The lumbar paravertebral region provides a novel site to assess neuromuscular block at the diaphragm

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Purpose: We evaluated a novel, paravertebral site for assessment of neuromuscular block at the diaphragm. The neuromuscular blocking effect of 0.1 mg·kg^{-1} cisatracurium at the adducting laryngeal muscles, the diaphragm and the adductor pollicis (AP) were compared.

Methods: In 24 patients undergoing thyroid surgery, evoked responses from the adducting laryngeal muscles and the AP muscle were obtained using surface electromyography (EMG). Skin electrodes were placed paravertebrally near T12/L1 or L1/L2 (novel position; $n = 12$) or conventionally ($n = 12$). After stimulation of the recurrent laryngeal, phrenic and ulnar nerves, the lag, onset time and maximum effect were measured (0.1 Hz, single twitch) as well as the time to reach 25% of T1/T0 (T 25%) using train-of-four stimulation every 20 sec.

Results: A mean maximum block of more than 94% was reached at all sites. Lag, onset time and T 25% at the adducting laryngeal muscles and the diaphragm were significantly ($P < 0.005$) shorter than at the AP muscle and did not differ significantly between the two diaphragmatic monitoring sites (conventional: 64 ± 21 sec, 166 ± 41 sec and 20 ± 3 min *vs* novel: 60 ± 16 sec, 161 ± 40 sec and 22 ± 2 min respectively).

Conclusion: Onset and duration of action of 0.1 mg·kg^{-1} cisatracurium was shorter at the larynx and the diaphragm than at the AP muscle. EMG results obtained from the novel, paravertebral site did not differ from the conventional monitoring site at the seventh or eighth intercostal space and suggest this alternative site is appropriate for monitoring of the diaphragm.

Objectif : Évaluer un nouveau site paravertébral pour l'estimation du bloc neuromusculaire diaphragmatique. Comparer, pour ce faire, l'effet de l'administration d'une dose de 0,1 mg·kg^{-1} de cisatracurium sur les muscles adducteurs laryngés, du diaphragme et adducteur du pouce (AP).

Méthode : Les potentiels évoqués des muscles adducteurs laryngés et de l'AP ont été obtenus par électromyographie (EMG) de surface chez 24 patients devant subir une intervention thyroïdienne. Des électrodes cutanées paravertébrales ont été placées près de T12/L1 ou L1/L2 (nouvelle position; n = 12) ou en position traditionnelle (n = 12). Après la stimulation des nerfs laryngé récurrent, diaphragmatique et cubital, on a mesuré la période de latence, le délai d'installation et l'effet maximal (0,1 Hz, une stimulation simple) ainsi que le temps d'atteindre 25 % du ratio T1/T0 (T 25 %) en utilisant une stimulation en train-de-quatre toutes les 20 s.

Résultats : Un bloc maximal moyen de plus de 94 % a été atteint à tous les sites. La période de latence, le délai d'installation et le T 25 % aux muscles adducteurs laryngés et au diaphragme ont été significativement (P < 0,005) plus courts qu'à l'AP et n'ont pas montré de différence significative entre les deux sites diaphragmatiques (traditionnel : 64 ± 21 s, 166 ± 41 s et 20 ± 3 min vs nouveau : 60 ± 16 s, 161 ± 40 s et 22 ± 2 min respectivement).

Conclusion : Le délai d'installation et la durée d'action de 0,1 mg·kg^{-1} de cisatracurium ont été plus courts au larynx et au diaphragme qu'à l'AP. Les résultats de l'EMG obtenus au nouveau site de monitorage paravertébral ne diffèrent pas de ceux du site traditionnel au septième ou huitième espace intercostal et montrent la valeur de ce nouveau site de monitorage du diaphragme.

MONITORING of the diaphragmatic response using surface skin electrodes was introduced into clinical research in 1986 by Donati *et al.*[1] These authors investigated the seventh or eighth intercostal space between the midclavicular and anterior axillary line as a possible monitoring site. This site has been successfully used in assessment of neuromuscular block (NMB) at the diaphragm for research purposes over the last decade.

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Its use, however, is limited by the fact that the electrodes often have to be placed within the surgical field, specially in abdominal or cardiothoracic surgery. Open and closed abdominal surgery could benefit from monitoring of NMB of the diaphragm since diaphragmatic function will influence abdominal pressure.

In this study, a novel site for diaphragmatic surface electromyography (EMG) recording in the paravertebral region was compared with the established site at the seventh or eighth intercostal space. We simultaneously determined the onset and peak effect of 0.1 $mg \cdot kg^{-1}$ cisatracurium at the adducting laryngeal muscles[2,3] and the adductor pollicis (AP) muscle using surface electrodes.

Materials and methods

After approval of the local Ethics Committee and written informed consent, 24 patients undergoing thyroid surgery were included in the study. Pregnant women, patients with neuromuscular, hepatic or renal disease and patients receiving medication known to interact with neuromuscular blocking drugs were excluded.

Two minutes after the start of a remifentanil infusion at 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, anesthesia was induced using a target- controlled infusion of propofol (target concentration: 4 $\mu g \cdot ml^{-1}$), programmed to reach the target concentration within 30 sec. After induction of anesthesia was completed, the patients were ventilated via face-mask for three minutes and the trachea was intubated using a Woodbridge® tube (Mallinckrodt, UK, size 7.0: female, size 8.0: male) with the surface laryngeal electrode (Magstim company, UK) attached 2 cm above the cuff and placed between the vocal cords for an optimal EMG tracing.[3] Two Ag/AgCl-skin-electrodes were placed over the right thenar area for EMG recording of the AP muscle using the Relaxograph® (Datex, Finland), and two Ag/AgCl-skin-electrodes were used to stimulate the ulnar nerve.

Anesthesia was maintained with a target-controlled infusion of propofol (target concentration: 3 $\mu g \cdot ml^{-1}$) and remifentanil at 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Mechanical ventilation (30% oxygen in air) was adjusted to achieve an end-tidal CO_2 -pressure of 25–40 mmHg.

Patients were randomly assigned to one of two groups. In the "novel" group (n=12), two Ag/AgCl-skin- electrodes were placed on the right of vertebrae T12/L1 or L1/L2 (wherever the maximal response was obtained), 2–3 cm apart, for EMG-monitoring of the right diaphragmatic muscular crux[4] (Figure 1). In the "conventional" group (n=12), two Ag/AgCl-skin-electrodes were placed at the right seventh or eighth intercostal space between the midclavicular and anterior axillary line.[1]

The right phrenic and recurrent laryngeal nerves were stimulated transcutaneously using an external bipolar nerve stimulator (Multiliner®, Tönnies Inc., Germany) at the inferolateral edge of the sternocleidomastoid muscle for the phrenic nerve. Two Ag/AgCl electrodes were positioned over the notch of the thyroid cartilage and sternum to stimulate the recurrent laryngeal nerve.[5] The site where only minimal or no concomitant stimulation of the brachial plexus occurred was selected to stimulate the phrenic nerve. The probe of the external nerve stimulator delivers a current between 0 and 70 mA. Single twitch-stimulation (0.1 Hz, pulse width: 0.2 msec) was applied on the right side of the neck to determine the supramaximal stimulation and recorded using Multiliner® (Toennies Inc., Germany) software. The current was increased from 0 mA to the current producing a maximal EMG-response and then increased by a further 10 mA to assure supramaximal stimulation. Single twitch stimulation was applied to the ulnar nerve (0.1 Hz) and the automatic calibration setup of the Relaxograph® was applied to determine supramaximal stimulation at the AP muscle. Train-of-four stimulation (2 Hz, 0.1 msec) was applied every 20 sec to determine clinical duration of NMB.

The amplitudes of the diaphragmatic and the laryngeal compound action potentials (peak-to-peak) were measured and recorded (Figure 2).

After no change in the neuromuscular response could be detected for five minutes, the patients received 0.1 $mg \cdot kg^{-1}$ cisatracurium *iv*, injected in five seconds into a fast-flowing infusion of Ringer's lactate solution. No further dose of any muscle relaxant was administered. Body temperature was kept above 35.6°C using a heating blanket (Bair Hugger®, Augustine Medical Inc., MN, USA).

The time from the end of injection of the muscle relaxant to the first twitch depression, the maximum twitch depression (lag time, onset time) as well as maximum block (% reduction of the maximal neuromuscular response) of NMB were measured. Clinical duration of NMB was defined as the time to reach 25% of T1/T0 (T 25%).

Difference of means ± and standard deviation of onset time at the diaphragm and the AP muscle of a pilot study[6] was used to determine group size for a power of more than 0.9 (beta error=10%). The results are expressed as mean standard deviation and range. The pharmacodynamic parameters were compared between larynx, diaphragm and AP muscles using the Kruskal-Wallis test. Differences were then compared using rank sum test, corrected for the number of comparisons. The pharmacodynamic parameters between

TABLE Lag, onset time, maximum block and T 25% after 0.1 mg·kg^{-1} cisatracurium

	Diaphragm (conventional) (n=12)	*Diaphragm (novel) (n=12)*	*Larynx (n=24)*	*Adductor pollicis (n=24)*
Lag time (sec)	64 ± 21 (40–80)	60 ± 16 (40–70)	55 ± 18 (40–80)	78 ± 21* (70–110)
Onset time (sec)	166 ± 41 (90–200)	161 ± 40 (80–205)	176 ± 55 (100–230)	235 ± 65* (160–300)
Maximum block (%)	94 ± 6 (92–100)	96 ± 3 (90–100)	98 ± 2 (96–100)	99 ± 1 (95–100)
T 25% (min)	20 ± 3 (16–24)	22 ± 2 (18–25)	20 ± 1 (15–23)	28 ± 4* (25–30)

Values are mean ± SD (range); *P <0.005 *vs* larynx and diaphragm

Lag and onset time=time from injection of cisatracurium to the first and maximal twitch-response respectively

Maximum block=maximum depression (%) of the twitch response in comparison to control response

T 25%=time to reach 25% of T1 / T0 control level

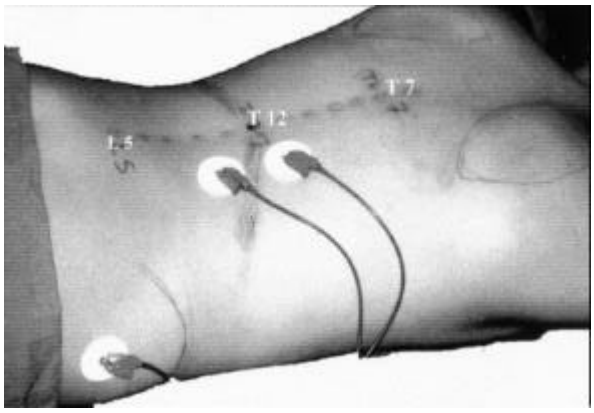

FIGURE 1 Position of the recording electrodes; marked are T 7, T 12, 12th rib; electrodes are placed paravertebrally, 2–3 cm apart at T 12 / L1 or L1 / L2, wherever the response is better.

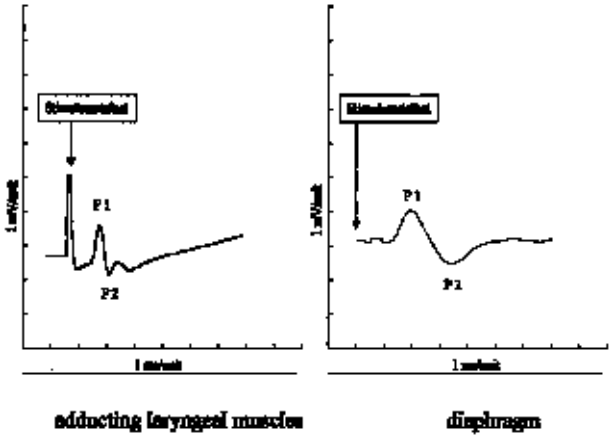

FIGURE 2 shows a compound action potential of the electromyographic response of the laryngeal muscles and the diaphragm (paravertebral site) for a representative patient; amplitude P1–P2 measured as muscular response.

the two diaphragmatic sites were compared using the paired rank sum test. A P <0.05 was considered to indicate a statistically significant difference.

Results

Mean age of patients was 48 ± 11 yr (24–60), with a mean weight of 75 ± 10 kg (60–88). Determination of the supramaximal stimulation at all sites of monitoring was successful in all patients, as was determination of the neuromuscular response at both diaphragmatic sites with a mean amplitude of 1.2 mV ± 0.3 mV. No side effects due to the simultaneous transcutaneous stimulation of the recurrent and phrenic nerves with a mean of 42 ± 6 mA (40–55), such as arrhythmias or skin irritation, were observed. All electrodes for diaphragmatic monitoring were left in place until surgery was completed; in no patient was skin irritation noted.

The pharmacodynamic data are presented in the Table.

Mean maximum NMB was more than 94% at all sites. Lag time, onset time and time to reach 25% of T1 / T0 of NMB were shorter at the larynx and the diaphragm than at the AP (P <0.005), without being different between the diaphragm and the larynx.

Lag, onset time, maximum effect and clinical duration were not different between the two diaphragmatic monitoring sites.

Discussion

As expected, the simultaneous determination at the larynx, the diaphragm and the AP revealed that NMB produced by 0.1 mg·kg^{-1} cisatracurium at the level of the respiratory muscles reaches a mean maximum block of 94–98% after 2.5 min, whereas NMB at the AP, with a mean maximum block of 99%, takes more than 3.5 min.

The seventh or eighth intercostal space, between the midclavicular and anterior axillary lines, have been used to monitor diaphragmatic NMB in research for more than 15 yr.[1] With the introduction of closed endoscopic techniques in modern surgery, monitoring the degree of NMB of the diaphragm during surgery may be

important since diaphragmatic tone greatly influences abdominal pressure. However, using the seventh or eighth intercostal space for intraoperative monitoring in laparoscopic surgery is impossible because the monitoring electrodes would remain within the sterile field. Since the lumbar diaphragm inserts with its muscular crura on the first two to three lumbar vertebrae, it seemed possible to monitor its response to phrenic nerve stimulation at a paravertebral site near vertebrae T12–L3 (Figure 1). By starting at T12 / L1 and moving the electrodes downwards, we were able to obtain signals in all patients. The signals from the patient's paravertebral region may reflect mainly the posterior portion of the diaphragm, just as the electrodes placed at the conventional site reflect its anterior portion. It is unknown to what extent these regional responses reflect the response of the entire diaphragm or that of the surrounding skeletal muscles.

Transcutaneous stimulation of the phrenic nerve was selected in such a way that no or only minimal concomitant stimulation of the brachial plexus occurred. The concomitant stimulation of the brachial plexus causes interference with monitoring of the diaphragm, especially due to parallel contraction of the shoulder and anterior thoracic muscles. In comparison to diaphragmatic monitoring at the seventh or eighth intercostal space, the "novel" site seems less prone to interferences by concomitant stimulation of these muscles. There is always the possibility of accidentally stimulating the brachial plexus in such a way that the latissimus dorsi muscle could be contracting and this would impair the measurements in the paravertebral region. However, this was not the case in any of our patients. One major setback at present – true for both sites – is the difficulty to stimulate the phrenic nerve transcutaneously at the neck. A stimulation using a needle stimulator produces quick and forceful phrenic nerve stimulation, but it cannot be used for ethical reasons. Transcutaneous stimulation of the phrenic nerve is time-consuming (in some patients up to 15 min was required to find the maximal signal) and great care has to be taken during measurements to ensure that no neck movement occurs. This difficulty to establish a quick, easy and reliable transcutaneous stimulation of the phrenic nerve is one of the major hurdles preventing the introduction of diaphragmatic monitoring into clinical practice.

We did not compare the two sites for diaphragmatic monitoring intra-individually since we were stimulating only one phrenic nerve. Insufficient stimulation and accidental concomitant stimulation of the brachial plexus could have caused a significant bias, making correlation and comparison of the two sites difficult. Bilateral stimulation of the phrenic nerve would have been technically arduous and could pose a risk to the patient by causing bradyarrythmias.

Only two studies objectively measured onset of NMB of cisatracurium at the larynx. Kim *et al.*[7] used the cuff pressure method[5] to determine onset times after 0.1 $mg \cdot kg^{-1}$ cisatracurium at the larynx and at the AP muscle. They measured a mean onset of 2.7 min at the larynx, much shorter than the mean onset time of 3.9 min at the AP. This is in concordance with our results for larynx, diaphragm and AP. In a former study,[3] we measured an onset time of 200 sec in ten patients, approximately 25 sec longer than determined in the current study, reflecting the expected interindividual variability. Again, the surface electrodes proved easy to use and reliable. Incidentally, Ag / AgCl-electrodes are routinely placed in the patient's back for electrocardiographic monitoring in our hospital setting; the use of a cushioned operating table avoids pressure induced irritation or damage to the patient's skin.

Our results show that monitoring of the onset of NMB at the AP muscle, a routine clinical practice, insufficiently reflects the onset of respiratory muscle NMB. Although this has been demonstrated for all neuromuscular blocking drugs, a potential hazard has been suggested in a recent study[8] in which cisatracurium was used during induction of anesthesia. Waiting for complete onset of NMB of 0.1 $mg \cdot kg^{-1}$ cisatracurium could create problems when short acting induction drugs such as etomidate, thiopental or propofol[9] are used for induction of anesthesia. Given the duration of action of these drugs is shorter than the onset of the NMB at the AP, the patient might have sufficient NMB at the hand but be awake during intubation.[8] Knowledge that early paralysis of the respiratory muscles will allow endotracheal intubation should avoid this problem.

In conclusion, we present a novel site for monitoring NMB at the diaphragm using skin electrodes in the lumbar paravertebral region. As expected, determination of the onset of NMB after 0.1 $mg \cdot kg^{-1}$ cisatracurium showed a much faster onset at the respiratory muscles (mean of 2.5 min) in comparison to almost four minutes at the AP. This novel site of monitoring the diaphragm provides an interesting alternative to assess NMB of the diaphragm, specially when the conventional, anterior site is not accessible for surgical reasons.

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