Title: THE EFFECTS OF ENFLURANE, HALOTHANE AND ISOFLURANE ON VECURONIUM NEUROMUSCULAR BLOCKADE IN HUMANS

Authors: S.M. Rupp, M.D., R.D. Miller, M.D., P.J. Gencarelli, M.D.

Affiliation: Department of Anesthesia, University of California, San Francisco, California 94143

Introduction. Enhancement of the neuromuscular effects of vecuronium (ORG NC45) by volatile anesthetics has been reported previously.[1,2] In this study we quantified and compared the potency, onset and duration of action times of vecuronium at two end-tidal concentrations of each anesthetic: enflurane, halothane and isoflurane.

Methods. Informed consent and approval from the local committee on human research was obtained to study 54 ASA I or II patients scheduled for elective surgery. Patients were premedicated with diazepam, 10 mg po. Anesthesia was induced with thiopental, 2-4 mg/kg, IV and one of the volatile inhaled anesthetics with 60 percent nitrous oxide. The trachea was intubated without the use of muscle relaxants. The concentration of the volatile anesthetics were determined continuously by mass spectrometry. End-tidal pCO_2 and esophageal temperature were maintained within the normal range. Neuromuscular function was measured by recording force of thumb adduction in response to supramaximal stimulation of the ulnar nerve at the wrist using a GRASS FT10 force transducer. The patients were divided into six groups. In three groups, the end-tidal anesthetic concentration was maintained at 1.2 MAC (in 60% N_2O): 0.45% halothane; 1.02% enflurane: 0.70% isoflurane. In the other three groups, the end-tidal anesthetic concentration was 2.2 MAC: 1.20% halothane; 2.80% enflurane; 1.84% isoflurane. After 25 minutes of stable end-tidal concentration of anesthetic, vecuronium was administered IV. The maximum percent depression of twitch tension (peak effect), time from administration to peak effect (onset time), and time from injection to return of muscle twitch tension to 90% of control (duration of action) were determined. A dose-response (log dose vs. peak effect) relationship for vecuronium was obtained by analysis of linear regression for each of the six groups. All regression lines were compared using the analysis of covariance. First the lines were tested to determine if they deviated from parallelism. Then the Student-Newman-Keuls test was applied to test for differences in elevation. An ED_{50} for each group was calculated from the regression analysis and these values were used to compare the potency of vecuronium between groups. Duration of action was compared between groups by plotting duration versus peak depression of twitch for each group, calculating a linear regression analysis and then comparing these regressions as was done for the dose-response relation. Statistical significance was the $P < 0.05$ level.

Results.

ANESTHETIC	ED_{50} (ug/kg)	ONSET (min)	DURATION (min)
1.2MAC HAL	16.9±1.2	6.2±0.2	20±11
2.2MAC HAL	13.8±1.2	6.1±0.2	18±3
1.2MAC ISO	14.7±1.1	6.1±0.3	15±5
2.2MAC ISO	* 9.8±1.2	6.9±0.5	24±7
1.2MAC ENF	# 12.8±1.2	7.0±0.5	25±13
2.2MAC ENF	* 6.3±1.3	* 9.7±0.6	* 50±21

All values mean ±SEM
* different from all other groups ($P < 0.05$)
# not different from 2.2MAC HAL but different from all other groups ($P< 0.05$)

Discussion. At a given MAC of anesthetic, enflurane is the most potent of the volatile anesthetics in its ability to augment a vecuronium-induced neuromuscular block followed by isoflurane and lastly halothane. Comparisons of ED_{50} within each anesthetic show that increasing the depth of anesthesia shifts the vecuronium dose-response curve to the left more for enflurane > isoflurane > halothane. The prolonged onset time of neuromuscular blockade at 2.2 MAC enflurane may be related to decreased muscle blood flow. The prolonged duration of vecuronium at 2.2 MAC enflurane is most likely related to enflurane's ability to depress twitch tension alone when used at concentrations greater than 2.5 percent.[3]

References.

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