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Title: INTUBATION CONDITIONS AND TIME-COURSE OF ACTION OF ORG 9426.  
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INTRODUCTION: Org 9426 is a new relaxant with a rapid initial rate of development of neuromuscular block. Other time-course characteristics are similar to those of vecuronium (1). The intubation conditions were studied 60 or 90 s following administration of 600 µg/kg Org 9426 (2x ED90) and compared to those created by 1.5 mg/kg suxamethonium, given 3 min following precurarisation with 10 mg gallamine iv.

METHODS: In agreement with FDA regulations 70 patients, ASA 1 or 2, age 18-60, M/F, were allocated to 7 groups of 10 patients (groups 1-7). They were randomized with respect to relaxant and intubation time. After induction with 1.5-2.5 mg/kg propofol and 1 mg alfentanil, anesthesia was maintained with N<sub>2</sub>O:O<sub>2</sub> (2:1) and 1% inspiratory concentration of halothane. After induction and calibration of the mechanomyography (0.1 Hz) groups 1 and 2 received gallamine, 3 min later followed by suxamethonium. Groups 3 and 4 received Org 9426, 3 min after calibration. Intubation was attempted at 60 (groups 1 and 3) or 90 s (groups 2 and 4). The conditions were scored with the scale of Krieg (2). In group 5, intubation was attempted 5 min following induction under similar anesthetic conditions but without the use of a relaxant. The neuromuscular function was not monitored in groups 6 and 7 in order to be able to mimic daily clinical practice as closely as possible. These patients received a similar anesthetic, however, without administration of halothane. In group 6, gallamine was given 2 min before and suxamethonium immediately after induction. In group 7, Org 9426 was given immediately after induction; intubation was attempted at 60 s following administration of suxamethonium or Org 9426.

RESULTS: Neuromuscular block of the adductor pollicis at intubation time amounted to mean values of 92%, 98%, 65%, 77% for groups 1, 2, 3 and 4, respectively. Patients in groups 1-4 and groups 6-7 could all be intubated under good to excellent conditions (class III and IV - score of Krieg) except one patient of group 6. This patient was easily intubated 120 s after suxamethonium. In group 5, 5 patients could not be intubated at all, and 5 patients could be intubated under satisfactory conditions. Onset time following Org 9426 amounted to 213 ± 71 s, clinical duration and recovery time were 24 ± 4 and 9 ± 3 min, respectively (mean ± SD).

DISCUSSION: The initial rate of block development of Org 9426 appears to be faster than that of other non-depolarizing agents, which may be responsible for the early development of good intubation conditions. Otherwise, it resembles vecuronium with regard to time-course of action. Org 9426 seems to be a suitable drug to replace suxamethonium for rapid sequence induction.

REFERENCES: 1. Br. J. Anaesth. 1990, 64:521-3.  
2. Acta Anaesthesiol. Scand. 1980, 24:423-35.

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TITLE: ORG 9426: ONSET, INTUBATING CONDITIONS, AND CLINICAL DURATION  
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Introduction: ORG 9426, a nondepolarizing steroidal muscle relaxant, has a faster onset of action than currently available relaxants.<sup>1</sup> We documented the onset and duration of paralysis and the conditions for tracheal intubation at two doses under conditions that approximate clinical use.

Method: With approval by the Protection of Human Subjects Committee and informed consent, 28 adults undergoing elective orthopedic surgery were studied. Anesthesia was induced with alfentanil (50 µg/kg) and thiopental (3 mg/kg). The ulnar nerve was stimulated supramaximally with repetitive trains of four (2 Hz for 2 s at 10-s intervals) using surface electrodes. The evoked compound electromyogram (EEMG) of thumb adduction was recorded using a Datex NMT monitor. The bolus dose of ORG 9426 was 350 µg/kg in 14 patients and 450 µg/kg in 14 patients. Intubation was begun when the EEMG was depressed by 80%; and conditions were scored using standard criteria. If the maximum blockade of the initial dose was less than 80%, a supplemental dose to a total of 600 µg/kg was given. After intubation, anesthesia was maintained with 70% N<sub>2</sub>O and either 0.6% end-tidal halothane or an infusion of alfentanil (1.5 µg/kg/min). The onset times from the bolus dose to 80% and 100% depression of the EEMG were determined. The times from the bolus dose until spontaneous recovery to 10 (T10), 25 (T25), 75 (T75), 90 (T90) % of the final baseline and the recovery indices (T10-25) and (T25-75) were determined. Differences were assessed by one-tailed t-test. Pulse and blood pressure were recorded at maximal blockade, 2, 5, and 10 min after the initial dose, and assessed by repeated measures analysis of variance. Standard errors (SEM) are shown for all mean values. Differences were considered significant at p < 0.05.

Results: The mean age was 28 yr (range 18-43 yr). There was a significant difference between the doses in maximum blockade, and in the time to 80% blockade, but not in the time to maximum blockade, time to complete intubation (table 1), or recovery indices (table 2). No patient who received 350 µg/kg developed complete blockade; and two patients required a supplemental dose. Five patients who received 450 µg/kg achieved 100% blockade. All intubating conditions were good or excellent. Scores of good reflected very slight movement of the diaphragm. No significant change in heart rate or blood pressure was observed.

Table 1 Onset of Effect

	350 µg/kg	450 µg/kg
Maximum blockade(%)	84 ± 5	96 ± 5
Time to 80%(s)	172 ± 18	117 ± 24
Time to maximum(s)	258 ± 15	214 ± 25
Intubation time(s)	206 ± 19	159 ± 25

Table 2 Spontaneous Recovery from Blockade

Interval	350 µg/kg		450 µg/kg	
	n	min	n	min
T10	5	16 ± 1	12	18 ± 1
T25	12	17 ± 2	14	21 ± 1
T90	12	29 ± 2	14	36 ± 2
T10-25	5	6 ± 2	12	4 ± 1
T25-75	12	8 ± 1	14	9 ± 1

Discussion: The maximum blockade of both doses of ORG 9426 were less than expected. During "balanced" anesthesia, Nagashima and Foldes estimated the ED95 to be 305 µg/kg in adults with an average age of 48 yr;<sup>2</sup> thus we expected that most patients given 350 and 450 µg/kg to have 100% blockade. In our patients, who were younger, it would appear that the ED95 was higher - about 450 µg/kg. With the ability to begin intubation at 117 seconds and a clinical duration of 21 minutes at the 450 µg/kg dose, ORG 9426 should be a clinically useful drug.

References: (1) Anesthesiology 73:A906, 1989.  
(2) Foldes (personal communication).