TITLE: ONSET, DURATION, AND RECOVERY FROM ORG 9426 IN THE ELDERLY

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ORG 9426 is a new, short-acting, steroidal, non-depolarizing neuromuscular blocking drug[1]. This study was performed to determine the differences in onset, duration, and recovery from neuromuscular blockade between young (25-40 yr) and elderly (65-80 yr) patients after subparalysing doses of ORG 9426 during balanced anesthesia.

METHODS: Following Ethics Committee approval and informed consent, 23 patients (17 young, 6 elderly) were studied during thiopental/N_2O/O_2 anesthesia. Neuromuscular blockade was assessed using TOF stimulation at 0.1 Hz of the ulnar nerve and recording the force generated in the adductor pollicis.

Following induction of anesthesia ORG 9426 was randomly administered in one of four doses (120, 160, 200 or 240 μg/kg). After maximal block of T1 a further increment to a toal of 300 μg/kg was given. The following variables were measured: Onset - time from injection to maximal T1 block; Duration - time from 300 μg/kg to 25% T1 recovery; Recovery - time between 10-25%, 25-50%, and 10-50% recovery of T1.

RESULTS: The initial dose of ORG 9426 produced subparalysing block in all patients. The Onset, Duration, and Recovery times are shown in the Table (mean ± SEM). (* P <0.05)

	Young	Old
Onset (s)	180.8 ± 13.4	235.7 ±16.9*
Duration (min)	9.5 ± 0.6	16.0 ± 1.1*
Recovery 10-25%	5.1 ± 0.8	6.9 ± 1.1
5-50%	4.6 ± 0.7	10.0 ± 1.6*
10-50%	8.5 ± 1.1	16.5 ± 2.5*

CONCLUSION: Onset, duration and recovery from ORG 9426 are prolonged in the elderly. The results are similar to those for vecuronium[2] but for both age groups these variables are shorter than for atracurium and vecuronium[3].

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TITLE: A COMPARISON OF THE EFFECTS OF DESFLURANE AND ISOFLURANE ON THE ACTION OF ATRACURIUM IN MAN

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Desflurane is a new volatile anesthetic agent currently under evaluation for clinical use in the United States. Desflurane has a low blood:gas solubility coefficient suggesting that desflurane should allow rapid induction of and emergence from anesthesia (1). There is also evidence that desflurane possesses significant muscle relaxation properties, and may potentiate the effect of non-depolarizing muscle relaxants(2). We have conducted a controlled, randomized study of the degree of neuromuscular blockade induced by atracurium at several dose levels, under either desflurane or isoflurane anesthesia.

Anesthesia consisted of induction with midazolam and thiopental, followed by desflurane or isoflurane plus 60% nitrous oxide in oxygen. The volatile anesthetic was administered at either 1.25 MAC or 0.65 MAC, and the atracurium dose was 0.05 mg/kg, 0.10 mg/kg, or 0.15 mg/kg. With the permission of our Institutional Review Board, and with informed written consent, forty eight ASA Class 1 or 2 patients undergoing elective surgery were randomly assigned to one of twelve groups, based on the anesthetic and dose, and the dose of atracurium administered. After a stable end-tidal concentration of anesthetic had been achieved, the predetermined dose of atracurium was administered . The response to train-of-four ulnar nerve stimulation with 0.2 ms supramaximal pulses was recorded every twelve seconds.

RESULTS/DISCUSSION: The mean ± SEM of the maximal percentage blockade achieved in each group is reported in the table below. N=4 in all groups except for ISO 0.65/Atra 0.05 (n=3) and ISO 0.65/Atra 0.10 (n=5). Probit analysis and linear regression revealed no significant differences between the isoflurane and desflurane groups, although there is a suggestion of greater potentiation by desflurane than isoflurane at 1.25 MAC and 0.05 mg/kg atracurium (p = 0.07). A larger group sample size might demonstrate a difference in the muscle relaxant potentiation, at least at high doses of the potent agents. The atracurium effect is clearly more than is expected with "balanced" anesthesia, where, for example, 0.1 mg/kg gave only a 14% block (2), compared to 80-100% at the two doses of both anesthetics in this study . The potentiation by the anesthetics appears to be dose-dependent. Future studies of the interaction of atracurium with desflurane may have to utilize lower doses of atracurium in order to generate useful dose-response curves.

AGENT	MAC	Atracurium (mg/kg)	% Max Block (mean±SEM)
DES	1.25	0.15	98 ± 2
ISO	1.25	0.15	97 ± 2
DES	1.25	0.10	96 ± 2
ISO	1.25	0.10	97 ± 1
DES	1.25	0.05	74 ± 8
ISO	1.25	0.05	41 ± 3
DES	0.65	0.15	96 ± 3
ISO	0.65	0.15	96 ± 1
DES	0.65	0.10	78 ± 11
ISO	0.65	0.10	81 ± 7
DES	0.65	0.05	39 ± 7
ISO	0.65	0.05	40 ± 16

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