sevoflurane (0.5–3% in a 50% oxygen/air mixture) was used to maintain anesthesia, with concentrations adjusted to maintain Bispectral Index values between 40 and 60 and mean blood pressure within 20% of baseline values. Anesthesia was supplemented with additional boluses of fentanyl (approximately 1–2 $\mu g \cdot kg^{-1} \cdot h^{-1}$). Tidal volumes of 6–8 ml/kg were used, and the respiratory rate was adjusted to maintain the end-tidal carbon dioxide between 30 and 34 mmHg. Core temperatures more than 35.0°C and upper extremity temperatures more than 32.0°C were achieved with upper body forced-air warming devices (Bair Hugger®; Augustine Medical, Minneapolis, MN).

Neuromuscular Management

Neuromuscular monitoring was applied to patients in both study groups on arrival to the operating room by a research assistant blinded to group assignment (TOF-Watch SX®; Bluestar Enterprises, Chanhassen, MN). The protocol was reviewed with all clinicians, as was the use of the TOF-Watch SX®. After the skin was cleansed and prepared, two surface

electrodes, separated by 3 cm, were placed over the ulnar nerve at the wrist. The acceleration transducer was attached to the distal phalanx of the thumb *via* a hand adapter that also applied a constant preload and allowed a reproducible baseline thumb position (TOF-Watch Hand Adapter®; Bluestar Enterprises). Uncalibrated TOF stimulation (four pulses of 0.2-ms duration at a frequency of 2 Hz) was used in patients in both groups, and the current intensity selected was 50 mA. During nerve stimulation, the monitored extremity was observed to ensure free movement of the thumb. For both study groups, clinicians were instructed to administer additional doses of rocuronium (5–10 mg) to maintain a TOF count of 2–3 (visual) during portions of the operation requiring neuromuscular blockade. No NMBAs were to be administered during the last 20–30 min of the anesthetic administration. At the conclusion of the surgical closure, when a TOF count of at least 3 was present, neuromuscular blockade was reversed with 50 μg/kg neostigmine and 10 μg/kg glycopyrrolate.

After neuromuscular monitoring was applied, clinicians providing intraoperative care opened envelopes to determine group assignment. In the acceleromyography group, clinicians were instructed to remove an opaque piece of cardboard covering the data panel of the TOF-Watch SX® and to use the TOF ratio information displayed to guide intraoperative management. Although the protocol recommended maintaining a TOF count of 2–3 during portions of the surgery requiring neuromuscular blockade, TOF ratio data could be used to guide NMBA dosing when surgical relaxation was no longer required (particularly during the last 45–60 min of the anesthetic administration). In addition, the protocol recommended that a TOF ratio more than 0.8 be achieved before tracheal extubation. However, the endotracheal tube could be removed before TOF ratios of 0.8 were attained if patients were unable to tolerate intubation. Additional criteria for extubation included sustained head lift or hand grip for more than 5 s, the ability to follow simple commands, and a stable ventilatory pattern with an acceptable arterial oxygen saturation. In the control group, the cardboard covering the display panel TOF-Watch SX® was not removed. The TOF-Watch SX® was used as a standard qualitative peripheral nerve stimulator because clinicians did not have access to TOF ratio data. The protocol in the control group required that tracheal extubation be delayed until no fade was detected visually with TOF stimulation (qualitative evaluation of residual neuromuscular blockade). Additional clinical criteria for tracheal extubation were identical to those of the acceleromyography group.

Data Collection

At the conclusion of the surgical procedure, the TOF-Watch SX® was removed and transported with the patient to the PACU. When the patient arrived at the PACU, a research assistant blinded to the group assignment reapplied the TOF-Watch SX® and measured TOF ratios in all subjects, as described above. Two consecutive TOF measurements (separated by 15 s) were obtained, and the average of the two values was recorded. If measurements differed by more than 10%, additional TOF measurements were obtained (to four TOF values), and the closest two ratios were averaged. Residual neuromuscular blockade was defined as a TOF ratio less than 0.9.

Immediately after TOF ratios were recorded, a standardized examination was performed to evaluate patients for symptoms and signs of muscle weakness. Testing for signs of muscle weakness (objective) was immediately followed by assessments for symptoms of residual paresis (subjective). The exam was designed based on the findings of Kopman *et al.* correlating signs and symptoms of residual paresis with the TOF ratio in awake volunteers.[15] To ensure a uniform and consistent evaluation of all subjects, testing was performed by a single research assistant (blinded to the TOF ratio data) and all evaluations for signs and symptoms of muscle weakness were performed in a standardized order. Complete examinations were performed at four time intervals: PACU admission and 20, 40, and 60 min after admission. Patients were asked to perform 11 tests of muscle strength (objective signs of weakness). Patients either passed (negative response) or failed (positive response) each test. These tests or signs included: 5-s head lift; 5-s hand grip; 5-s eye opening; 5-s tongue protrusion; tongue depressor test (prevent removal of a wooden tongue depressor from between the incisor teeth); ability to smile; ability to swallow; ability to speak; ability to cough; ability to track objects with eyes (follow finger of examiner); and ability to breathe deeply. Subjective symptoms of muscle weakness were measured in the following manner. After each test was completed, patients were questioned by the research assistant about whether the test was difficult to complete or uncomfortable to perform. For example, a patient might successfully maintain a 5-s eye opening yet note that it was "difficult to keep my eyes open" and subjectively experience "heavy eyelids." Subjective symptoms of muscle weakness were recorded as normal (negative response) or impaired (positive response). In addition to these 11 symptoms, all subjects were assessed for five other symptoms of residual paresis: blurry vision; double vision; facial weakness; facial numbness; and general weakness. Responses were assessed and recorded as described above. At the conclusion of each testing session, patients were asked to quantify overall muscle weakness on an 11-point verbal rating scale (0 = no muscle weakness, 10 = most severe muscle weakness experienced).

Aldrete scores were assessed when the patients arrived in the PACU and every 10 min for the next 60 min. The times required to meet discharge criteria (an Aldrete score of ≥8 of 10 points) and achieve actual discharge were noted. For discharge times longer than 60 min, the reasons for delayed discharge were described. Recovery data were collected by PACU nurses blinded to group assignment and TOF ratio measurements and were recorded on a data collection form.

Quality of recovery was quantified using the quality of recovery (QoR)-9 and a 100-mm visual analog scale (VAS). The QoR-9 scoring system was explained in detail to all subjects in the preoperative holding area and completed in the presence of a research assistant to ensure accurate comprehension of all questions. QoR-9 scores range from 0 (extremely poor quality of recovery) to 18 (extremely high quality of recovery). The QoR-9 has been demonstrated to have good validity, reliability, and clinical acceptability in patients undergoing a variety of surgical procedures.[14] The QoR-9 was completed again at the time of patient discharge from the PACU. As an alternative assessment tool, patients were asked at the same time to evaluate overall quality of recovery using a 100-mm VAS. Patients were requested to rate recovery by marking an "X" on a 100-mm line between 0 (extremely poor quality of recovery) and 100 (extremely high quality of recovery).

Patient demographic data were recorded from the preoperative anesthesia evaluation form. Duration of anesthesia, administration of crystalloids, blood loss, total doses and number of repeat doses of rocuronium, and core temperatures at the conclusion of the anesthetic administration were recorded from the anesthesia record. Additional data collected for research purposes included the TOF count at reversal and the timing from neostigmine administration until tracheal extubation, PACU admission, and TOF measurements in the PACU. The ability to achieve a TOF ratio more than 0.80 before extubation in the acceleromyography group was noted.

Statistical Analysis

In awake volunteers, 7 of 12 (58.3%) subjects experienced symptoms of weakness at a TOF ratio of 0.8.[8] We hypothesized that acceleromyography monitoring could reduce the incidence of symptoms of residual paresis by 50%. Group sample sizes of 52 each achieve 80% power to detect a difference of 0.29 between the null hypothesis that both group proportions are 0.58 and the alternative hypothesis that the proportion of group 2 is 0.29 with a significance level (α) of 0.05 using chi-square or Fisher exact test with continuity correction. Because patients may be unwilling or unable to answer questions about symptoms in the early postoperative period, 155 patients were enrolled to ensure an acceptable response rate.

The primary outcome variables were overall weakness scores, total number of symptoms of muscle weakness, and total number of signs of muscle weakness at the four measurement times in the PACU. These data are presented as mean ± SD as well as median and range. To examine the primary outcomes, two of which consisted of count data, generalized linear models were used with a Poisson distribution and log link. Several count distributions were considered (*e.g.*, negative binomial), but the results were consistent even with different distributional assumptions, so only the Poisson regression is presented. A group (control group *vs.* acceleromyography group) by time (0, 20, 40, and 60 min) factorial model was specified, with the group factor (*i.e.*, aggregating across time) designated as the primary analysis. PASW 18.0 (SPSS, Inc., Chicago IL) was used for these models. The criterion for rejection of the null hypothesis in analysis of each of the three primary outcome variables was $P < 0.05/3 = 0.0167$.

Discrete data were compared using Fisher exact test (NCSS, Kaysville, UT). The 99% confidence intervals for the differences in percentages were calculated using the Miettinen and Nurminen method. Ordinal data and continuous data that were not normally distributed are presented as median and range. These data were compared between groups using the Mann–Whitney U test (StatsDirect, Cheshire, United Kingdom). The median differences and their 99% confidence intervals were calculated. Normally distributed continuous data are presented as mean and SD. These data were compared using the unpaired *t* test (NCSS). Mean differences and their 99% confidence intervals were calculated.

The possible relationships between signs and symptoms of muscle weakness in the early postoperative period and the TOF ratio were sought using receiver operating characteristics (ROC) curve analysis. The ability of the total number of positive signs and the total number of positive symptoms determined for each individual during muscle strength assessment at PACU admission to detect the presence or absence of a TOF ratio less than 0.90 formed the basis of two ROC analyses. The third ROC analysis was based on the ability of muscle weakness assessed with an 11-point verbal rating scale to detect the presence or absence of a TOF ratio less than 0.90. Optimal cutoff point, area under the ROC curve and its 99% confidence interval, and the sensitivity and specificity and their 99% confidence intervals were determined for each of the three variables assessed (StatsDirect).

Given the large number of comparisons being made, the criterion for rejection of the null hypothesis was a two-tailed $P < 0.01$ to help minimize the chance of a type I error.

Results

One hundred fifty-five patients were enrolled in this clinical trial. Five patients were excluded from data analysis for protocol violations. Patient characteristics are presented in table 1. There were no differences between groups in sex, age, weight, height, preexisting medical conditions (data not shown), ASA physical status, or type of surgical procedure. Intraoperatively, the two groups did not differ in duration of anesthesia, use of crystalloids, blood loss, or core temperature at the end of the procedure (table 2). Neuromuscular management data are presented in table 2. Total doses of rocuronium used and numbers of repeat doses were similar in both groups. A TOF ratio of ≥80% was achieved in 87% of subjects in the acceleromyography group before tracheal extubation. TOF ratios on admission to the PACU were significantly higher in the acceleromyography group (0.98, range 0.48–1.28) than in the control group (0.88, range

Table 1. Patient Characteristics

	Control Group	Acceleromyography Group	Difference (99% CI)
Number	74	76	—
Sex (male:female)	39 (52.7%):35 (47.3%)	42 (55.3%):34 (44.7%)	−2.6% (−23.1% to 18.1%)
Age (yr)	51.0 ± 14.7	54.1 ± 15.3	−3.1 (− 9.5 to 3.3)
Weight (kg)	85.6 ± 21.1	84.1 ± 21.5	1.6 (−7.5 to 10.6)
Height (cm)	171.3 ± 11.4	171.9 ± 9.2	−0.5 (−4.9 to 3.9)
ASA physical status	2 (1–3)	2 (1–3)	0 (0 to 0)
Surgical procedures	—	—	—
Gynecologic surgery	6 (8.1%)	5 (6.6%)	1.5% (−11.1% to 14.6%)
General surgery	31 (41.9%)	23 (30.3%)	11.6% (−8.6% to 31.1%)
Thoracic surgery	7 (9.5%)	5 (6.6%)	2.9% (−9.9% to 16.3%)
Orthopedic surgery	10 (13.5%)	15 (19.7%)	−6.2% (−22.4% to 10.0%)
Vascular surgery	0 (0%)	2 (2.6%)	−2.6% (−12.4% to 5.8%)
Neurologic surgery	11 (14.9%)	6 (7.9%)	7.0% (−7.1% to 21.8%)
Urologic surgery	9 (12.2%)	17 (22.4%)	−10.2% (−26.5% to 6.1%)
Plastic surgery	2 (2.7%)	4 (5.3%)	−2.6% (−13.9% to 8.1%)

Data are mean ± SD, median (range), or number of patients (%).
ASA physical status = American Society of Anesthesiologists physical status.

0.33–1.26, $P = 0.004$). The number of patients with TOF ratios less than 0.9 (14.5% *vs.* 50%, $P < 0.0001$) and TOF ratios less than 0.7 (4.0% *vs.* 18.9%, $P = 0.004$) was smaller in the acceleromyography group than in the control group. Tracheal extubation was performed in 10 patients in the acceleromyography group before a TOF ratio of 0.8 was achieved because of an inability to tolerate intubation; TOF ratios less than 0.9 were measured in the PACU in 80% of this subgroup. Three of these 10 patients had TOF ratios less than 0.7 (0.48, 0.57, 0.58) and received reversal at a TOF count of 3, 1, and 4, respectively.

The primary outcome variables for this investigation were overall weakness scores (graded on a 0–10 scale), total number of symptoms of muscle weakness, and total number of signs of muscle weakness on admission to the PACU and every 20 min thereafter to 1 h (see Supplemental Digital Content 1, http://links.lww.com/ALN/A777, which is a table listing these outcome measures). Generalized linear models revealed the acceleromyography group had less overall weakness and fewer symptoms of muscle weakness across all time points ($P < 0.0001$ for both analyses), but the number of signs of muscle weakness was small from the time of arrival in the PACU and did not differ between the groups across time points. Median overall weakness (0–10 scale) in the acceleromyography group on admission to the PACU was 4 and decreased to 2 in 1 h, whereas in the control group, it was 6 on admission to the PACU and decreased to 4 in 1 h. The median number of symptoms of muscle weakness in the acceleromyography group on admission to the PACU was 2 and decreased to 0 in 1 h, whereas in the control group, it was 5

Table 2. Perioperative Data

	Control Group	Acceleromyography Group	Difference (99% CI)	*P* Value
Anesthesia duration (min)	145 (64–381)	156 (65–387)	−11 (−38 to 19)	0.367
Blood loss (ml)	50 (20–900)	100 (10–1,400)	0 (−50 to 15)	0.552
Crystalloid volume (ml)	1,350 (130–3,995)	1,500 (400–6,500)	−100 (−450 to 200)	0.394
Temperature at end of procedure (°C)	36.2 ± 0.6	36.2 ± 0.6	0 (−0.3 to 0.2)	0.699
Temperature at arrival postanesthesia care unit (°C)	36.6 ± 0.3	36.6 ± 0.4	0 (−0.2 to 0.1)	0.934
Total rocuronium dose (mg)	60 (30–160)	60 (20–160)	0 (−10 to 10)	0.440
Number of rocuronium repeat doses	1 (0–10)	1 (0–11)	0 (−1 to 1)	0.948
Number of twitches at reversal	4 (1–4)	4 (0–4)	0 (0 to 0)	0.009
Time neostigmine to extubation (min)	10 (1–43)	10 (1–37)	0 (−4 to 2)	0.662
Time neostigmine to post-anesthesia care unit (min)	16.5 (5–47)	18 (6–45)	−1 (−5 to 2)	0.196
Time neostigmine to train-of-four (min)	20 (8–52)	20.5 (6–48)	−1 (−5 to 2)	0.370
Train-of-four ratio in PACU	0.88 (0.33–1.26)	0.98 (0.48–1.28)	− 0.1 (− 0.18 to − 0.01)	0.004
Train-of-four ratio <0.9	37 (50.0%)	11 (14.5%)	35.5% (16.4% to 52.6%)	<0.0001
Train-of-four ratio <0.7	14 (18.9%)	3 (4.0%)	15.0% (1.8% to 29.8%)	0.004

Data are mean ± SD, median (range), or number of patients (%).
PACU = postanesthesia care unit.

on admission to the PACU and decreased to 1 in 1 h. The median number of signs of muscle weakness was 0 in both groups at all times assessed from the time of PACU admission.

At PACU admission, the most frequently observed symptoms in the study population as a whole were general weakness (59.6% of subjects), subjective difficulty completing 5-s eye opening (52.7%), subjective difficulty tracking object with eyes (43.2%), blurry vision (41.8%), and subjective difficulty speaking (36.3%). Twenty minutes after PACU admission, general weakness (57.0% of all subjects), subjective difficulty completing 5-s eye opening (40.9%), blurry vision (32.2%), and subjective difficulty speaking (25.5%) were the most frequently observed symptoms of residual paresis. General weakness (45.6% of all subjects), subjective difficulty completing 5-s eye opening (30.2%), subjective difficulty speaking (16.1%), and blurry vision (14.1%) were observed 40 min after PACU admission. At the time of the 60-min evaluation, symptoms that still persisted included generalized weakness (36.2% of all subjects), subjective difficulty completing 5-s eye opening (15.4%), blurry vision (8.7%), subjective difficulty speaking (8.1%), and subjective difficulty tracking object with eyes (7.4%). In contrast, signs of muscle weakness were present in less than 6% of patients at all assessment times, with the exception of inability to track objects with eyes (14.4% of all subjects) at PACU admission.

The ROC analysis revealed that, although the number of signs of muscle weakness at PACU admission had good specificity (0.940) for a TOF ratio less than 0.9, it had poor sensitivity (0.435) (see Supplemental Digital Content 2, http://links.lww.com/ALN/A778, which provides a table of the ROC analysis of the relationships between signs and symptoms of muscle weakness and the presence or absence of a TOF ratio less than 0.90). This was reflected by the low area under ROC curve for the signs of muscle weakness. Symptoms of muscle weakness at PACU admission had good sensitivity and specificity for a TOF ratio less than 0.9 whether they are expressed as the number of symptoms or overall muscle weakness. The number of symptoms with a cutoff point of five symptoms had a sensitivity of 0.870 and a specificity of 0.820 with a ROC area of 0.913, whereas overall muscle weakness with a cutoff point of six had a sensitivity of 0.783 and a specificity of 0.830 with a ROC area of 0.883. Thus, the presence or absence of symptoms of muscle weakness was predictive of the presence or absence of a TOF ratio less than 0.9, but the presence or absence of signs of muscle weakness was not.

Aldrete scores during the first 60 min in the PACU were similar in the acceleromyography and control groups ($P = 0.23–0.72$). No differences between groups were observed in the time required to meet discharge criteria (control group: 65 min, range 21–285 min; acceleromyography group: 67.5 min, range 22–240 min; $P = 0.68$) or achieve actual discharge (control group: 98 min, range 29–340 min; acceleromyography group, 90 min, range 45–260 min; $P = 0.31$). The primary reasons for PACU LOS more than 60 min were unavailability of ward beds and pain management issues.

Global QoR-9 scores did not differ between study groups during the preoperative evaluation (control group: 17, range 11–18; acceleromyography group: 18, range 11–18; $P = 0.28$) or at PACU discharge (control group: 14, range 5–16; acceleromyography group: 14, range 9–16; $P = 0.042$). In only one category, general well-being, were higher scores measured in the acceleromyography group at PACU discharge (control group: 1, range 0–2; acceleromyography group: 2, range 1–2; $P < 0.0001$). However, global quality of recovery measured on a 0–100 VAS was improved in the acceleromyography group (85, range 50–100) compared with the control group (70, range 0–100; $P < 0.0001$) at the time of discharge from the PACU.

There were no adverse events related to neuromuscular monitoring.

Discussion

The current investigation demonstrates that symptoms of muscle weakness are common after general anesthesia with NMBAs. The use of acceleromyography monitoring was associated with a lower incidence of residual neuromuscular blockade and attenuated the severity of patient-perceived muscle weakness during the PACU admission. We also observed that the presence or absence of symptoms of muscle weakness was predictive, respectively, of the presence or absence of a TOF ratio less than 0.9. In contrast, clinical signs or bedside tests of muscle weakness were poor prognosticators of residual paresis and were not useful in assessing a patient's subjective sense of well-being. In addition, global quality of recovery measured on a 0–100 VAS was improved in patients monitored with acceleromyography. These findings support the concept that residual neuromuscular blockade is an important factor in the determination of patient satisfaction during recovery from anesthesia.

Incidence of Residual Neuromuscular Blockade

Three previous randomized studies have demonstrated that intraoperative acceleromyography monitoring reduces the incidence of residual neuromuscular blockade.[10,19,20] These findings are not unexpected. Higher TOF ratios should be obtained in the PACU if nearly complete neuromuscular function is demonstrated before tracheal extubation. The incidence of residual block, defined as a TOF ratio less than 0.9 with acceleromyography, was 50% in our control group. Recent studies have determined that TOF ratios less than 0.9 are observed in 38–64% of postoperative patients who do not receive quantitative neuromuscular monitoring.[1–5] The incidence of residual blockade was significantly less in patients randomized to receive acceleromyography monitoring (14.5%) than in the control group. In the acceleromyography group, the only patients exhibiting TOF ratios less than 0.85 in the PACU were those whose tracheas were extubated before a TOF ratio of 0.8 was achieved in the operating room.

Our findings suggest that acceleromyography monitoring reduces residual paresis by allowing a more rational and accurate titration of NMBAs during the last 45–60 min of anesthetic administration. Previous studies have demonstrated that the use of acceleromyography monitoring in the operating room does not result in a reduction in the total dose of rocuronium or pancuronium.[10,19,20] However, other neuromuscular management variables at the conclusion of anesthetic administration are influenced by TOF ratio data. In our investigation, clinicians were allowed access to TOF data throughout the anesthetic administration. These data are unlikely to affect clinical management during portions of the surgery requiring moderate neuromuscular blockade (TOF count 2–3, TOF ratio of 0). The primary utility of acceleromyography monitoring is realized when surgical muscle relaxation is no longer required. We observed that the percentage of patients receiving a repeat dose of NMBAs during the last 45 min of surgery was lower in the acceleromyography group (6.6%) than in the control group (18.9%, $P = 0.027$). In addition, the percentage of patients with a TOF count of 4 at the time of reversal was higher in the acceleromyography group (80.3%) than in the control group (55.4%, $P = 0.014$); the time required to attain a TOF ratio of 0.9 is significantly shorter when neostigmine is administered at a higher TOF count.[21] However, these differences were not statistically significant using our established level of significance ($P < 0.01$).

Symptoms of Muscle Weakness during Postoperative Recovery

The relationship between various TOF ratios and symptoms of residual paralysis has been examined in awake volunteers after NMBA administration. At a TOF ratio of 0.7–0.81, volunteers complained of difficulty swallowing, dysarthria, diplopia, blurred vision, and difficulty keeping their eyes open.[22,23] Awake subjects noted visual disturbances, decreased grip strength, inability to maintain incisor teeth apposition, severe facial weakness, difficulty speaking, and generalized weakness at a TOF ratio of 0.7–0.75.[15] Visual problems and generalized fatigue persisted at a TOF ratio of 0.85–0.9, and visual disturbances were described by 70% of volunteers for as long as 90 min after TOF ratios had recovered to 1.0. In contrast, no previous investigations have examined systematically surgical patients for symptoms of muscle weakness related to residual neuromuscular blockade.

Our observations in the clinical setting support the findings from awake volunteer studies.[15,22,23] At all four measurement times in the PACU, general weakness and visual symptoms (difficulty tracking objects with eyes, maintaining eye opening, blurry vision) were the most frequently described patient complaints related to residual paresis. Difficulty speaking was also commonly noted during the first 60 min of the PACU admission. These observations suggest that ocular and pharyngeal muscles may be particularly sensitive to small degrees of residual block. Subtle effects of NMBA on all muscle groups in the postoperative period likely accounted for the high incidence of generalized weakness.

Sixty minutes after PACU admission, a variety of symptoms of muscle weakness were still noted by patients. In the control group, 55% of subjects noted general weakness, and overall muscle weakness was graded 4 on a scale of 0–10. The reasons for the persistence of symptoms after the TOF ratio had likely recovered to unity are uncertain. We (and others)[24] hypothesize that prolonged occupation of the neuromuscular junction by NMBAs may have contributed to these symptoms. At a TOF ratio of 0.95–1.0, a significant percentage of junctional receptors may still be occupied by the NMBA.[24,25] Currently, there are no methods to detect receptor occupancy or determine the time course until the neuromuscular junction is free of NMBA binding. It is possible that a small degree of receptor occupancy may persist after the TOF ratio has fully recovered and produce subjective symptoms of weakness.

Signs of Muscle Weakness during Postoperative Recovery

Postoperative signs of muscle weakness were observed less frequently than were symptoms in the control and acceleromyography groups. A number of previous investigations have established that profound neuromuscular blockade must be present before subjects are unable to complete tests of muscle strength. At a TOF ratio of 0.65 to 0.75, all 12 awake volunteers were able to protrude the tongue, swallow, sustain a 5-s head lift, speak, and open their eyes.[26] A 5-s head lift could be performed by all seven volunteers at a TOF ratio of 0.6.[27] In the clinical setting, 71% of patients with TOF ratios less than 0.7 were able to perform a 5-s head lift on arrival to the PACU.[28]

In the current investigation, the median number of signs of muscle weakness was 0 in the acceleromyography and control groups at all four measurement times. Our findings support the previous observations that most patients are able to perform tests of muscle strength at TOF ratios more than 0.6 to 0.7. Although most patients successfully completed these tests with small degrees of neuromuscular blockade, many subjectively experienced difficulty completing the task or felt uncomfortable during the performance of the test. Thus, symptoms may be a more sensitive measure of lesser degrees of receptor occupancy.

Acceleromyography Monitoring and Symptoms and Signs of Muscle Weakness

Two primary findings related to intraoperative acceleromyography monitoring were observed in this investigation. First, patients in the acceleromyography group had a lower incidence of residual paresis, as documented with quantitative neuromuscular monitoring. Second, patients in this group also exhibited fewer symptoms of muscle weakness in the PACU. It is likely that these two outcome measures are interrelated because we also observed an association between

residual block (TOF ratio less than 0.9) and general weakness in the postoperative period.

In the current study, the total number of symptoms of muscle weakness described by patients in the PACU was significantly lower across all time points in the acceleromyography group than in the control group ($P < 0.0001$ at each assessment period). Acceleromyography monitoring appeared to have the largest beneficial effect on the symptom of general weakness. An absolute reduction in the incidence of general weakness of 32.6% to 38.1% ($P < 0.0001$ at all times) was noted in the acceleromyography group throughout the study period. Other postoperative symptoms that were observed less frequently in the acceleromyography group included subjective difficulty breathing deeply, facial weakness, and visual impairment. Overall muscle weakness, assessed on a 0–10 scale in the PACU, was also noted to be less severe across all time points in the acceleromyography *versus* the control group.

In contrast, acceleromyography monitoring appears to minimally affect signs or tests of muscle weakness in the PACU. Signs of muscle weakness in the PACU did not differ between groups across time points. These findings are not surprising. Typically, TOF ratios less than 0.5–0.6 must be present before subjects fail standard tests of neuromuscular recovery. In our investigation, few patients in either group had this degree of neuromuscular blockade at the time of clinical assessment.

PACU Length of Stay and Quality of Recovery

Previous studies have not examined the effect of acceleromyography monitoring on PACU LOS. The times required to meet discharge criteria and achieve actual PACU discharge did not differ between study groups in our investigation. Aldrete scores were also similar during the PACU admission. Thus, Aldrete scores do not appear to be sensitive predictors of residual paresis and are not influenced by mild or moderate muscle weakness. Most standard criteria used to assess recovery in the PACU are unaffected by smaller degrees of residual block (hemodynamic stability, nausea and vomiting, pain), and patients typically are not questioned about symptoms of muscle weakness after surgery.

Global quality of recovery, as measured with the QoR-9 scoring system, was not improved in subjects receiving acceleromyography monitoring. Validated quality of recovery scoring systems do not incorporate questions that evaluate patients for symptoms of residual paresis directly. Therefore, these tools are unlikely to detect patients with unpleasant symptoms of muscle weakness. Only two of the nine dimensions of the QoR-9 potentially would be affected by residual blockade (breathe easily and general well-being). General well-being scores were improved in the acceleromyography group at the time of discharge from the PACU. Because none of the available scoring systems assess patient-perceived muscle weakness, we asked subjects to describe global quality of recovery on a 100-mm VAS scale. Median scores were significantly higher in the acceleromyography group (85) than in the control group (70). We hypothesize that the improved quality of recovery scores (general well-being on the QoR-9 and the higher global VAS) were attributable to a reduction in the incidence of general weakness during PACU admission.

Limitations

There are limitations to this investigation. The ability of acceleromyography to detect residual block (a mechanomyographic TOF ratio less than 0.9) is improved when calibration and normalization are performed with the TOF-Watch SX® monitor before NMBA administration.[29,30] Average control TOF ratios of 1.13 have been observed with acceleromyography, compared with a value of 0.96 with mechanomyography (the current "gold standard").[29] Because baseline values with acceleromyography usually exceed 1.0, an isolated measurement at the end of anesthesia likely underestimates the true incidence of residual paresis unless normalization to control values is performed. Thus, the TOF ratios presented probably are 11–12% higher than would have been measured using mechanomyographic or electromyographic monitoring. Furthermore, the accuracy of acceleromyography in awake postoperative patients has been questioned.[31] To improve performance and reduce variability during recovery,[29,30] we applied a constant preload to the thumb and performed a series of stimuli, rather than a single TOF ratio, in the PACU. In addition, patients were examined for symptoms and signs of residual muscle weakness for only 60 min. We did not determine whether symptoms extended beyond this time.

Conclusion

Unpleasant symptoms of muscle weakness often are observed in the early postoperative period. As stated in a recent editorial, "It is possible that rigorous management of residual blockade might lead to more comfort, a more rapid discharge, and more satisfaction."[32] Our findings demonstrate that unpleasant symptoms of muscle weakness are reduced and patient satisfaction is improved when quantitative acceleromyography monitoring is used in the operating room. However, PACU LOS was unaffected by the type of neuromuscular monitoring used intraoperatively. The relationship between residual neuromuscular blockade and symptoms of muscle weakness, overall quality of recovery, and PACU LOS may be further defined in future studies using other, more effective neuromuscular reversal agents, such as sugammadex.

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