Impaired Upper Airway Integrity by Residual Neuromuscular Blockade

Increased Airway Collapsibility and Blunted Genioglossus Muscle Activity in Response to Negative Pharyngeal Pressure

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**Background:** Residual neuromuscular blockade increases the risk to develop postoperative complications. The authors hypothesized that minimal neuromuscular blockade (train-of-four [TOF] ratio 0.5–1) increases upper airway collapsibility and impairs upper airway dilator muscle compensatory responses to negative pharyngeal pressure challenges.

**Methods:** Epiglottic and nasal mask pressures, genioglossus electromyogram, respiratory timing, and changes in lung volume were measured in awake healthy volunteers (n = 15) before, during (TOF = 0.5 and 0.8 [steady state]), and after recovery of TOF to unity from rocuronium-induced partial neuromuscular blockade. Passive upper airway closing pressure (negative pressure drops, random order, range +2 to −30 cm H2O) and pressure threshold for flow limitation were determined.

**Results:** Upper airway closing pressure increased (was less negative) significantly from baseline by 54 ± 4.4% (means ± SEM), 37 ± 4.2%, and 16 ± 4.1% at TOF ratios of 0.5, 0.8, and 1.0, respectively (P < 0.01 vs. baseline for any level). Phasic genioglossus activity almost quadrupled in response to negative (−20 cm H2O) pharyngeal pressure at baseline, and this increase was significantly impaired by 57 ± 44% and 32 ± 6% at TOF ratios of 0.5 and 0.8, respectively (P < 0.01 vs. baseline). End-expiratory lung volume, respiratory rate, and tidal volume did not change.

**Conclusion:** Minimal neuromuscular blockade markedly increases upper airway closing pressure, partly by impairing the genioglossus muscle compensatory response. Increased airway collapsibility despite unaffected values for resting ventilation may predispose patients to postoperative respiratory complications, particularly during airway challenges.

NONDEPOLARIZING neuromuscular blocking agents are used during general anesthesia to facilitate tracheal intubation and to improve surgical conditions. However, residual effects of neuromuscular blocking agents often last longer than surgery, and their symptoms are difficult to distinguish from those of hypnotics and narcotics. Therefore, intraoperative quantitative monitoring of neuromuscular function such as acceleromyography has been suggested to diagnose impaired neuromuscular transmission.

The train-of-four (TOF) ratio of the adductor pollicis muscle is commonly used to measure neuromuscular blockade, and a TOF ratio of 0.7 predicts adequate recovery of tidal volume and respiratory rate. A TOF ratio of 0.7 has been proposed as a reliable indicator for the return of sufficient muscular function to permit endotracheal extubation. Other data, however, have shown that even minimal neuromuscular blockade can evoke diplopia, inability to clench the teeth, misdirected swallowing, and to impair maximum inspiratory airflow and forced inspiratory volume. Furthermore, previous work from our group using respiratory gated cine magnetic resonance imaging has demonstrated that inspiratory upper airway volume is decreased, even with residual neuromuscular blockade at a TOF ratio of 0.8. Thus, upper airway collapsibility might be increased during residual neuromuscular blockade, independent of anesthesia; to our knowledge, this has not been evaluated. Furthermore, if upper airway integrity is impaired by minimal neuromuscular blockade independent of anesthetic effects, it would be interesting to assess whether this relates to impaired muscle function of airway openers, such as the genioglossus muscle, or to factors such as lung volume or respiratory timing. Accordingly, we tested the hypothesis that residual neuromuscular blockade (TOF ratio 0.5 and 0.8) increases upper airway critical closing pressure (Pcrit) and impairs the upper airway dilator genioglossus muscle response to negative pharyngeal pressure challenges.

**Materials and Methods**

**Subjects**

After institutional review board approval (Essen Medical School, Essen, Germany) and obtaining written informed consent, we studied 15 healthy male volunteers (age, 36 ± 7 yr; weight, 85 ± 15 kg; height, 183 ± 8 cm; means ± SD). Experiments were conducted at Essen Medical School, Essen, Germany, in a laboratory equipped with an anesthesia workstation and in the presence of board-certified anesthesiologists for safety.
reasons. Standard anesthesia monitoring (electrocardiogram, pulse oximetry, end-tidal carbon dioxide concentration, and oscillometric blood pressure measurements) was used continuously throughout the experiments.

**Measurements**

To assess $P_{\text{crit}}$, we used an experimental respirator ($P_{\text{crit}}$ 3000; Respironics Inc., Murrysville, PA) to generate positive and negative pharyngeal airway pressures, and the pressure within the nasal mask upstream to the collapsible pharyngeal area was measured electromanometrically by a differential pressure transducer (Validyne MP45; Validyne Engineering, Northridge, CA) via an air-filled tube connected to a dedicated port in the nasal mask. Epiglottic (downstream) pressure was measured by a custom-built catheter tip micromanometer (Millar Instruments, Houston, TX) calibrated in warm (37°C) saline before placement. This catheter was inserted through a nostril, and its correct position was assumed when the catheter tip, observed through the volunteer’s open mouth upon advancement, just disappeared behind the base of the tongue. Respiratory flow was measured using a pneumotachograph (Model 3830; Hans Rudolph, Kansas City, MO) with a direct-current-amplifier (MIO-0501; FMI, Seechem, Germany) and a differential pressure transducer (Model DP45-32 with CD15 Carrier Demodulator; Validyne Engineering) connected to the mask. The pneumotachograph was calibrated with a large volume (2 l) syringe.

To assess $P_{\text{crit}}$, mask pressure was randomly decreased from baseline to pressures between $-100$ and $-30 \text{ cm H}_2\text{O}$ for four breathing cycles. Afterwards, airway pressure was returned to $+2 \text{ cm H}_2\text{O}$, i.e., to a pressure not associated with flow limitation at baseline in all volunteers. At least 1 min was allowed to elapse before the next induced airway pressure change.\textsuperscript{14,15}

$P_{\text{crit}}$ was calculated from the flow-limited breaths, as described previously.\textsuperscript{15} Flow limitation was defined as unchanged inspiratory flow despite a further decrease in pharyngeal (epiglottic) pressure\textsuperscript{16} and a flattened flow tracing in a flow-time plot.\textsuperscript{17} Mask pressure was then plotted versus flow for the flow limited breaths and fitted using a linear regression model. A representative calculation of the critical closing pressure is shown in figure 1.

Genioglossus muscle electromyogram was measured via 32-gauge hook-wire electrodes (length, 50 mm; Vysys Healthcare, Hoechberg, Germany) that were inserted transcutaneously into the genioglossus muscle via 26-gauge needles after visualization of the submental region by ultrasound and local anesthesia of the skin with lidocaine 2%. The electrodes were referenced to a ground electrode placed on the upper arm. The genioglossus electromyogram signal was filtered (band-pass filter, 30–1000 Hz), amplified, and rectified (Grass Amplifier Model G62C-3; Grass Technologies, West Warwick, RI) and displayed as raw signals and as a moving time average (time constant, 100 ms) of the filtered and rectified signal. The amplifier was adjusted to yield a full-scale deflection of the respective recorder channel when the volunteer pressed his tongue with maximum force against his teeth with the mouth closed. The amplitude of the moving time average recorded during the second and third consecutive breaths after a mask pressure drop were averaged and used for quantitative analysis of the genioglossus muscle electromyogram.
Tidal volume and variables of respiratory timing were measured by respiratory inductance plethysmography (LifeShirt; VivoMetrics, Ventura, CA). The transducers were fitted according to the manufacturer’s sizing chart and calibrated. Data were digitally recorded (LifeShirt200 recorder, VivoMetrics), stored on a memory card, and processed on a computer (VivoLogic V 3.1 software, VivoMetrics). Respiratory rate, tidal volume, inspiratory and expiratory time, inspiration to expiration ratio, and changes in end-expiratory lung volume were averaged from 20 breaths preceding the mask pressure drop maneuvers.

The degree of neuromuscular blockade was continuously measured by accelerometry of the adductor pollicis muscle with ulnar nerve stimulation (TOF-watch SX®; Organon, Dublin, Ireland). The skin on the forearm was cleansed with an alcohol wipe. The skin was first prepared with an abrasive paste (NuPrep Gel; D.O. Weaver, Aurora, CO), then cleaned with 80% ethanol, and finally dried with gauze. We randomly used the volunteers’ right (n = 7) or left (n = 8) ulnar nerve for stimulation. Two stimulation surface electrodes (PNS electrode; NDM, Dayton, OH) were placed over the ulnar nerve, with one electrode positioned on the ulnar side of the flexor carpi radialis tendon and the other positioned 3 cm proximal to the first. The transducer was positioned with the flat side against the thumb. A supramaximal stimulation current was determined with a 5-mA increase in stimulation current during five consecutive stimuli increasing twitch height by less than 5%. This was checked twice, and this stimulation current was subsequently used for measurements, providing a stable signal. During a subsequent 30-min period for signal stabilization, we used single-twitch stimulation, during which an increasing response was observed (staircase phenomenon). The TOF-Watch SX was then calibrated using the CAL 1 sequence (Operating Manual TOF-Watch® SX; Organon) to set the T1 response to 100% (baseline). Stimulation was continued in the TOF mode, and a supramaximal stimulation current was applied throughout the experimental protocol. The data obtained by the TOF-watch SX were transferred to and stored in a personal computer using the TOF-link interface and the TOF-watch SX monitoring software (Organon).

For safety reasons, arterial oxygen saturation (digit II) and end-tidal carbon dioxide concentration (sample port in the nasal mask) were measured using an anesthesia monitor (Dräger®, PM8050, Lübeck, Germany).

**Experimental Protocol**

Surface electrodes (PNS Electrode, NDM) were attached to the cleansed skin (see above) over the ulnar nerve, each nostril was decongested (0.3 ml of 0.05% oxymetazoline; Novartis, Munich, Germany), and 0.5 ml of 4% lidocaine (Astra Chemicals, Wedel/Holstein, Germany) was applied to one nostril to ease catheter advancement. To monitor an electrocardiogram, three stick-on surface electrodes were placed on the chest and shoulders, and a pulse oximeter was placed on digit II.

Thereafter, a submental skin area topographically corresponding to a tongue region 3–4 mm lateral to the frenulum on each side was anesthetized intradermally by lidocaine, and the hook electrodes inserted into the genioglossus muscle. A nasal mask was then administered and held in place with a head strap. After placing an intravenous 20-gauge catheter into a forearm vein, the degree of neuromuscular blockade was measured continuously by accelerometry (TOF-watch SX®, Organon) after determination of the supramaximal stimulation current. With the calibrated transducers in place, the volunteer was then asked to perform the following maneuvers: (1) swallow several times, (2) push the tongue against the front teeth as hard as possible several times, and (3) inspire as hard as possible several times while the inspiratory line of the airway was occluded.

After baseline measurements, 0.1 mg/kg rocuronium (Organon Teknika, Eppelheim, Germany) was injected and followed by a continuous infusion (10–80 mg/h), as guided by TOF measurements. Initially, a TOF ratio of 0.5 was always targeted. When steady state conditions were achieved at a TOF ratio of 0.5, rocuronium administration was adjusted to maintain a neuromuscular blockade at that degree for at least 5 min before measurements were performed. A TOF ratio range of 0.45–0.55 (deviation of up to 10%) was considered acceptable, and all measurements were performed within that range. The rocuronium infusion was subsequently decreased to achieve a TOF ratio of 0.8. After a stable TOF ratio of 0.8 (± 10%) was recorded for at least 5 min measurements were performed before the rocuronium infusion was terminated. A final series of measurements was performed at time of recovery of the TOF ratio to unity.

Pressure and flow signals were recorded in parallel on digital tape (Model RD 200 T; TEAC, Wiesbaden-Erbenheim, Germany) and with a digital recording system (Powerlab® 16/38; ADInstruments, Colorado Springs, CO), and also documented on a thermoarray recorder (Dash® 16; AstroMed, West Warwick, RI). Data were assessed using Chart 4.0® software (ADInstruments).

**Statistical Analyses**

Data are presented as means ± SD with the exception of the genioglossus electromyogram, which is given as means ± SEM. Statistical analyses were performed using SPSS 11.0 (SPSS Inc., Chicago, IL). We tested the a priori hypotheses that during partial neuromuscular blockade (1) passive Pcrit is less negative with TOF ratios of 0.5, 0.8, and unity than at baseline and (2) electromyogram activity of genioglossus muscle in response to negative pharyngeal pressure is decreased. Differences in Pcrit (primary criterion) between baseline
and neuromuscular blockade were compared with the Student t test for paired samples. On the basis of our previous study of the effects of partial neuromuscular blockade on muscle activity during swallowing, we estimated (paired t tests) that 15 volunteers would provide a 99% and 80% power to detect with an α-error P of 0.05 a change in critical airway closing pressure of 20% and 10% during partial neuromuscular blockade (at TOF ratios 0.5 and 0.8, respectively).

We selected genioglossus electromyogram activity as a secondary criterion to be tested only if significant results in testing the primary criterion were obtained. We used a linear mixed model for repeated measures, including neuromuscular function (baseline, TOF ratios of 0.5, 0.8, and 1) and mask pressure (from +1 to -30 cm H$_2$O) as repeated variables. First, all data (15 volunteers, 4 levels of neuromuscular function, 7 levels of mask pressure = 420 data points) were entered into the model to test for an effect on genioglossus activity of neuromuscular function and of mask pressure. In the second step, we tested for specific differences in genioglossus activity between baseline and a TOF ratio of 0.5, 0.8, and 1, respectively. A total of 210 data points were entered into the model to enable comparison to baseline. Finally, we used covariance analysis to determine the variance of the increase in upper airway passive closing pressure during neuromuscular blockade that can be explained by its effects on genioglossus activity and inspiration/expiration ratio.

All other comparisons were made with an exploratory intention. We compared by paired t tests between baseline and partial neuromuscular blockade variables of breathing, change in end-expiratory lung volume, tidal volume, respiratory rate as well as respiratory timing.

Results

Pcrit

A representative recording from one subject at different degrees of neuromuscular blockade and different mask pressures is shown in figure 2. Critical airway closing pressure averaged -54.7 ± 18.7 cm H$_2$O at baseline, but it significantly increased (to less negative values) during partial neuromuscular blockade (fig. 3). Specifically, Pcrit increased by 54 ± 4.4% and 37 ± 4.2% at TOF ratios of 0.5 and 0.8, respectively, and Pcrit was still significantly increased by 16 ± 4.1% (P < 0.01 vs. baseline) even after the TOF ratio had returned to unity.

Onset of flow limitation was observed at a mean mask pressure of -12.6 ± 3.3 cm H$_2$O at baseline without neuromuscular blockade, but it occurred at significantly higher pressures (-5.8 ± 1.8 cm H$_2$O and -9.8 ± 2.9 cm H$_2$O) at TOF ratio s of 0.5 and 0.8, respectively (fig. 3).

Genioglossus Muscle Activity

Genioglossus muscle activity increased as mask pressure decreased, but the increase in activity was significantly less during partial neuromuscular blockade (P < 0.05). This was particularly true for comparison of values at a TOF ratio of 0.5 compared to baseline (P = 0.004). Interestingly, at mask pressures close to atmospheric pressure, mean genioglossus activity did not differ from baseline at a TOF ratio of 0.5, but values were significantly lower during neuromuscular blockade when the airway was challenged by negative pharyngeal pressures (fig. 4).

Other Respiratory Variables

End-expiratory lung volume, respiratory rate (13 ± 3 breaths/min), tidal volume (352 ± 120 mL), and mean inspiratory flow (150 ± 106 mL/s) did not change significantly during partial neuromuscular blockade. Inspiratory-to-expiratory ratio averaged 0.56 ± 0.2 at baseline, and tended to increase (P = 0.064) at TOF ratio s of 0.5 (0.63 ± 0.17), 0.8 (0.61 ± 0.2), and unity (0.6 ± 0.17). Oxygen saturation did not change significantly.

Association between Genioglossus Activity, Respiratory Timing, and Upper Airway collapsibility

Based on the findings of increased Pcrit and decreased genioglossus activity during minimal neuromuscular blockade, we performed a covariance analysis to evaluate the variance of the Pcrit increase during neuromuscular blockade that can be explained by its effects on genioglossus activity and inspiratory-to-expiratory ratio. These variables together with the target degree of neuromuscular blockade (baseline, TOF = 0.5, TOF = 0.8, TOF = 1) explained 26% (r-square) of the variance of the change in Pcrit (P < 0.015) and thus independently influenced upper airway collapsibility during neuromuscular blockade.

Neuromuscular Transmission Data

The stimulation current used amounted to 45.6 ± 7.5 mA. Baseline TOF ratio before administration of neuromuscular blocking drugs averaged 1.044 ± 0.042, and TOF ratio at unity was 1.028 ± 0.018. Normalized TOF ratios (normalized to a baseline TOF ratio of 1) during partial neuromuscular blockade amounted to 0.48 ± 0.02, 0.79 ± 0.05, and 0.98 ± 0.04, respectively, at the three target TOF ratios of 0.5, 0.8, and unity.

Discussion

Minimal neuromuscular blockade (TOF ratio 0.5–1) markedly increased upper airway collapsibility and impaired the genioglossus response to negative pharyngeal pressure challenges.
To maintain upper airway patency during inspiration, it appears reasonable that the forces generated by the respiratory pump muscles decreasing intraluminal upper airway pressure and tending to collapse the airway should be balanced by dilating forces. The upper airway dilator muscles deliver these dilating forces, but it is largely unknown whether this balance is maintained during recovery from neuromuscular blockade. It has been shown in animals\textsuperscript{21,23} and in humans\textsuperscript{10,11} that upper airway muscles are more susceptible to effects of neuromuscular blocking agents than the diaphragm.\textsuperscript{11,21,23} Sundman and Eriksson\textsuperscript{10} showed an increased incidence of misdirected swallowing and a decreased upper esophageal sphincter resting tone during minimal neuromuscular blockade (TOF ratio 0.5–1) that persisted even with recovery of the TOF ratio to unity. Likewise, we have previously shown that genioglossus activity during swallowing and maximum voluntary

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pressure compared with activity near atmospheric pressure almost quadrupled at negative pharyngeal way dilator muscle activity during minimal neuromuscular interplay between air flow and genioglossus upper airway increased inspiratory airway volume by elucidating the Our results also extend our previous findings on de- nioglossus activity increases markedly and significantly as neg- ative values of mask pressure, i.e., air- way integrity is impaired. *P < 0.05 versus baseline.
tongue contraction is impaired at a TOF ratio of 0.8.11. Our results also extend our previous findings on de- creased inspiratory airway volume by elucidating the interplay between air flow and genioglossus upper air- way dilator muscle activity during minimal neuromuscu- lar blockade.

In the absence of neuromuscular blockade, genioglos- sus activity almost quadrupled at negative pharyngeal pressure compared with activity near atmospheric pres- sure. However, during minimal neuromuscular block- ade, this obviously compensatory increase in genioglossus muscle activation to maintain an open airway was markedly impaired. Our data show that a decrease in maximum genioglossus activation as observed during minimal neuromuscular blockade is sufficient to evoke markedly increased airway collapsibility. Effects on genioglossus activation of minimal neuromuscular blockade explain significant variance of its effects on the upper airway critical closing pressure. Thus, our data suggest that minimal neuromuscular blockade evokes increased upper airway collapsibility by blunting upper airway dilator compensatory responses to negative pharyngeal pressure.

The relation between the decrease in genioglossus activity evoked by neuromuscular blockade and its ef- fects on upper airway closing pressure compares very well to findings in patients with obstructive sleep apnea. Patients with obstructive sleep apnea have small upper airways for anatomical reasons, and they show a de- creased genioglossus electromyogram activity during sleep onset that parallels the observed upper airway collapse.24,25 Our healthy volunteers did not have any evidence of pathologic airway anatomy; consistent with that, their airways did not collapse at atmospheric pressure in the absence of neuromuscular blockade. Obstruc- tive sleep apnea patients also have higher genioglossus activity in the awake state than normal volunteers presumably compensating for their anatomical disposition responsible for small upper airways. However, this mechanism no longer works during sleep when genio- glossus muscle activity decreases and upper airway ob- struction ensues. Similarly, in postoperative patients un- der the influence of opioids and/or sedatives, in addition to residual neuromuscular blockade, an impaired ability of the upper airway dilator muscles to produce a compen- satory increase in activity might put a patient at risk for airway collapse. An increased risk for airway collapse as evoked by residual neuromuscular blockade is also plausible during additional challenges of the airway, such as by airway secretions, edema, anatomical narrowing, obesity, or obstructive sleep apnea.

The effects of minimal neuromuscular blockade on airway patency could potentially be partly compensated by changes in respiratory timing. During partial neuromuscular blockade, we observed a trend (P = 0.068) towards an increased ratio of inspiratory-to-expiratory time compared with baseline (by approximately 10%). An increased inspiratory time may have helped to stabi- lize the airway during inspiration such that increased airway collapsibility evoked by upper airway dilator mus- cle dysfunction was ameliorated.13,16 A suggestion that is supported by the results of covariance analysis. Inspirato-ry-to-expiratory ratio was negatively associated with upper airway critical closing pressure.

Our data also show that minimal neuromuscular block- ade (TOF ratio 0.5–0.8) and possibly even a TOF ratio of

Fig. 3. Upper airway critical closing pressure (Pcrit) and airway pressure associated with beginning of flow limitation in awake healthy volunteers at baseline before neuromuscular blockade, with impaired neuromuscular transmission and a target train-of-four (TOF) ratio of 0.5 and 0.8, and after recovery of the TOF ratio to unity. Data are means (± SD) from 15 volunteers. Upper airway closing pressure (black bars) significantly increased during partial neuromuscular blockade and was still abnormal, even with recovery of the TOF ratio to unity. With neuromuscular transmission intact at baseline, evidence of flow limitation (gray bars) was first observed at an average pressure of –12 cm H2O. With partial neuromuscular blockade at a TOF ratio of 0.5 and 0.8, flow limitation occurred at significantly less negative values of mask pressure, i.e., air- way closing pressure (Pcrit) was first observed at an average pressure of –12 cm H2O. With partial neuromuscular blockade at a TOF ratio of 0.5 and 0.8, flow limitation occurred at significantly less negative values of mask pressure, i.e., air- way closing pressure (Pcrit) was first observed at an average pressure of –12 cm H2O. With partial neuromuscular blockade at a TOF ratio of 0.5 and 0.8, flow limitation occurred at significantly less negative values of mask pressure, i.e., air-

Fig. 4. Genioglossus muscle activity as a function of negative mask pressure without (open circles) and with (full triangles) partial neuromuscular blockade at a target train-of-four (TOF) ratio of 0.5. Data are means (± SEM) from 15 volunteers. Genioglossus activity increases markedly and significantly as negative pressure is applied. However, the magnitude of this effect is significantly attenuated with partial neuromuscular blockade. *P < 0.05 versus baseline (same mask pressure); #P < 0.05 versus mask pressure +2 cm H2O (same level of neuromuscular function). MTA = moving time average; AU = arbitrary units.
unity do not rule out impaired integrity of the airway. This is in accordance with a recent study showing that even small degrees of residual block have at least short-term clinical effects.26

Respiratory rate, tidal volume and oxygen saturation remained unchanged during neuromuscular blockade in our volunteers, a finding consistent with previous studies.11,27 In postoperative patients, the degree of neuromuscular blockade studied (TOF ratio 0.5–0.8) can lead to airway obstruction associated with oxygen desaturation in the recovery room.26,28 The increased respiratory consequences of partial neuromuscular blockade in patients in a postanaesthesia care unit26,28 compared with those observed in our study may be explained by effects of narcotics/sedatives/anesthetics potentiating those of partial neuromuscular blockade.

We targeted a TOF ratio of 0.5 and 0.8. The lowest degree of partial neuromuscular blockade reliably detectable by optical or manual evaluation of the muscular response to TOF stimulation (i.e., without quantitative neuromuscular transmission monitoring)29 or with “bedside” tests of neuromuscular function used by many clinicians, such as head lift and tidal volume,30 is a TOF ratio of approximately 0.5.29,30 Quantitative neuromuscular transmission monitoring is not routinely applied by many clinicians31,32; it is therefore likely that upper airway collapsibility induced by partial paralysis will not be detected in patients with a TOF ratio between 0.5 and 1. Possibly, quantitative monitoring of the TOF ratio is useful to prevent patients from being exposed to the risks of an unidentified impairment of upper airway patency.

Intraoperative acceleromyography monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanaesthesia care unit.28 However, impaired upper airway integrity was observed, even with recovery of the TOF ratio to unity, although evoked mean genioglossus activity had already recovered to baseline. This observation may imply that residual neuromuscular blockade of airway muscles may not be reliably detected in the periphery by accelerometry. Furthermore, many studies have found that the control TOF ratio (measured before administration of a neuromuscular blocking agent) is greater than 1 when acceleromyography is used.33 Therefore, some authors suggest that the TOF ratio derived by accelerometry should be normalized to the baseline TOF value to better reflect mechanomyographic readings.33,34 In our study, baseline TOF ratio averaged 1.04. Accordingly, a (not normalized) TOF ratio of unity after recovery represents a normalized TOF ratio of only 0.98. These differences are quite minor, and it is unclear whether upper airway closing pressure would have fully returned to baseline levels at recovery of the normalized TOF ratio to unity. In fact, upper airway collapsibility was significantly impaired even when genioglossus activity had recovered to baseline. Accordingly, mechanisms other than genioglossus dysfunction may contribute to the persistent increase of Perit, such as velopharyngeal airway dilator muscle dysfunction. Imaging studies during complete35 or partial11 neuromuscular blockade and in patients with obstructive sleep apnea36 suggest that the soft palate plays an important role in mediating airway narrowing during airway muscle paralysis35,11 and sleep.36 Thus, further work on the function of airway openers other than the genioglossus muscle should be performed.

Reversal of residual neuromuscular blockade is an important goal for patients’ postoperative safety,37 and it is associated with a decreased risk of 24-h postoperative morbidity and mortality.37,38 We believe that even small degrees of neuromuscular blockade should be reversed, if waiting for spontaneous recovery is not considered reasonable. However, the beneficial effects of reversal agents must be counterbalanced with the potential risk of side effects, particularly when high doses of neostigmine are given without monitoring neuromuscular transmission.21 Further studies should focus on the optimal doses of reversal agents required to reverse minimal neuromuscular blockade.

In summary, minimal residual neuromuscular blockade in the awake state, in the absence of anesthetics and surgery, and to a degree insufficient to evoke respiratory symptoms markedly increased upper airway collapsibility and impaired the genioglossus muscle compensatory response to pharyngeal negative pressure challenges. Increased upper airway collapsibility due to residual neuromuscular blockade, is likely to put a patient at risk during recovery, particularly in the presence of airway challenges.

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