

TITLE: ORG 9426: SINGLE-DOSE RESPONSE, ONSET, AND DURATION WITH HALOTHANE ANESTHESIA
AUTHORS: WC Tullock MD, DH Wilks MD, BW Brandom MD, P Diana MD, DR Cook MD
AFFILIATION: Department of Anesthesiology, Montefiore Hospital, and the University of Pittsburgh School of Medicine, Pittsburgh, Pa 15213

Introduction: ORG 9426 is a nondepolarizing steroidal muscle relaxant that has been shown in several animal species to have a fast onset and a short to intermediate duration of action. Our study evaluates the dose response in humans.

Method: With approval by the Protection of Human Subjects Committee and informed consent, 32 adult patients undergoing elective surgery were studied. Anesthesia was induced with fentanyl (1.2-4.5 µg/kg) and thiopental (2-11 mg/kg). Intubation was accomplished without muscle relaxant. Anesthesia was maintained with 0.6% halothane and 60% N₂O. 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 (EMG) of thumb adduction was recorded using a Datex NMT monitor. Patients were randomly assigned to receive an initial dose of 80, 100, 120, or 160 µg/kg of ORG 9426. After maximal response to the initial dose, a supplemental dose was given so that all patients received a total dose of 300 µg/kg. The initial dose-response relation was constructed using log-probit transformation and least-squares regression analysis. The time between the initial dose and maximal response was taken as the onset time. The time between the supplemental dose and spontaneous recovery to 10 (T10), 25 (T25), 75 (T75), 90 (T90) % of the final baseline and the time intervals (T10-25), (T25-75) and (T10-90) were determined. 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.

Results: The mean age was 39 (range 18-65). End-tidal halothane and CO₂ concentrations were $0.59 \pm 0.02\%$ and 32 ± 0.5 mmHg, respectively. The equation $y = 3.2x - 1.56$ describes the dose-response relation. The ED₅₀ was 105 µg/kg; the ED₉₀ was 259 µg/kg. No significant change in heart rate or blood pressure was observed ($P < 0.05$). 19 patients had 100% blockade after the supplemental dose, the other 13 patients had a mean maximal block of $10 \pm 2\%$ (range 1-34) of baseline.

		Dose Response	
Dose (µg/kg)	n	Onset (s)	% Blockade
80	7	142 ± 14	32 ± 10
100	7	144 ± 11	60 ± 9
120	9	160 ± 13	57 ± 8
160	9	160 ± 13	65 ± 8

		Spontaneous Recovery			
Interval	n	min	Interval	n	min
T10	28	16 ± 0.9	T10-25	28	4 ± 0.3
T25	31	20 ± 0.9	T25-75	30	8 ± 0.4
T90	29	30 ± 1.3	T10-90	28	15 ± 0.3

Discussion: The onset time of ORG 9426 (142 to 160 s) is shorter than that reported for vecuronium and mivacurium (5 to 7 min) for doses producing the same range of blockade.^{1,2} The T25-75 recovery index for ORG 9426 (8 min) is similar to that for vecuronium (9 to 12 min). With vecuronium the absence of cardiovascular effects allows the use of higher doses to speed onset time.³ Our data support a similar trial with ORG 9426.

References: 1. Anesthesiology 55:6-11, 1981
 2. Anesthesiology 70:31-35, 1989
 3. Anesth Analg 70:86-90, 1990

A878

TITLE: RECOVERY OF RESPIRATORY MUSCLE FUNCTION IN SURGICAL OUTPATIENTS
AUTHORS: A. Stanec, M.D., W. Nuesa, M.D., A. Akturk, M.D., M. Pillon, M.D., K. Capek, R.R.T.
AFFILIATION: Anes. Dept., St. Joseph's Hospital and Medical Center, Paterson, NJ 07503

Previous studies proposed that maximum inspiratory pressure (MIP) of 25 cm H₂O and vital capacity (VC) of 15 ml/kg were acceptable for maintaining adequate ventilation after extubation. These values have been reported to be interchangeable with train of four (TOF) ratio of 0.7. In conscious volunteers these "minimal values" were inadequate for airway protection and/or obstruction.¹ The purpose of this study was to determine the respiratory muscle function recovery from shorter acting non-depolarizing relaxants.

Thirty ASA I patients undergoing outpatient orthopedic procedures under general anesthesia were studied. Institutional Board Review and informed consent were obtained. Anesthesia was induced with fentanyl and sodium thiopental in usual doses. Endotracheal intubation was accomplished with intubating doses of atracurium or vecuronium. Ventilation was controlled and steady state conditions were maintained. An adductor pollicis monitor (APM) was used to measure the force of adductor pollicis muscle contraction evoked by supramaximal stimulation of the ulnar nerve at the wrist. Respiratory muscle function was tested by MIP and VC. Control values were obtained in unpremedicated patients in the Operating Room (OR) holding area. Control clinical tests in-

cluded the ability to maintain a head lift and a hand grip. All measurements were repeated in the OR prior to and after reversal, and 15, 30 and 60 min after reversal in the Post Anesthesia Care Unit (PACU). Control TOF, 50 and 100 Hz responses were obtained after induction of anesthesia and repeated prior to and after reversal. All respiratory values were measured in triplicate.

The control values from this study fell within the accepted normal range (in the absence of anesthetics and relaxants). In the OR, prior to reversal, in patients with TOF ratio 0.6-0.7, the MIP and VC values were decreased by 66 and 57% respectively. In the PACU 30 min after reversal, with TOF ratio of 0.9 - 1.0, the MIP and VC values were decreased by 28 and 23% respectively. Prior to discharge from PACU (60 min after reversal) the MIP and VC values were 15 and 10% less than the controlled values.

The concern that residual respiratory muscle weakness may be present in patients recovering from anesthetic and muscle relaxant agents, is a valid one. Our data suggests that in determining recovery of respiratory muscles, higher values of MIP and VC than those generally accepted should be considered. The percentage decrease from each patient's control values is a better indicator of respiratory muscle function recovery than the absolute value measured. We conclude that MIP and VC are simple to measure in conscious patients and may be used as a guide in determining an individual patient's ability to protect his airway prior to discharge from the PACU.

References

1. Anesthesiology 70:381-385, 1989