Title: ENFLURANE POTENTIATION OF NEUROMUSCULAR BLOCKADE BY ATRACURIUM

Authors: F. M. Ramsey, M.D., P. A. White, C.R.N.A., E. H. Stullken, M.D., L. L. Allen, R.Ph., R. C. Roy, M.D.

Affiliation: Department of Anesthesia, Bowman Gray School of Medicine of Wake Forest University, 300 S. Hawthorne Road, Winston-Salem, NC 27103
and
Burroughs Wellcome Co., Medical Division, 3030 Cornwallis Road, Research Triangle Park, NC 27709

Introduction. Atracurium (BW33A) is an intermediate acting non-depolarizing neuromuscular blocking agent currently undergoing clinical trials in the United States. Previous clinical studies in humans have shown it to have a potency similar to metocurine but a duration of action only 40-50% of the duration of longer acting muscle relaxants in current clinical use.[1] Additional reported advantages include lack of cummulative effects and absence of significant hemodynamic side effects.[2,3] This study was performed to determine the effect of enflurane anesthesia on the neuromuscular dose response curve of atracurium.

Methods. Forty-six patients, ASA status I or II, 18 to 60 years old were studied. Approval was obtained from the institutional Human Research Practices Committee and written informed consent was obtained from all patients. Neuromuscular dose-response curves were plotted following bolus administration of atracurium in 15 patients under balanced anesthesia (thiopental, fentanyl, N_2O/O_2) and 31 patients under N_2O/O_2, enflurane anesthesia (MAC end tidal = 1.16 ± SE.03). Monitoring included blood pressure by cuff, heart rate by tachograph, continuous EKG, and temperature by esophageal thermistor. All patients were intubated without muscle relaxants and ventilated mechanically to maintain normocarbia, documented by arterial blood gas analysis. Evoked twitch response of the adductor pollicis muscle to supramaximal stimulation of the ulnar nerve at 0.1 Hz was recorded on a Grass polygraph. After establishing stable baseline control twitch response a single, sequentially increasing, dose of atracurium was administered to 3 subgroups of patients in the balanced anesthesia group (B) and 3 subgroups of patients in the enflurane group (E). No further muscle relaxants were administered until full spontaneous recovery of twitch occurred to 95% of control. When necessary, residual block was antagonized with neostigmine and atropine. Maximum percent neuromuscular block (NMB) following each dose of atracurium was measured. Probit values of the maximum percent block versus log dose of atracurium were plotted for the three doses in each group and lines of best fit were computed by the method of least squares linear regression analysis. The slopes and intercepts of the two lines were computed and compared to each other to determine if enflurane caused a shift in position of the curve or altered its slope. Predicted ED_{25}, ED_{50}, ED_{75}, and ED_{95} values of atracurium were extracted from the dose-response curves for both anesthetic techniques. An enflurane potentiation factor (PF) was determined by dividing the dose of atracurium required to produce a given degree of block during enflurane anesthesia by the dose required to produce an equivalent degree of block during balanced anesthesia.

Results. The neuromuscular data and probit analysis are presented in Table 1. The potentiation factors attributable to enflurane at the ED_{25}, ED_{50}, ED_{75} and ED_{95} are presented in Table 2. Standard errors of the means were omitted to conserve space.

TABLE 1

Grp	N	Dose µg/kg	NMB (%)	Log Dose	Probit	Slope	Intercept
	5	60	7.7	1.78	2.79		
B	5	150	45.8	2.18	4.79	6.35	-8.64
	5	250	89.4	2.40	6.83		
	11	80	35.2	1.90	4.50		
E	10	100	41.4	2.00	4.61	6.34	-7.76
	10	180	93.1	2.26	6.62		

TABLE 2

Group	Predicted Doses ED_{25}	ED_{50}	ED_{75}	ED_{95}
B	110.3	140.6	179.3	254.9
E	80.9	103.1	131.6	187.1
PF=E/B	0.73	0.73	0.73	0.73

Discussion. Enflurane potentiates the neuromuscular blocking effects of atracurium. The nearly identical slopes of the dose response curves establishes that the two curves are parallel. The greater intercept (-7.76 vs. -8.64) computed for enflurane places the dose response curve during enflurane above and to the left of the curve during balanced anesthesia. The constancy of the potentiation factor at 0.73 confirms the relationship. Therefore, the dose of atracurium during enflurane anesthesia can be reduced by approximately 25-30% to achieve the same degree of neuromuscular block accomplished during balanced anesthesia.

References

1. Payne JP, Hugh R. Brit J Anes (1981) 53,45.
2. Basta SJ, et al. Anes and Analg (1982) 61, 169. (Abstract)
3. Lee C, et al. Anes and Analg (1982) 61, 199. (Abstract)