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Cisatracurium neuromuscular block at the adductor pollicis and the laryngeal adductor muscles in humans

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We have compared the dose–response relationship (n=30) and time course of neuromuscular block (*n*=20) of cisatracurium at the laryngeal adductor and the adductor pollicis muscles. ED_{95} values for cisatracurium were 66.8 (95% confidence interval 61.3–72.3) μg kg^{-1} at the larynx and 45.2 (42.1–48.3) μg kg^{-1} at the adductor pollicis muscle ($P<0.0001$). After administration of cisatracurium 0.1 mg kg^{-1}, onset time was 2.7 (2.2–3.2) min at the larynx and 3.9 (3.0–4.8) min at the adductor pollicis ($P<0.0001$). Time to 95% recovery of the first twitch of the TOF was 26.9 (20.1–33.7) min and 45.6 (39.7–51.5) min, respectively ($P<0.0001$). We found that the laryngeal adductors were more resistant to the action of cisatracurium than the adductor pollicis muscle, but onset and recovery were faster at the larynx.

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Cisatracurium has been shown in humans to be approximately three times more potent than atracurium and to release less histamine.[1] In most studies of non-depolarizing neuromuscular blocking agents, neuromuscular block occurs more rapidly at the larynx than at the adductor pollicis muscle after injection and the dose of blocker required for laryngeal muscle block is larger than for comparable adductor pollicis block. The laryngeal adductors, which close the glottis, are important clinically, and the time course of cisatracurium on these muscles has not been investigated. In this study, we have compared the dose–response relationship and neuromuscular blocking effects of cisatracurium on the larynx and adductor pollicis muscle in humans.

Methods and results

After obtaining approval from the Hospital Ethics Committee and written informed consent, we studied 50 patients, ASA I or II, undergoing elective inpatient surgery requiring general anaesthesia and tracheal intubation. Patients with neuromuscular disorders and those receiving drugs which might interfere with neuromuscular function were excluded. For dose–response studies, anaesthesia was induced with fentanyl 4–5 μg kg^{-1} and propofol 2–2.5 mg kg^{-1} i.v., and maintained with propofol 8–10 mg kg^{-1} h^{-1} and intermittent bolus doses of fentanyl 1–2 μg kg^{-1}.

To monitor contraction of the laryngeal adductor muscles, the inflatable cuff of a Mallinckrodt tube (7.5 mm inner diameter; Athlone, Ireland) was positioned between the vocal cords under direct vision and inflated with air to a pressure of at least 1.3–1.7 kPa. The recurrent laryngeal nerve was stimulated using surface electrodes placed on the forehead (positive) and at the notch of the thyroid cartilage (negative).[2] With both muscle groups, square-wave supramaximal stimuli of 0.2 ms were delivered in a train-of-four (TOF) sequence at 2 Hz every 10 s, using a Myotest DBS (Biometer Co., Odense, Denmark). The resultant contraction of the adductor pollicis muscle after stimulation at the ulnar nerve near the wrist was recorded using a Myograph 2000 (Biometer Co., Odense, Denmark) with a preload of 300 g. The evoked force of vocal cord adduction was evaluated by quantification of the pressure changes in the inflatable cuff. Pressure changes were detected using a pressure transducer (P23XL, Viggo-Spectramed, Singapore) and recorded on a strip-chart recorder (90651A, SpaceLabs, Redmond, USA).

A subgroup of 30 patients were allocated randomly to receive cisatracurium 30, 40 or 50 μg kg^{-1} using a single-dose method. From the dose–response curves, the respective ED_{95} and ED_{50} (effective dose resulting in 95% and 50% block) values at the adductor pollicis muscle and the larynx were measured.

For the time course studies, 20 patients received a bolus dose of cisatracurium 0.1 mg kg^{-1}. The following variables were measured at both muscles: time from the end of injection until first depression of T1 (first twitch of the TOF response) (lag time); maximum depression of T1

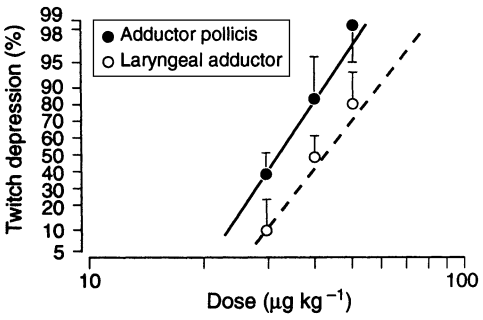

Fig 1 Log dose–probit plot for twitch depression after cisatracurium at the adductor pollicis or the laryngeal adductor muscles. Individual points represent mean (95% confidence intervals) twitch depression (% control) with each dose.

(onset); times from the end of injection until 1%, 25%, 75% and 95% recovery of T1 (T1 (1, 25, 75, 95)); and time from 25% to 75% recovery of T1 (recovery index).

Unless otherwise specified, results are expressed as mean (95% confidence intervals). Data were analysed using the SPSS statistical package (version 7.5) with one-way analysis of variance with Bonferroni correction, analysis of covariance or paired *t* test as appropriate. $P<0.05$ was considered significant.

The groups were similar in age, weight, height and sex. The slopes of the dose–response curves at the larynx and adductor pollicis muscles were 5.4 (3.6–7.2) and 6.1 (4.7–7.5), respectively (Fig. 1). The slopes were not significantly different but the laryngeal adductor response was shifted to the right. ED_{95} was 66.8 (61.3–72.3) μg kg^{-1} at the larynx compared with 45.2 (42.1–48.3) μg kg^{-1} at the adductor pollicis ($P<0.0001$). Corresponding values for ED_{50} were 40.4 (36.3–44.5) μg kg^{-1} and 31.1 (28.7–33.5) μg kg^{-1}, respectively ($P<0.0001$). Lag time, onset time and recovery times (but not recovery index) were significantly shorter at the larynx than at the adductor pollicis ($P<0.0001$) (Table 1). There were no significant haemodynamic changes during the measurement period.

Comment

We have demonstrated that dose–response curves at the larynx were significantly shifted to the right compared with those at the adductor pollicis muscle. Approximately 1.5 times as much cisatracurium was required to produce an effect at the larynx compared with the adductor pollicis. The main hypothesis for the resistance of the larynx to neuromuscular block concerns the role of muscle fibre type and size. The laryngeal muscles have fast contraction times compared with mainly slow fibres in the adductor pollicis.[3] The calculated density of functional acetylcholine receptors is greater in fast contraction fibres than in slow fibres.[4] Laryngeal muscles contain very small fibres whereas larger fibres are found in peripheral muscles. Muscle sensitivity to non-depolarizing drugs increases with fibre size.[5]

Table 1 Onset and recovery times (mean (95% confidence intervals)) after cisatracurium 0.1 mg kg^{-1}. Lag time and onset time=times (min) to first and maximum depression of the first twitch response (T1) of the train-of-four after administration of cisatracurium; T1 (1, 25, 75, 95)=time interval (min) between administration of cisatracurium and recovery of T1 to 1%, 25%, 75%, 95% of control; Recovery index=time interval between T1 (25%) and T1 (75%). ***$P<0.0001$

	Larynx	Adductor pollicis
Lag time (min)	0.4 (0.3–0.5)	0.7 (0.6–0.8)***
Onset time (min)	2.7 (2.2–3.2)	3.9 (3.0–4.8)***
T1 (1) (%)	7.9 (6.1–9.7)	19.5 (15.1–23.9)***
T1 (25) (%)	10.7 (7.6–13.8)	25.9 (19.8–32.1)***
T1 (75) (%)	20.8 (15.6–26.1)	37.3 (32.1–42.5)***
T1 (95) (%)	26.9 (20.1–33.7)	45.6 (39.7–51.5)***
Recovery index (%)	10.4 (7.6–13.2)	11.6 (9.3–13.9)

The more rapid onset of cisatracurium at the larynx than at the adductor pollicis suggests that time to peak effect is related to blood flow. Duration of effect of cisatracurium was 20 min less at the larynx than at the adductor pollicis (Table 1). This may be a result of the relative resistance of the larynx to neuromuscular block compared with the adductor pollicis.[2 6]

In summary, we observed, as expected, a relative resistance to the effect of cisatracurium at the larynx compared with the adductor pollicis muscle.

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