General Anesthesia

Monitoring neuromuscular blockade at the vastus medialis muscle using phonomyography

[Le monitoring du bloc neuromusculaire du muscle vaste interne du membre inférieur avec phonomyographie]

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Purpose: The vastus medialis muscle has been recently proposed as a new site for monitoring neuromuscular blockade (NMB). The purpose of this study is to compare NMB at the vastus medialis with the adductor pollicis muscle using phonomyography (PMG).

Methods: Fifteen patients were enrolled in the study. Anesthesia was induced with remifentanyl 0.25 to 0.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, followed by propofol 2 to 2.5 $\text{mg}\cdot\text{kg}^{-1}$ iv. Analgesia was provided by remifentanyl 0.05 to 0.25 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ iv throughout surgery. A small piezo-electric microphone was attached to the middle of the thenar mass of the right hand to record acoustic signals produced by the contraction of the adductor pollicis muscle. A second microphone was fixed to the medial part of the thigh, 10 cm over the patella, to record the response from the vastus medialis muscle. The ulnar nerve and the *im* branches of the femoral nerve were stimulated using train-of-four stimulation every 12 sec. Onset, maximum effect, and offset of neuromuscular block were measured after mivacurium 0.2 $\text{mg}\cdot\text{kg}^{-1}$ iv and compared.

Results: At the vastus medialis muscle, the onset of NMB was significantly shorter at 1.9 ± 0.6 min vs 2.8 ± 0.7 min, the maximum effect less pronounced at $85 \pm 11\%$ vs $96 \pm 2\%$ and recovery of NMB to 25%, 75%, 90% of twitch control height more rapid than at the adductor pollicis muscle at 17 ± 2.2 min vs 21.6 ± 4.2 min, 26.7 ± 6.5 vs 21 ± 4.1 min and 30.7 ± 6.6 vs 35.9 ± 7.1 min, respectively.

Conclusions: PMG can be used to measure NMB at the vastus medialis muscle. We found a shorter onset time, less pronounced maximum effect and more rapid recovery of NMB at the vastus medialis muscle than at the adductor pollicis muscle.

Objectif: Le muscle vaste interne du membre inférieur a été proposé récemment comme nouveau site de monitoring du bloc neuromusculaire (BNM). Notre but est de comparer le BNM au muscle vaste interne et à l'adducteur du pouce en utilisant la phonomyographie (PMG).

Méthode : Quinze patients ont été recrutés. L'anesthésie a été induite avec 0,25 à 0,5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ de rémifentanyl suivi de 2 à 2,5 $\text{mg}\cdot\text{kg}^{-1}$ de propofol iv. L'analgesie a été produite avec 0,05 à 0,25 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ de rémifentanyl iv tout au long de l'opération. Un petit microphone piézo-électrique a été attaché au milieu de l'éminence thénar de la main droite pour enregistrer les signaux acoustiques produits par la contraction de l'adducteur du pouce. Un second microphone a été fixé à la partie interne de la cuisse, 10 cm au-dessus de la rotule pour enregistrer la réponse du muscle vaste interne. Le nerf cubital et les branches *im* du nerf fémoral ont été stimulés en train-de-quatre à toutes les 12 s. Le délai d'installation, l'effet maximal et la cessation du bloc neuromusculaire ont été mesurés et comparés après l'administration iv de 0,2 $\text{mg}\cdot\text{kg}^{-1}$ de mivacurium.

Résultats : Au muscle vaste interne, le délai d'installation du BNM a été significativement plus court à $1,9 \pm 0,6$ min vs $2,8 \pm 0,7$ min, l'effet maximal moins prononcé à $85 \pm 11\%$ vs $96 \pm 2\%$ et la récupération du BNM, à 25 %, 75 %, 90 % d'intensité de la stimulation témoin, plus rapide qu'à l'adducteur du pouce à $17 \pm 2,2$ min vs $21,6 \pm 4,2$ min, $26,7 \pm 6,5$ vs $21 \pm 4,1$ min et $30,7 \pm 6,6$ vs $35,9 \pm 7,1$ min, respectivement.

Conclusion : La PMG peut être utilisée pour mesurer le BNM au muscle vaste interne du membre inférieur. Le délai d'installation était plus court, l'effet maximal moins prononcé et la récupération plus rapide du BNM au muscle vaste interne du membre inférieur qu'au muscle adducteur du pouce.

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PHONOMOYOGRAHY (PMG) has been presented as a novel method to record neuromuscular blockade (NMB) with high sensitivity, simple installation and applicability at several muscles, including the laryngeal muscles,^{1,2} the corrugator supercilli,³ and the adductor pollicis.⁴ It can be used interchangeably with mechanomyography.^{1,4} It is based on the fact that contracting muscles create low-frequency sounds by the lateral movement of muscle fibrils.⁵⁻⁷ Muscles of the hand have long been used in research and clinical practice as targets of NMB and reference sites for neuromuscular monitoring. In addition, monitoring of the hand muscles is essential for determination of complete muscular recovery after NMB during surgery. Recently, the vastus medialis was proposed as a peripheral muscle for monitoring NMB.⁸ However, that study focused on the influence of patient positioning on measurements of NMB at the vastus medialis muscle without presenting a complete pharmacodynamic profile of this muscle in comparison to the adductor pollicis muscle. In order to define the role of this muscle for neuromuscular monitoring, it is important to present onset and recovery of NMB in comparison to the standard monitoring at the adductor pollicis muscle. In our study, onset, maximum effect, and recovery of NMB at the vastus medialis muscle and the adductor pollicis of the right hand are measured and compared using PMG.

Methods

After approval of the local Ethics Committee and obtaining informed and written consent, 15 patients undergoing elective general surgery using general anesthesia with a laryngeal mask airway were included in the study. Patients with neuromuscular, hepatic or renal disease and patients receiving medications known to interact with neuromuscular blocking drugs were excluded. After arrival in the operating theatre, routine monitoring (non-invasive blood pressure, pulse oximetry, 5-lead electrocardiography) was applied. Anesthesia was induced with remifentanyl 0.25 to 0.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ followed by propofol 2 to 2.5 $\text{mg}\cdot\text{kg}^{-1}\cdot\text{kg}^{-1}$ *iv*. After loss of consciousness and ventilation via face-mask for two minutes with 100% oxygen, a laryngeal mask airway (size 4 for women, size 5 for men, LMA Company, Henley on Thames, UK) was inserted, and controlled ventilation was started with minute ventilation set to maintain a PETCO₂ of 25 to 35 mmHg. Anesthesia was maintained with 1 to 1.5 MAC of sevoflurane in a gas mixture of 30% oxygen in air to maintain a bispectral index of 50 (BIS, A-2000 monitoring system, Aspect Medical Company, Newton,

MA, USA). Analgesia was provided by remifentanyl 0.05 to 0.25 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ *iv* throughout surgery.

A small piezo-electric microphone (1.6 cm diameter, Model 1010, Grass Instruments, Astro-Med, Inc., West Warwick, USA; frequency response: 2.5 Hz to 5 kHz, signal output: 20–40 mV into 1 MW) was attached to the middle of thenar mass of the right hand using tape to record the acoustic signals produced by the contraction of the adductor pollicis muscle. Two electrodes were positioned to the medial part of the distal forearm, over the ulnar nerve, as shown in Figure 1. The arm was fixed to a routine arm board with the thumb able to move uninhibited. A second microphone was fixed to the medial part of the thigh, over the vastus medialis muscle. This microphone was fixed about 10 cm above the upper edge of the patella,^{8,9} medial to the rectus femoris muscle (Figure 2). The microphone was positioned between two electrodes fixed over the skin to stimulate *im* branches of the femoral nerve.⁸ The acoustic signals were amplified and band pass filtered between 0.5 Hz and 1000 Hz using an AC/DC amplifier. The phonomyographic signals were continuously sampled at 100 Hz using the Polyview® software package (Astro-Med Inc., Longueuil, QC, Canada), digitized and stored on a portable microcomputer. The twitch amplitude from PMG signals was measured maximum-to-maximum.

In all patients, the ulnar nerve and the *im* branches of the femoral nerve were stimulated using supramaximal train-of-four (TOF) stimulations each 12 sec via surface electrodes using a constant current stimulator (Innervator®, Fisher and Paykel Healthcare, Auckland, New Zealand). The current intensity was set to a maximum of 70 mA. Supramaximal stimulation was attained for both muscles by measuring the amplitudes of the twitch responses during increased stimulation currents and choosing the stimulation current where no acoustic signal saturation occurred.

After the start of the stimulation, mivacurium 0.2 $\text{mg}\cdot\text{kg}^{-1}$ was injected within five seconds into a fast flowing solution of Ringer's lactate. Onset, maximum effect, and offset of NMB were determined. Recordings of signals were continued until TOF ratios were greater than 0.9 in all patients.

The first twitch response of the TOF stimulation was used to analyze the onset time (time to reach maximum decrease of twitch response) and the time to reach 25%, 50%, 75% and 90% of control twitch response (T1/T0). The maximum effect was determined as the maximum decrease of the twitch response and was also recorded. TOF ratios of 0.5, 0.7, 0.8 and 0.9 were also calculated.

TABLE Pharmacodynamic data and bias (adductor pollicis - vastus medialis)

	<i>Adductor pollicis</i>	<i>Vastus medialis</i>	<i>P-value</i>
Maximum effect (%)	96 ± 2	85 ± 11	0.001
Onset (min)	2.8 ± 0.7	1.9 ± 0.6	0.000
T 25% (min)	21 ± 4.1	17 ± 2.2	0.006
T 50% (min)	25 ± 4.7	21.6 ± 4.2	0.002
T 75% (min)	30.7 ± 6.6	26.7 ± 6.5	0.002
T 90% (min)	35.9 ± 7.1	30.6 ± 7.1	0.001
TOF 0.5 (min)	27.3 ± 4.6	22.2 ± 3.4	0.000
TOF 0.7 (min)	32.2 ± 5.7	25.7 ± 4.2	0.000
TOF 0.8 (min)	35.4 ± 3.7	30.4 ± 5.4	0.014
TOF 0.9 (min)	41 ± 5	32 ± 6.8	0.003

All times are in minutes. TOF = train-of-four. Data presented as mean ± standard deviation.

Results are expressed as mean ± standard deviation. Repeated-measures of ANOVA followed by post-hoc *t* test was performed to compare all values (onset, maximum effect and recovery of T1/T0 and TOF) whenever significant differences were found. $P < 0.05$ was regarded as showing a significant difference. Mean amplitude of first recorded twitch was compared between both signals using a standard paired *t* test. Sample size was calculated using an expected difference of mean of three minutes at T 25% for a Power of 0.8 and $\alpha = 0.05$. The means of the difference of all pharmacodynamic parameters and 95% confidence intervals were also calculated.

Results

We were able to obtain pharmacodynamic data in 15 patients who consisted of four men and eight women with a mean age of 47 ± 21 yr, mean weight of 75 ± 8 kg and mean height of 165 ± 12 cm. After the injection of mivacurium, there was no period of systemic hypotension in any patient. Acoustic control signals at the vastus medialis muscle from three patients were too small to allow measurement of NMB and were subsequently excluded from analysis; they were replaced by three subsequent patients where signal recording was without a problem. Control twitch amplitudes were significantly higher at the adductor pollicis muscle than at the vastus medialis muscle. The mean amplitude of the control twitch was 1.6 ± 0.6 V vs 1 ± 0.5 V, respectively ($P = 0.01$).

Pharmacodynamic data are presented in the Table; at the vastus medialis muscle, the maximum effect was

FIGURE 1 Positioning of the microphones to monitor neuromuscular blockade at the adductor pollicis (thenar region). The arm was fixed to a routine arm board using a gluing tape. The thumb is free to move in reaction to the stimulation.

significantly smaller, onset and offset of NMB faster than at the adductor pollicis muscle. Mean onset, peak effect and recovery are presented in Figure 3a, the means of the differences of all pharmacodynamic parameters with confidence intervals are presented in Figure 3b, respectively.

Discussion

Onset and offset of NMB are faster at the vastus medialis muscle than at the adductor pollicis muscle with a less pronounced maximum effect.

The differences between the pharmacodynamic profile of the adductor pollicis muscle and the vastus medialis muscle could be explained by multiple factors: the dimension of muscular fibres,¹⁰ differences in blood perfusion^{11,12} and the density of acetylcholine receptors. One previous study found a significant difference in proportion of type I and type II fibres between the adductor pollicis muscle and the vastus medialis muscle (superficial and deeper parts).¹³ The proportion of type I fibres in the adductor pollicis muscle was found as $80.4 \pm 8.7\%$ and the proportion in the superficial and the deeper part of the vastus medialis muscle as $43.7 \pm 7.0\%$ and $61.5 \pm 9.5\%$, respectively. This observation could explain in part the differences in pharmacodynamic profile found between both muscles.

Recently, the corrugator supercilii muscle has been advocated as a muscle which more closely reflects

FIGURE 2 Positioning of the microphone to monitor neuromuscular blockade at the vastus medialis. The microphone was fixed about 10 cm above the upper edge of the patella, medial to the rectus femoris muscle. The microphone is positioned between two electrodes fixed over the vastus medialis muscle to stimulate the *im* branches of the femoral nerve.

onset and offset of NMB at the larynx.¹⁴ Although we did not study the corrugator supercilii muscle in the present study, it is interesting to note that NMB after mivacurium 0.2 mg·kg⁻¹ resembles the NMB found at the vastus medialis muscle in the present study.¹⁵ The fact that the proportion of type I fibres in corrugator supercilii found to be at 51%,¹⁶ is similar to the proportion of type I fibres in the vastus medialis muscle (44%) might explain the similar pharmacodynamic profiles of the two muscles. Whether the vastus medialis muscle reflects well NMB at the larynx or the diaphragm, should be the focus of future studies.

In a previous study, the comparison of NMB at the vastus medialis muscle (via acceleromyography) and the adductor pollicis (via mechanomyography) was performed.⁸ It was found that onset time after vecuronium 0.1 mg·kg⁻¹ was faster at the vastus medialis than at the adductor pollicis muscle. Although the complete pharmacodynamic profile was not presented or recorded, those authors presumed a faster recovery of NMB at the vastus medialis muscle than at the adductor pollicis muscle. This hypothesis has been confirmed by our findings.

We used the same technique of nerve stimulation as was proposed in the previous study.⁸ This form of nerve stimulation differs from the usual stimulation of an afferent motor nerve, as it is a direct stimulation of *im* branches of the nerve. The motor nerve supplying the vastus medialis muscle originates from the posterior divisions of the femoral nerve and is enter-

FIGURE 3A All twitches as means (SD) of all patients for the adductor pollicis of the right hand (grey square) and the vastus medialis muscle (black triangle). * $P < 0.05$ shows a statistically significant difference.

FIGURE 3B This figure shows the mean of the differences for all pharmacodynamic parameters; error bars reflect confidence intervals (95%).

ing the vastus medialis from its deep surface,¹⁷⁻¹⁹ in a bi-layered fascial envelope next to the Hunter's canal (adductor canal), where direct stimulation is not possible. This was pointed out in a commentary²⁰ in response to Saitoh's study. However, the technique of stimulating *im* nerve branches has been used at other muscles, such as the larynx.^{21,22} Whether this form of stimulation changes the monitoring results, cannot be answered. However, this form of stimulation is less selective and might explain why in some patients, the control amplitude was too weak for any

FIGURE 4 Qualitative comparison between signals from the adductor pollicis (a), the vastus medialis muscle from a thigh with a low proportion of fat (b) and the vastus medialis muscle from a thigh with a high proportion of fat (c). Figures 4a and b show a typical phonomyographic signal with a biphasic signal wave. Figure 4c presents a multiphasic acoustic signal, in a rebound pattern. Dotted lines shows peak-to-peak measurement of the signal amplitude.

neuromuscular monitoring, hence the replacement of three patients. In general, our experience with stimulation and recording of signals of the vastus medialis muscle showed that the more ‘muscular’ the thigh of a given patient, the higher the signal amplitude and the easier the signal recording. The more fat tissue was moved at the moment of stimulation, the more

artefact interferences are noticed, the lower the signal amplitude. Due to the fact that we recorded the original signals, we were able to exclude these low-quality signals. Monitoring the muscle response simply by recording digitized data, as done previously,⁸ most probably does not record these artefacts since acceleromyographic probe movement will still occur. Similar problems of signal recording can be noticed in recording of other, more profoundly, located muscles with fat tissue in between the muscle and the skin, such as the diaphragm. In our experience, independent from the monitoring method used to measure neuromuscular transmission, monitoring becomes difficult when larger fat layers lay between muscle and skin with the monitoring device attached. Obviously these problems do rarely occur when hand muscles are used for monitoring.

In general, signals from the vastus medialis muscle were less powerful than signals from the adductor pollicis muscle. This could be explained by the efficacy of stimulation or by quantity of fat tissue between the muscle and the microphone. The amount of fat located between the muscle and the skin also seems to cause a change in the waveform of the acoustic signal from the vastus medialis muscle. Examples of acoustic signals from patients with different fat distribution are presented in Figure 4. Signals from the thigh with a high proportion of fat are characterized by one or two repetitions of the signal, in a rebound pattern. We hypothesize that the acoustic response depends on the focus of stimulation and physical characteristics of the leg and vastus medialis (muscle formation, fat distribution).

In conclusion, the vastus medialis muscle was found to have a shorter onset time, maximum effect and action time than adductor pollicis of the right hand. TOF recovery at vastus medialis is also significantly more rapid than adductor pollicis muscle. Whenever hand muscles or foot muscles are not easily accessible, monitoring of the vastus medialis muscle might be considered as an alternative monitoring site. This might be the case in spine surgery or neurosurgical procedures. However, one must be aware that the pharmacodynamic response is significantly different from the response of those other muscles.

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