Simultaneous determination of neuromuscular block at the larynx, diaphragm, adductor pollicis, orbicularis oculi and corrugator supercilii muscles


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We simultaneously determined the neuromuscular blocking effect of mivacurium 0.2 mg kg⁻¹ at five muscles in 20 women undergoing gynaecological surgery. Evoked electromyographic responses were obtained using surface electromyography (EMG) at the adducting laryngeal muscles, the diaphragm (lateral to vertebrae T12/L1 or L1/L2) and the adductor pollicis muscle and accelerometric (AMG) responses were measured at the orbicularis oculi and the corrugator supercilii muscle. Onset time and times for the first twitch response (T₁/T₀) to return to 25, 75 and 90% at the adducting laryngeal muscles and the diaphragm were significantly (P<0.005) shorter than at the adductor pollicis, the corrugator supercilii or the orbicularis oculi muscles (mean (sd) onset time: 89 (26) s and 78 (17) s to 202 (45) s, 152 (41) s, 194 (40) s; T₁/T₀=25%: 10.4 (1.5) and 11.4 (1.2) min versus 20.5 (3.9), 15.9 (3.3), 16.3 (3.7) min; T₁/T₀=90%: 15.5 (1.6) and 16.1 (1.6) min versus 27.4 (4.6), 21.5 (3.8), 23.3 (5.1) min). Onset and clinical duration of neuromuscular block at the larynx and the diaphragm after mivacurium 0.2 mg kg⁻¹ are shorter than in the peripheral muscles. Monitoring of neuromuscular block in the diaphragm was successfully used in all patients.

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In recent years, attempts have been made to measure onset and offset of neuromuscular block at various muscles The monitoring of the response of the larynx and the diaphragm to neuromuscular blocking drugs has enhanced our knowledge about the action of these agents and delivered more accurate data on the onset and clinical duration of neuromuscular block at those muscles. The determination of neuromuscular block by the introduction of a cuff-pressure technique for measurements at the larynx¹ and electromyographic (EMG) monitoring of the diaphragm² have replaced simple clinical observation in the study of neuromuscular block.³ The great inter-individual range of the pharmacodynamic profile of non-depolarizing neuromuscular blocking drugs makes the intra-individual comparison of onset and offset interesting.

We simultaneously determined the onset and offset of neuromuscular block produced by mivacurium 0.2 mg kg⁻¹ at the larynx, diaphragm, adductor pollicis, orbicularis oculi and corrugator supercilii muscle using non-invasive, superficial electrodes. To record the diaphragmatic response, we modified the technique of skin EMG by placing the electrodes at the back of the patient, lateral to vertebrae T12/L1 or L1/L2, just inferior to the 12th rib, thus presenting a novel site for monitoring diaphragmatic neuromuscular block.

Materials and methods

After approval of the local ethics committee and written informed consent, 20 women undergoing gynaecological surgery were included in the study. Pregnant women, patients with neuromuscular, hepatic or renal disease and patients receiving medications known to interact with neuromuscular blocking drugs were excluded.

Anaesthesia was induced using alfentanil 20 μg kg⁻¹ followed by a target-controlled infusion of propofol (target concentration 4 μg ml⁻¹) programmed to reach the target concentration within 30 s. After induction of anaesthesia, the trachea was intubated through the mouth using a Woodbridge tube (Mallinkrodt, UK, size 7.0) with the surface laryngeal electrode (Magstim company, UK) attached 2 cm above the origin of the cuff. The electrode
was placed between the vocal cords for optimal EMG tracing. Anaesthesia was maintained with a target-controlled infusion of propofol (target concentration 3 \( \mu \text{g mL}^{-1} \)) and alfentanil in increments of 10 \( \mu \text{g kg}^{-1} \) given at the discretion of the anaesthetist; mechanical ventilation was adjusted to achieve an end-tidal carbon dioxide-pressure of 3.5–4.5 kPa.

Two Ag/AgCl-skin-electrodes were attached lateral to vertebrae T12/L1 or L1/L2 (wherever the maximum response was better) on the right paravertebral side of the back, inferior to the 12th rib, and placed 2 cm apart for monitoring of the response of the right diaphragmatic muscular crux to phrenic nerve stimulation (Fig. 1). One Ag/AgCl-electrode was used as a ground electrode and placed on the hip bone distant to the recording site. The phrenic and recurrent laryngeal nerves were stimulated transcutaneously using one external bipolar nerve stimulator (Multiliner\textsuperscript{®}, ToÈnnies company, Germany) on the right side at the inferolateral edge of the sternocleidomastoid muscle for the phrenic nerve. In addition, two Ag/AgCl electrodes were positioned over the notch of the thyroid cartilage on the same side for the recurrent laryngeal nerve. The stimulation site was selected, which produced only minimal or no concomitant stimulation of the brachial plexus. The probe of the external nerve stimulator is attached at the neck with an elastic band. It delivers a current between 0 and 70 mA. Single twitch-stimulation (0.1 Hz, pulse width 0.2 ms) was performed on the right neck to determine the supramaximal stimulation and recorded using modified Multiliner\textsuperscript{®} (Toennies, Germany) nerve conduction software. The current was increased from 0 mA to the current with the maximal EMG response and then increased by 10 mA to assure supramaximal stimulation. The amplitudes of the diaphragmatic and the laryngeal compound action potentials (peak-to-peak) were measured and recorded (Fig. 2). After stimulation of the right ulnar nerve using Ag/AgCl-electrodes attached to the forearm, evoked EMG-single twitch responses (0.1 Hz; pulse width 0.2 ms) from the adductor pollicis muscle via Ag/AgCl-electrodes placed over the base of the thenar area were recorded. The automatic calibration of the Datex Relaxograph\textsuperscript{®} NMT 100 (Datex Instrumentarium Corporation, Helsinki, Finland) was used to determine supramaximal stimulation (0–70 mA).

An AMG probe was placed on the medial part of the right suprareiliary arch was equipped with an AMG probe (TOF\textsuperscript{®} guard, eye-adapter, Organon Teknika, Finland) to record the neuromuscular response of the corrugator suprareilii muscle. Another AMG probe was placed on the left upper eye lid to record evoked responses of the orbicularis oculi muscle. Stimulation of the upper branches of the facial nerves was performed on both sides using two Ag/AgCl-electrodes (size 1 \( \times \) 1.5 cm) attached to the skin 2 cm anterior to the ear lobe. The automatic calibration set-up of the TOF-guard\textsuperscript{®}NMT (Organon Helsinki, Finland) was used to determine supramaximal stimulation on both sides (single twitch, 0.1 Hz). After no change in the neuromuscular response could be detected at all five sites for 10 min,
the patients received mivacurium 0.2 mg kg⁻¹, injected within 15 s into a fast-flowing infusion of Ringer solution. No further dose of neuromuscular blocking drug was given. Body temperature was measured at the forehead and kept above 35.6°C using a heating blanket (Bair Hugger, MN, USA).

The time from the end of injection of mivacurium to the first twitch depression (lag time), the maximum twitch depression (onset time) and the maximum block (%-reduction of the maximal neuromuscular response) were measured. To determine clinical duration of neuromuscular block, single-twitch responses every 15 s were used; time for the first twitch response (T₁/T₀) to return to 25, 75 and 90% was measured.

**Statistical analysis**

The results are expressed as mean (standard deviation (SD)) and range. The pharmacodynamic parameters were compared between the different monitoring sites using analysis of variance (ANOVA), followed by Fisher’s least significant difference strategy for multiple comparisons; P<0.05 was regarded as showing a significant difference.

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**Figure 3** Onset and clinical duration of neuromuscular block after mivacurium 0.2 mg kg⁻¹. Values are mean; error bars indicate standard deviation. The larynx, the diaphragm and the adductor pollicis muscle monitored using EMG, the orbicularis oculi and the corrugator supercili muscle are measured using AMG. (A) Lag time (black column) and onset time (white column): time from injection of mivacurium to the first and maximal effect; *P<0.005 versus larynx and diaphragm, #P<0.025, §P<0.005 versus adductor pollicis muscle, respectively. Mean time in box. (B) T₁/T₀=25% (white column), T₁/T₀=75% (black column), T₁/T₀=90% (striped column): time from injection to recovery of the twitch response to 25, 75 and 90%. *P<0.05 versus larynx and diaphragm, #P<0.005 versus larynx and diaphragm, §P<0.05 versus corrugator supercili muscle.
Results

In 20 female patients with a mean age of 44 (SD 16) yr (range 18–78 yr) and a mean weight of 64 (10) kg (46–81 kg), determination of the supramaximal stimulation at all five monitoring sites was successful. No side effects as a result of the simultaneous transcutaneous stimulation of the recurrent laryngeal and phrenic nerve with a mean current of 45 (6) mA (range 30–55 mA) such as arrhythmias or skin irritation were noted.

Mean maximum block was more than 98% at all sites. It was 99 (SD 4%) (range 88–100%) and 99 (4%) (range 82–100%) at the larynx and the diaphragm, respectively. The mean maximum block at the adductor pollicis, the corrugator supercilii and the orbicularis oculi muscle was 99 (2%) (93–100%), 99 (3%) (84–100%) and 98 (4%) (86–100%), respectively. There was no statistically significant difference between the muscles.

Onset times and clinical duration of neuromuscular block are presented in Figure 3A and Figure 3B. Lag time and onset time of neuromuscular block were significantly shorter at the larynx and the diaphragm than at the other muscles (P<0.005), without being significantly different between the diaphragm and the larynx or between the orbicularis oculi and the corrugator supercilii muscle.

The lag and onset time at the adductor pollicis muscle were significantly longer than the times at the corrugator supercilii muscle (P<0.025); although the lag time at the adductor pollicis muscle was significantly longer than the lag time at the orbicularis oculi muscle (P<0.005), the onset times at the adductor pollicis and the orbicularis oculi muscle did not differ statistically (202 versus 194 s). Time for the first twitch response (T1/T0) to return to 25, 75 and 90% was shorter for the larynx and the diaphragm than for the other muscles (P<0.05 versus the orbicularis oculi and the corrugator supercilii muscle, P<0.005 versus the adductor pollicis muscle).

The clinical duration of neuromuscular block at the corrugator supercilius muscle was significantly shorter than at the adductor pollicis muscle (P<0.05), but not statistically different from the clinical duration at the orbicularis oculi muscle.

Discussion

The simultaneous determination of neuromuscular block after mivacurium 0.2 mg kg⁻¹ at the larynx, diaphragm, adductor pollicis, orbicularis oculi and corrugator supercilius muscle revealed that onset at the respiratory muscles (larynx, diaphragm) reaches a mean maximum block of 99% after 80–90 s, whereas the onset at the orbicularis oculi and the corrugator supercilius muscle is more than 150 s and at the adductor pollicis muscle is more than 3 min. Time for T1/T0 to reach 25% was 10–12 min at the larynx and the diaphragm, more than 15 min at the orbicularis oculi and corrugator supercilius muscle and more than 20 min at the adductor pollicis muscle.

The onset times determined in this study correspond well with times determined by judging the intubating conditions at the larynx and the diaphragm, but the responses are in contrast to visual observation of the orbicularis oculi response to stimulation.

Le Corre and colleagues⁷ estimated the onset of several neuromuscular blocking drugs at the orbicularis oculi muscle and found that visual estimation was a good predictor of excellent or good intubation conditions. They concluded that loss of orbicularis oculi responses are acceptable predictors of good intubation conditions. They estimated an onset time of 99 s at the orbicularis oculi muscle after mivacurium 0.2 mg kg⁻¹ and performed tracheal intubation with good to excellent intubation conditions. This would be in concordance with the diaphragmatic and laryngeal onset times measured in this study (78 and 89 s) but not with another study which compared the effects of mivacurium 0.2 mg kg⁻¹ at the diaphragm and the geniohyoid muscles. D’Honneur and colleagues⁸ determined the onset time at the diaphragm, using surface EMG at 158 s longer than it was in our study. The major difference between their study and this one is the different calibration time: whereas D’Honneur and colleagues only waited 3 min before measurements were started, the current study set-up used a 10-min calibration time of supramaximal stimulation. McCoy and colleagues⁹ found that the longer the duration of control stimulation the shorter the onset measured.

Rimaniol and colleagues⁶ studied the effect of mivacurium 0.15 and 0.25 mg kg⁻¹ at the orbicularis oculi muscle using AMG. They found that for mivacurium 0.15 mg kg⁻¹ the onset of neuromuscular block was not different between the orbicularis oculi and the adductor pollicis muscle (235 (SD 76) versus 232 (67) s), but the offset was significantly shorter at the orbicularis oculi muscle. For mivacurium 0.25 mg kg⁻¹, the onset was significantly shorter at the orbicularis oculi muscle than at the adductor pollicis muscle (90 (25) versus 160 (30) s). In the current study, the onset of block after mivacurium 0.2 mg kg⁻¹ was shorter at the orbicularis oculi muscle than at the adductor pollicis muscle (194 (40) versus 202 (45) s) but failed to reach statistical significance.

We stimulated the phrenic and the recurrent laryngeal nerve transcutaneously without difficulty. It could be that in patients with large necks or an enlarged thyroid gland, transcutaneous stimulation of the phrenic nerve using a surface probe might be difficult; in those patients, we prefer percutaneous stimulation via needle electrodes. Concomitant stimulation of the brachial plexus was absent or minimal and did not affect the monitoring of the diaphragmatic response; monitoring the diaphragm on the patient’s back is certainly advantageous to rule out artefacts from concomitant stimulation of the brachial plexus.
Donati and colleagues\textsuperscript{2} introduced surface EMG of the diaphragm to monitor neuromuscular block into research practice; it was an easy and objective way to measure onset and offset of block at this muscle. Skin electrodes attached at the 7th or 8th intercostal space between the midclavicular and the anterior axillary line, however, cannot be used during open and laparoscopic abdominal surgery as they are within the surgical fields.

Because the muscular crura of the lumbar diaphragm are inserted into the first two to three lumbar vertebrae, it seemed possible to monitor the response to phrenic stimulation on the patient’s back, lateral to vertebrae T12/ L1 or L1/L2 (Fig. 2). Future studies will show whether this location can be used for routine intra-operative monitoring of the diaphragm.

The corrugator supercilii muscle, a small muscle of the superciliary arch, located medially under the eyebrow, is inserted into the forehead skin and responsible for vertical frowning of the forehead. It can be monitored using an AMG probe attached to the medial part of the superciliary arch at a 90° angle to the muscle contraction direction, in a similar way to the AMG measurement of the orbicularis oculi muscle.\textsuperscript{6, 10}

The only study of neuromuscular block at the corrugator supercilii muscle was recently presented as an abstract by Plaud and Donati.\textsuperscript{11} They measured maximum block and recovery to $T_1/T_D=25\%$ after rocuronium 0.6 mg kg$^{-1}$ at the corrugator supercilius muscle and the larynx. They concluded that the neuromuscular response measured at the corrugator supercilii muscle was a good reflection of the laryngeal muscle response. We found significant differences in onset time and clinical duration between the larynx and the corrugator supercilii muscle but the maximum block was not significantly different.

The morphological difference between the orbicularis oculi muscle and the corrugator supercilius muscle has been the focus of a recent anatomical study. Goodmurphy and colleagues\textsuperscript{12} have found that the orbicularis oculi muscle fibres are small, rounded and 89\% fast-twitch type-II muscle fibres, whereas the corrugator supercilii muscle fibres were larger, polygonal, and 49\% of fast-twitch type II. The capillary index (capillary area per unit of contractile area) of the corrugator supercilius muscle, however, was 2.4 times the capillary index of the orbicularis oculi muscle. The difference in capillary index and the larger size of the muscle fibres\textsuperscript{13} might explain the faster onset of neuromuscular blocking drugs at the corrugator supercilii muscle. Further studies of the action of other neuromuscular blocking drugs at the corrugator supercilii muscle are needed to define the role of this muscle as a predictor of the laryngeal muscle response.

In conclusion, we present the first simultaneous determination of neuromuscular block at the larynx, diaphragm, adductor pollicis, orbicularis oculi and corrugator supercilius muscle. Surface electrodes were used to record evoked responses at all sites. The monitoring of the diaphragmatic response at the back of the patient allows intra-operative monitoring during abdominal surgery. In contrast to previous findings with rocuronium,\textsuperscript{11} onset and clinical duration of neuromuscular block after mivacurium at the corrugator supercilii muscle did not accurately reflect onset and clinical duration of neuromuscular block at the larynx or the diaphragm. More studies are needed to define the role of this muscle for neuromuscular monitoring in clinical practice.

References

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