TITLE: **EFFECTS OF HYPERPARATHYROIDISM ON THE VECURONIUM-INDUCED NEUROMUSCULAR BLOCKADE**

AUTHORS: **E.Roland* MD, E.Rouple* MD, J.M.K.H.Wierda*** MD, E.Sarfati** MD, S.Villiers*MD, C.Dubost** MD, B.Eurin* MD**

AFFILIATION: Dept Anesth* & Surg**, Hop Univ. Saint-Louis, Paris, France
Dept Anesth., Groningen Univ. Hosp.,The Netherlands***

Introduction: Ionized plasma calcium (Ca++) concentration plays an important role in neuromuscular transmission and blockade (NMB) [1]. Primary hyperparathyroidism (HPT) has beeen shown to interfere with vecuronium (Vec) NMB [2]. This study was designed to compare the dose-response curve, the steady state dose requirement (SSDR),the recovery of vecuronium-induced NMB in patients with HPT to control patients.

Methods: After informed consent and ethical committee approval, 20 patients (ASA I or II) were studied: 10 with HPT scheduled for parathyroidectomy and 10 controls. All patients were premedicated with Hydroxyzine 2.5-4.5 mg./kg. Anesthesia was induced with thiopental 6-8 mg/kg iv and maintained with N2O 60-70 % and incremental doses of fentanyl. Tracheal intubation was performed under topical anesthesia. Single supramaximal stimuli (0.1 Hz) were delivered to the ulnar nerve at the wrist. The heigh of the twitch (HT) of the adductor pollicis were recorded. After measurement of the control twitch height (CH), the dose-response curve was determined according to cumulative dose response technique (CDR): patients received incremental doses of Vec until 95 % NMB was obtained [3]. Then,the SSDR was determined by adjustement of rate infusion in order to maintain the HT between 5 and 15 % of CH during 20 min. Spontaneous Recovery Index (RI 25-75) was measured after Vec infusion was stopped. Linear regressions were obtained between NMB in % of CH and log of cumulative Vec dose. A regression line was calculated for each patient from which ED 50, ED 90, ED 95 were derived. Groups were compared using Mann & Withney U test; p< 0,05 was regarded statistically significant.

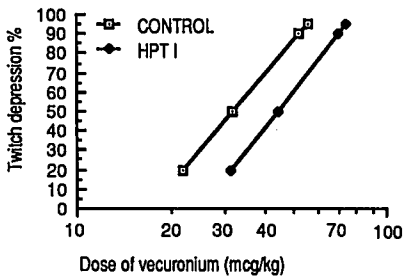
Results: The mean dose response curve of patients with HPT was shifted to the right (Fig) with stastistically different intercepts. The ED 50, 90 and 95, SDDR and RI 25-75 values are shown in the Table. A significant correlation was found between ED 50 values and Ca++ (r=0.56, F-test, p=0.00027).

		HPT	CONTROL
ED 50	(mcg/kg)	44.2 ± 9.4 *	31.8 ± 5.1
ED 90	(mcg/kg)	70.4 ± 16.3*	52.3 ± 8.0
ED 95	(mcg/kg)	74.6 ± 16.5 *	55.6 ± 8.7
SSDR	($mg/m^2/h$)	3.85 ± 1.0.2	3.61 ± 0.90
RI 25-75	(mn)	12.3 ± 4.8	9..8 ± 1.9
Ionized Ca++	(meq/l)	3.18 ± 0.35 *	2.45 ± 0.08

Values are given as mean ± SD * Significantly (p< 0.05) different from control

Conclusion: This study shows that ED 50, using CDR technique, is 39 % more important for patients with HPT than for control group. This resistance to Vec may be partialy related to high Ca++ level in HPT, whereas SSDR and RI were not affected by HPT.

Reference: *1 - Br J Anaesth 52 : 863-866, 1980.*
2 - Anesthesiology 71: A 814 , 1989
3 - Anesthesiology 53: 161-166 , 1980



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Title: DOSE-RESPONSE AND RECOVERY OF ORG 9426 UNDER ENFLURANE ANESTHESIA

Authors: RR Bartkowski M.D., Ph.D., TA Witkowski M.D., SS Azad M.D., RH Epstein M.D., A Marr C.R.N.A., J Lessin R.N.

Affiliation: Department of Anesthesiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107

ORG 9426 is a new steroidal analog of vecuronium. It has been reported to have a brief duration of action and rapid onset.[1] This study investigated its dose-response and recovery characteristics in 40 ASA 1-2 patients between 18-65 years of age. All patients gave informed consent in a protocol approved by our IRB.

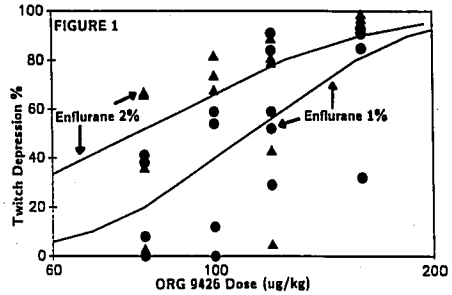
Methods: All patients received diazepam 100-150 ug/kg 30-60 minutes before anesthetic induction. Anesthesia was induced with thiopental 4-8 mg/kg and fentanyl 4-8 ug/kg. Intubation was accomplished under enflurane and N2O/O2 without the aid of muscle relaxant. Anesthesia was maintained with enflurane 1% (n=20) or 2% (n=20) and N2O/O2 at a 60/40 ratio. After 15-25 minutes of stable end-tidal enflurane concentration, ORG 9426 was injected as a bolus. Patients were randomized to one of four doses: 80, 100, 120, 160 ug/kg. After the maximum block was achieved, additional ORG 9426 was given to a total of 300 ug/kg and enflurane reduced to 0.5-0.8%. Neuromuscular transmission was assessed by stimulation of the ulnar nerve at the wrist with surface electrodes and measurement of the force of thumb adduction with a Grass FT-10 transducer. Stimulation was by train of four at 12 second intervals.

Probit analysis for continuous data was used to determine the ED50 and ED95 for the population. All data are presented as mean ± S.D.

Results: The response to the initial dose is shown in figure 1. The ED50 for ORG 9426 at 1% and 2% enflurane are 112 and 78 ug/kg. The corresponding values for ED95 are 214 and 195 ug/kg. Recovery times are: dose-25%: 27.4 ± 7.3 min. and, 25%-75%: 12.0 ± 2.6 min.

Discussion: ORG 9426 has a rapid recovery even under enflurane anesthesia which has been shown to potentiate blockers. Enflurane potentiation is evident in that ED50 and ED95 which are less than the values of 168 and 285 ug/kg reported by Nagashima[2] under balanced anesthesia.

These findings indicate that ORG 9426 is promising because of its brief duration. It's action is potentiated markedly by enflurane in a manner similar to other nondepolarizing blockers.



1. Anesth Anesth 70:S437, 1990.
2. Anesthesiology 71:A773, 1989.