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Phonomyography as a Novel Method to Determine Neuromuscular Blockade at the Laryngeal Adductor Muscles

Comparison with the Cuff Pressure Method

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Background: **Neuromuscular blockade at the laryngeal adductor muscles may be measured using the cuff of a endotracheal tube placed between the vocal cords. Phonomyography is an alternative method of neuromuscular monitoring. In this study, phonomyography is applied to determine blockade at the larynx and compared with the cuff pressure method.**

Methods: **After the authors obtained approval from the ethics committee and informed consent, 28 patients were entered in the study. After induction of anesthesia, a endotracheal tube was inserted. Its cuff was placed in the trachea in routine fashion (n = 14) or between the vocal cords (n = 14). In all patients, a small condenser microphone was placed in the vestibular fold, just lateral to the tube, next to the laryngeal adductor muscles. The recurrent laryngeal nerve was stimulated supramaximally with single twitch stimulation (0.1 Hz) for onset, and train-of-four stimulation every 12 s during offset of neuromuscular blockade was produced by 0.1 mg/kg mivacurium. Onset and recovery of neuromuscular blockade measured by the two methods were compared using the *t* test ($P < 0.05$), and a Bland-Altman test was performed to define agreement between the two methods. Onset and recovery of neuromuscular blockade measured by phonomyography with the cuff placed between the vocal cords or in the trachea were compared using the *t* test ($P < 0.05$).**

Results: **Mean onset, maximum effect, and time to reach 25% and 75% of control twitch response for phonomyography *versus* cuff pressure method were 145 s (SD, 25) *versus* 156 s (SD, 33), 89% (SD, 4) *versus* 91% (SD, 4), 9 min (SD, 4) *versus* 10 min (SD, 3), and 27 min (SD, 4) *versus* 29 min (SD, 4), respectively, without being significantly different. Mean bias was −2%, with limits of agreement of −20 and +18% for all signals (cuff method minus phonomyography). There was no significant difference in onset and offset of neuromuscular blockade measured using phonomyography with the cuff placed between the vocal cords or in the trachea.**

Conclusions: **Both methods can be used interchangeably to determine neuromuscular blockade of the laryngeal adductor muscles. Phonomyography allows measurement of laryngeal blockade with the endotracheal tube in the normal position.**

NEUROMUSCULAR blocking agents are given to facilitate tracheal intubation, and adequate relaxation of the vocal cords is one of their desired effects. More than a decade ago, Donati *et al.*[1] presented a method of neuromuscular monitoring at the larynx using the cuff of an endotracheal tube placed between the vocal cords. This method has been the gold standard in research to measure the force of the contraction of the laryngeal adductor muscles and to determine the degree of neuromuscular blockade.

This form of laryngeal mechanomyography, however, has several disadvantages. The cuff pressure is subject to variations with the respiratory cycle, and initial placement of the endotracheal cuff between the vocal cords without neuromuscular blockade very often produces coughing and subsequent displacement of the cuff. Neuromuscular blockade itself changes the tone of the vocal cord muscles and surrounding area and can produce drifts in baseline pressure.[2] Using a single-cuff endotracheal tube for measuring the neuromuscular blockade further bears the risk of accidental extubation and requires great care.

Electromyography using either a special endotracheal tube with implemented wire electrodes[3] or a surface electrode[4] has been successfully used to measure neuromuscular blockade at the larynx. However, electromyography and mechanomyography do not measure the same physical phenomenon, and both methods are not interchangeable.[5,6] Phonomyography is a relatively new method to measure neuromuscular blockade.[7–9] It is based on the fact that muscle contraction generates sounds of low frequency.[10,11] Earlier studies[7,8] have used an air chamber microphone to measure neuromuscular blockade at the adductor pollicis muscle and produced contradictory results as to whether phonomyography and other methods of monitoring neuromuscular blockade can be used interchangeably. To improve the quality of the phonomyographic recordings, we chose a small condenser microphone without an air interface, capable of picking up low-frequency signals to monitor neuromuscular blockade at the corrugator supercilii muscle.[9] Phonomyography was easy to use, produced stable signals, and was easy to interpret with a low rate of artifacts.[9]

This study presents phonomyography of the larynx as a new method to measure neuromuscular blockade at the laryngeal adductor muscles and compares it with the established cuff pressure method.

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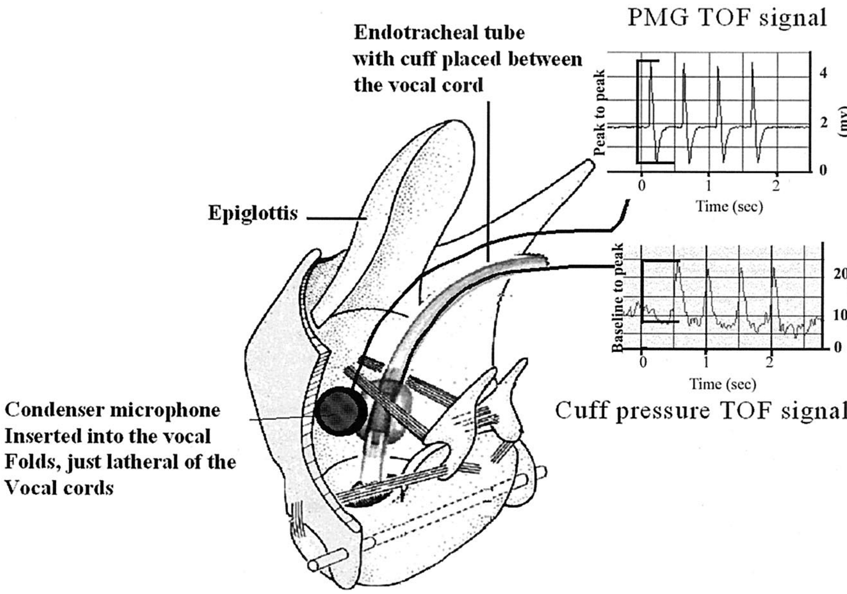

Fig. 1. Illustration of the location of cuff and microphone with the respective train-of-four (TOF) signals. Black bars indicate the amplitude of the signal as measured with both methods. Amplitude was measured as (negative) peak to (positive) peak with phonomyography, baseline to peak with cuff pressure method. PMG = phonomyography.

Materials and Methods

After we obtained approval from the local ethics committee and informed consent, 28 patients undergoing general surgery in controlled ventilation using an endotracheal tube were included in the study. Patients with coexisting neuromuscular disease or patients on medication known to interact with neuromuscular transmission were excluded.

After arrival in the operating room, routine monitoring (noninvasive blood pressure, pulse oximetry, electrocardiography) was started. Anesthesia was induced with a continuous infusion of 0.25–0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil; 2 min later 2–3 mg/kg propofol was injected. After loss of consciousness and ventilation *via* face mask for 2 min with 100% oxygen, the trachea was intubated using a routine endotracheal tube (Mallinckrodt, St. Louis, MO; size 8 for men, size 7 for women) without the use of neuromuscular blocking agents. The cuff was placed in the trachea in routine fashion (n = 14) or placed between the vocal cords and connected to a pressure transducer (n = 14). The cuff of the endotracheal tube was inflated with up to 10 ml of air (sufficient to prevent leakage). Anesthesia was maintained with 1–1.5 minimum alveolar concentration of sevoflurane in a breathing gas mixture of 30% oxygen in air. Analgesia was provided with 0.05–0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil. Minute ventilation was set to maintain an end-tidal carbon dioxide pressure of 3.5–4.5 kPa. Superficial stimulation of the recurrent laryngeal nerve using routine electrocardiographic surface electrodes[1] was commenced using a constant current stimulator (Innervator®; Fisher and Paykel Healthcare, Auckland, New Zealand) that generated single-twitch square pulses of 0.2 ms with a current intensity between 0 and 70 mA (single twitch 0.1 Hz for onset, train-of-four stimulation every 12 s for offset of neuromuscular blockade, the frequency of mechanical ventilation was synchronized with the stimulation frequency to avoid stimulation during inspiration or exhalation). Supramaximal stimulation for phonomyography and the cuff pressure method was determined using single-twitch stimulation at 0.1 Hz. The cuff pressure signal was amplified using an AC/DC amplifier (Model 7P122; Grass Instruments, Astra-Med, Inc., West Warwick, RI), and its amplitude was measured. A small condenser microphone (diameter: 1.6 cm, Model 1010; Grass Instruments, Astra-Med, Inc.; frequency response: 2.5 Hz to 5 kHz, signal output: 20–40 mV into 1 MΩ) was inserted into the left vestibular folds just lateral to the vocal cords to record the acoustic signals produced by the contraction of the laryngeal adducting muscles using a Maggil straight forceps (fig. 1). Its correct position was again verified at the end of the measurement period. The microphone signal was amplified and bandpass filtered between 0.5 and 1,000 Hz using an AC/DC amplifier (Model 7P122; Grass Instruments, Astra-Med, Inc.). The signals were continuously sampled at 100 Hz using the Polyview® software package (Astra-Med, Inc.), digitized, and stored on a portable microcomputer. The single-twitch phonomyography signal was measured peak to peak (fig. 1), its peak frequency determined by Fast Fourier transformation using the Polyview® software package. After at least 5 min of supramaximal stimulation and stable baseline values for both recordings, 0.1 mg/kg mivacurium was injected within 5 s into a fast-flowing solution of Ringer lactate.

The first twitch response was used to analyze onset time (time to reach maximum decrease of twitch response) and time to reach 25% and 75% of control twitch response. The maximum effect was determined as the maximum decrease of the twitch response and was also recorded.

Table 1. Onset, Offset, and Maximum Effect of Neuromuscular Blockade at the Adducting Laryngeal Muscles After 0.1 mg/kg Mivacurium

	Phonomyography* (N = 14)	Phonomyography† (N = 14)	Mechanomyography (N = 14)
Onset time, s	137 (37)	145 (25)	156 (33)
Maximum effect, %	90 (6)	89 (4)	91 (4)
T 25%, min	9 (5)	9 (4)	10 (3)
T 75%, min	27 (6)	27 (4)	29 (4)

* Results obtained with the endotracheal cuff placed in the trachea. † Results obtained with the endotracheal cuff placed between the vocal cords.

Maximum effect = maximum decrease in twitch height in comparison to control twitch height; Onset time = time to reach maximum effect; T 25% = time to reach 25% of control twitch height; T 75% = time to reach 75% of control twitch height.

These data were compared between the two methods using the *t* test; $P < 0.05$ was considered as showing a significant difference. The mean difference of all signals determined using both methods and the limits of agreement between the two methods were analyzed using Bland-Altman test.[12] Pharmacodynamic data derived using phonomyography with the cuff first in the trachea or between the vocal cords were compared using the *t* test; $P < 0.05$ was considered as showing a significant difference. Data are presented as mean values (SD).

Results

In all patients, pharmacodynamic results with both methods could be obtained. Placement of the microphone was possible under direct laryngoscopy and with the aid of a Maggil straight forceps in all patients within 1 min. The microphone was still in the correct position at the end of the measurement period in all patients. When the cuff was placed between the vocal cords, 6.7 ml (SD, 2.1) of air was inflated to prevent leakage. Recordings of signals were continued for 1 h after mivacurium injection, and at this point, train-of-four ratios were greater than 0.9 in all patients. In three patients, cuff pressure signals reached only 90% of the initial amplitude at the end of the measurement period. A typical phonomyography signal is shown in figure 1. The peak frequency response was 6.5 Hz (SD, 2; range, 4.5–8.6 Hz).

Onset, maximum effect, and time to reach 25% and 75% of control twitch were very similar for both methods (table 1). Mean bias was −2% with limits of agreement of −20 and +18% for all signals (cuff method minus phonomyography; fig. 2). There was no significant difference between onset, maximum effect, and offset of neuromuscular blockade measured using phonomyography when the endotracheal cuff was placed in the trachea or between the vocal cords (table 1).

Discussion

Onset and offset of neuromuscular blockade measured using phonomyography produced results that were very similar to those obtained using the cuff pressure method, which is considered the gold standard. The advantage of phonomyography lies in the fact that it is independent of the endotracheal tube, thus allowing intubation and placement of the cuff in a routine fashion, therefore avoiding the risk of accidental extubation. In comparison to the cuff pressure method, the baseline of phonomyography is stable, there are no changes caused by respiration, and the signal detection is generally less prone to artifacts, especially with higher degrees of neuromuscular blockade. The stable position and record-

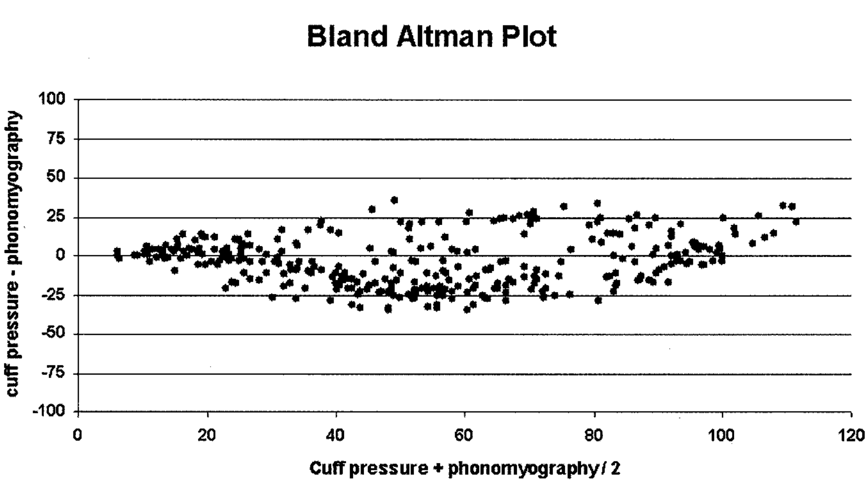

Fig. 2. Bland-Altman plot for all evoked signals (% of control amplitude height); mean bias was −2%, with limits of agreement of −20 and +18% for all signals (cuff method minus phonomyography).

ing capacity of the microphone does not rely on the endotracheal cuff placed between the vocal cords but can be easily achieved with the endotracheal cuff placed in the trachea.

A problem with the cuff pressure method has recently been described by Girling *et al.*[2] and consists of the fact that the intracuff pressure changes during neuromuscular blockade of the larynx, thereby underestimating the actual degree of block. These investigators therefore proposed that reinflation of the cuff during blockade is necessary to ensure proper contact and valid results. However, care must be taken to reinflate to exactly the same level, otherwise the final value might be different from the initial control. In the current study, we noticed that the results obtained from phonomyography and the cuff pressure method differed more in the initial periods of recovery, with the cuff pressure method generally being less sensitive to detect the earliest phases of recovery. We explain this by the cuff losing contact with the "relaxed" vocal cords, therefore overestimating the actual degree of neuromuscular blockade. Loss of contact between monitoring sensor (the cuff, an electromyographic electrode, or a microphone) is a theoretical problem of all methods of monitoring laryngeal neuromuscular blockade since, in contrast to monitoring superficial muscles, the sensors are not attached (either inserted or glued) to the muscle or the overlying skin. Verification of secure contact and position of the microphone at the end of the measurement period ensures correct results. The opening of the vocal cords and the respiration-induced movement of the cuff between the vocal cords—or across—can disturb the proper tracing of neuromuscular blockade. The mechanism of recording the force of the contraction of the laryngeal adductor muscles by measuring pressure changes bears the problem that changes in the position of the cuff as a "pressure" balloon caused by longitudinal movements of the cuff, changes in intracuff pressure, or changes in vocal cord opening can influence the recording quality and the changes of cuff pressure recorded. This remains a problem even with a modified cuff pressure technique, where the risk of accidental extubation is eliminated by using a special endotracheal tube with two cuffs (one placed in the trachea, one placed between the vocal cords to monitor the response of the vocal cords).

We took great care when placing the microphone beside the laryngeal adductor muscles. It is performed in such a way that there is a direct contact with the laryngeal adductor muscles, controlling the correct position of the microphone after complete offset of neuromuscular blockade. The size of the microphone proved actually to be more of a help than a hindrance since it prevented the movement of the microphone during the study period and kept it in place.

The first two studies using phonomyography to monitor neuromuscular blockade were contradictory. Dascalu *et al.*[7] found minimal bias and narrow limits of agreement between phonomyography, acceleromyography, and mechanomyography when used during clinical conditions to monitor neuromuscular blockade at the adductor pollicis muscle, whereas Bellemare *et al.*[8] found that at low and moderate degrees of neuromuscular blockade after a bolus injection of rocuronium, there was a significant bias and unacceptable limits of agreement between mechanomyography and phonomyography at the adductor pollicis muscle. Both studies used similar microphones with air chambers but did not provide technical specifications of the microphones used (such as frequency response). These microphones are too bulky to be used internally. To determine neuromuscular blockade at the corrugator supercilii muscle, we have successfully used a small condenser microphone whose frequency response is such that it can detect signals down to a frequency of 2 Hz.[9] In that study, we presented a frequency domain analysis of the signals and determined a peak frequency of 4 Hz, well within the range of our microphone. The peak frequency determined here is slightly higher at 6.5 Hz. Technical aspects, such as the distance between the microphone and the muscle, the angle between the microphone and the morphology of the muscle itself, play an important role in the physiology of the signal reception and have an influence on the signal height.[11] The condenser microphone has several advantages: it is small, can be glued directly onto the skin or inserted into the throat, and the acoustic signals are stable with a flat baseline. Subjectively, the analysis of the evoked acoustic signals was easier and faster than the analysis of the cuff pressure signals. Our first experience showed that its position beside the vocal cords remains stable and does not need to be corrected. No microphone was displaced. The microphone is attached to a cable, preventing any "loss" or movement of the microphone into the esophagus. At this point, the microphone needs to be placed into the vestibular folds using a Maggil forceps; we have now attached the microphone to an flexible introductory tube, which allows the placement without the use of the Maggil forceps and further stabilizes its position. The time for introduction of the microphone (< 1 min) seems already very fast. At this point, phonomyography of the larynx is an easy-to-apply method, and results of neuromuscular blockade can be used interchangeably with results derived using the cuff pressure method. We favor phonomyography because of the more stable baseline, ease of signal analysis, absence of respiratory artifacts, and absence of risk of accidental extubation or cuff displacement.

We believe that phonomyography of the larynx can be used to detect neuromuscular blockade not only at the laryngeal adductor muscles, but also at the abductor laryngeal muscle. The encouraging results of this study should lead to a reexamination of the validity of phonomyography using a condenser microphone at other muscles, such as the adductor pollicis muscle. In theory, phonomyography is applicable to all muscles of interest in neuromuscular research, such as the diaphragm, the larynx, and the peripheral muscles. If validation of phonomyography at these muscles against mechanomyography or electromyography (diaphragm) supports the first promising findings of our study of good agreement with the method of reference, a novel model could be used in neuromuscular research where simultaneously neuromuscular blockade is recorded at all muscles of interest using the same noninvasive method. The ease of applying a small microphone over peripheral muscles, such as the corrugator supercilii muscle or the adductor pollicis muscle, used to monitor neuromuscular blockade in daily routine, should lead to the development of this method and simple devices using this method to monitor neuromuscular blockade.

We conclude that phonomyography and the cuff pressure method can be used interchangeably to detect neuromuscular blockade at the laryngeal adductor muscles. Phonomyography allows measurement of laryngeal blockade with the endotracheal tube in the normal position.

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