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ORGANON 9426 NEUROMUSCULAR BLOCKADE AT THE ADDUCTOR MUSCLES OF THE LARYNX AND ADDUCTOR POLLICIS IN MAN

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It was previously demonstrated that larger doses of vecuronium are required to induce neuromuscular blockade (NMB)of the laryngeal muscles than the adductor pollicis (AP) (1). Organon 9426 is a new nondepolarizing muscle relaxant with a shorter onset of action than vecuronium at the AP (2).The aim of this study was to determine the onset of action of Organon 9426 at the laryngeal adductor muscles.
Methods: The protocol was approved by our local Ethical Committee. Fourteen ASA I or II patients, 24-63 years old, were studied after giving informed consent. Anesthesia was induced with propofol (2-2.5 mg/kg) and fentanyl (3-5 g/kg). Tracheal intubation was performed without muscle relaxant and the inflatable cuff of the tracheal tube was positioned under direct vision between the cocal cords. The cuff was inflated to 10-12 mm Hg with air. The lungs were mechanically ventilated to maintain end-tidal CO_2 within normal limits. Anesthesia was then maintained with propofol and intermittent doses of fentanyl. The use of nitrous oxide or halogenated agents was avoided. Bilateral adduction of the vocal cords was produced by supramaximal stimulation of the recurent laryngeal nerve over the notch of the thyroid cartilage every 10 seconds. The vocal cord response was evaluated by measuring the pressure change produced in the cuff of the tracheal tube. Simultaneously the ulnar nerve was stimulated at the wrist and the force of contraction of the AP was measured. Organon 9426 0.25 (n=7) or 0.50 (n=7) was given as a bolus. First twitch height (T_1) was measured. A Student's t test for paired data was used. All the results are expressed as mean ± SEM.
Results: At both doses Organon 9426 produced NMB more rapidly on the vocal cords than on the AP. With both doses maximum blockade was less intense and recovery was much more rapid at the vocal cords than at the AP (table 1)
Discussion: This study demonstrates that Organon 9426 has a rapid onset of action particularly on the laryngeal adductor muscles. A dose of at least 0.5 mg/kg could be necessary to produce good conditions for tracheal intubation, because such a dose is necessary to block the laryngeal adductor muscles.
In conclusion Organon 9426 could be a valuable alternative when a rapid onset of NMB at the vocal cords is required.
References:
1. Anesthesiology 73 : A884, 1990
2. Br J Anaesth 64 : 521-523, 1990

Table 1 : Mean ± SEM, $p < 0.05$ between both muscles

	Dose	Vocal cords	Add.Poll.
Max block (%)	0.25	37 ± 8	69 ± 8
	0.50	77 ± 5	98 ± 1
Onset (min)	0.25	1.6 ± 0.1	3.0 ± 0.3
	0.50	1.3 ± 0.1	2.4 ± 0.2
Rec 90 % (min)	0.25	7 ± 1	20 ± 4
	0.50	22 ± 3	37 ± 4

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TITLE: NEUROMUSCULAR BLOCKING EFFECT OF ORG 9426 ON HUMAN DIAPHRAGM.

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The sensitivity of the neuromuscular junction to muscle relaxants differs according to muscle groups[1]. While the neuromuscular blocking effect (NMBE) of muscle relaxants is usually monitored on the adductor pollicis muscle (APM), its main clinical implication is the paralysis of respiratory muscles. In the present study, we compared the NMBE of Org 9426 (ORG) on the diaphragm and the APM.

Six ASA I surgical patients were studied with informed consent and approval by the Ethics Committee. Anesthesia was induced with thiopental (6-8 $mg.kg^{-1}$) and fentanyl (2 $mcg.kg^{-1}$) IV. Tracheal intubation was performed after local anesthesia. Anesthesia was maintained with nitrous oxide 60% in oxygen and repeated doses of fentanyl (1 $mcg.kg^{-1}$). End-tidal CO_2 was monitored and maintained to 5%. The phrenic nerves were stimulated bilaterally at the neck using supramaximal single twitch stimulation (0.1 Hz). The evoked response was evaluated by the transdiaphragmatic pressure, which is defined as gastric minus esophageal pressure. The pressures were recorded using two balloon catheters connected to a differential pressure transducer. Supramaximal single twitch stimulation was also applied to the ulnar nerve at the wrist and and the force of the thumb was measured. After stabilization of twitch responses, ORG (0.6 $mg.kg^{-1}$) was administered. The following parameters were determined: the onset time (OT), the time from injection to 5% (T5), 25% (T25), 75% (T75), and 90% (T90) recovery of the twitch height (TH) and the recovery index (RI). Data were compared by paired t-test.

Following ORG complete neuromuscular blockade was achieved on the two muscles. The NMBE was shorter on the diaphragm than on the adductor pollicis muscle (Table). The onset time and the recovery index did not differ significantly.

Table. Effect of Org 9426 (0.6 $mg.kg^{-1}$).
Results are expressed as mean ± SD (min).

	OT	T5	T25	T75	T90	RI
Diaphragm:	1.1:	18.8:	21.7:	28.4:	33.9:	6.7:
	± 0.2:	± 7.2:	± 7.6:	± 9.2:	± 8.1:	± 4.2:
Adductor Pollicis :	1.2:	29.6:	37.3:	48.3:	56.2:	11.0:
	± 0.1:	± 8.9:	±12.0:	±17.3:	±20.2:	± 5.5:
p	: NS	:<0.02:	<0.02:	<0.02:	<0.05:	NS :

It can be concluded that muscle paralysis is rapidly achieved after Org 9426 (0.6 $mg.kg^{-1}$) and that there will be no residual diminution of the diaphragmatic elicited response when the TH of the adductor pollicis muscle has returned to control values.

Reference.
1. Anesthesiology 58: 414-417, 1983.