

Title: NEUROMUSCULAR BLOCKING EFFECTS OF ATRACURIUM DURING N₂O-FENTANYL OR ISOFLURANE ANESTHESIA

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Introduction. Atracurium (EW33A) is a new non-depolarizing muscle relaxant of short-intermediate duration now undergoing clinical trials.(1) In this study we compare its neuromuscular blocking effects during isoflurane and N₂O-fentanyl anesthesia.

Methods. We obtained informed consent and approval from the local committee on human research to study 50 ASA I or II patients undergoing elective surgery. All patients were premedicated with morphine sulphate, 0.15 mg/kg IM, and diazepam, 10 mg po. In 25 patients (Group I), anesthesia was induced with thiopental, 4-6 mg/kg IV, fentanyl 7-10 ug/kg IV and N₂O 60%. In 25 patients (Group II), anesthesia was induced with thiopental, 4-6 mg/kg IV, and the inhaled anesthetic isoflurane (0.75% end-tidal) with 60% N₂O. In all patients the trachea was sprayed with 4% lidocaine and then intubated without the use of muscle relaxants. The concentration of isoflurane (in Group II), N₂O and CO₂ were monitored continuously by mass spectrometry. End-tidal PCO₂ and esophageal temperature were maintained within the normal range. The ulnar nerve was stimulated at the wrist with supramaximal impulses of 0.15ms duration at 0.15 Hz. The resultant force of thumb adduction was measured by a Grass FT03 force displacement transducer and recorded on a polygraph. Heart rate and blood pressure were measured by a Dinamap[®] at one minute intervals and recorded on a printer. ECG was monitored continuously. After 30-45 minutes of stable anesthesia the patients received atracurium 0.04-0.25 mg/kg IV. We measured peak effect (maximum % twitch tension depression), the onset time (time to peak twitch tension depression) and duration (time from injection to 95% recovery). The first 20 patients in each group were used to generate a log dose versus maximum twitch tension depression relationship. The last 5 patients in each group were given a dose approximately 2 times the ED₉₅ (the dose required to depress twitch tension by 95%) as determined by the previous 20 patients. The log dose vs. peak depression of twitch regressions were compared by t test, first to determine if they deviated from parallelism, then to determine differences in elevation. Onset times within each anesthetic group were compared by analysis of variance. The maximum changes in heart rate and mean arterial blood pressure that were recorded in the ten minutes after injection were compared to pre-injection values for significance by t test.

Results. The ED₅₀ (the dose required to depress twitch tension by 50 percent of control) for the N₂O-fentanyl group was 0.083 mg/kg whereas the corresponding value for the isoflurane group was

0.068 mg/kg (P < 0.05). The dose-response regressions did not deviate from parallelism. There were no significant changes in heart rhythm, heart rate or mean arterial pressure at any dose given.

GROUP I NITROUS OXIDE-FENTANYL

Dose (mg/kg)	Onset (min)	Block (%)	Recovery (min)
0.06	6.2±1.7	4±4	12±1
0.07	7.6±2.0	35±22	23±7
0.08	6.3±0.7	51±17	21±2
0.10	7.0±1.4	67±20	21±3
0.25	2.8±0.7*	100	49±15

GROUP II ISOFLURANE

Dose (mg/kg)	Onset (min)	Block (%)	Recovery (min)
0.04	6.4±0.9	15±13	19±4
0.06	6.4±1.4	35±34	20±8
0.07	6.6±1.1	31±14	18±7
0.08	5.8±1.6	82±20	33±14
0.25	2.3±0.9*	100	55±14

All values mean ± S.D.

n=5 for all dosage levels

* Different from other doses within the same anesthetic (P < 0.05)

Discussion. Our results indicate that isoflurane anesthesia shifts the dose-response curve of atracurium to the left when compared to N₂O-fentanyl anesthesia. There is no difference in onset time and duration of effect at comparable doses between the two groups. However, when compared to the standard nondepolarizing muscle relaxants (i.e. pancuronium, d-tubocurarine) the duration of action is shorter. Also, both groups demonstrated markedly shorter onset times at twice the ED₉₅ without producing cardiovascular effects. The use of higher doses may result in even shorter onset times without cardiovascular effects. If this occurs, atracurium may be useful in providing relaxation for intubation of the trachea.

Reference

1. Payne JP, Hughes R: Evaluation of atracurium in anesthetized man. Br J Anaesth 53:45-54, 1981