TITLE: EFFECT OF A MIXTURE OF PANCURONIUM AND VECURONIUM ON HEART RATE DURING ANESTHESIA FOR CARDIAC OPERATIONS

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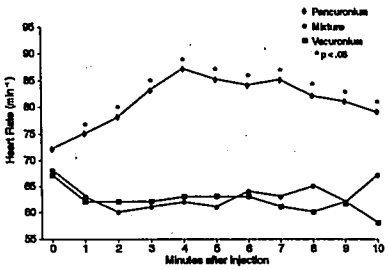
Administration of muscle relaxants frequently causes undesirable hemodynamic changes that may be detrimental to patients with unstable oxygen supply/demand balance. Pancuronium can markedly increase heart rate, and vecuronium can cause significant bradycardia, particularly when used in conjunction with potent narcotics.[1] We wished to determine if a mixture of pancuronium and vecuronium would provide better stability of heart rate, than either drug alone, when given to produce neuromuscular blockade during cardiac operations.

After Institutional Review Board approval, 21 consenting patients scheduled for cardiac operations were randomly assigned to receive vecuronium (0.1 mg/kg), pancuronium (0.1 mg/kg), or a mixture of vecuronium (0.05 mg/kg) and pancuronium (0.05 mg/kg). Patients with pacemakers or atrial fibrillation were excluded. The test drugs were diluted to equal concentrations, coded, and labeled by the pharmacist according to a randomization schedule. Anesthesia was induced with an infusion of fentanyl (50 μg/kg,iv). Heart rate and blood pressure were recorded before induction and once every minute for 10 min after the administration of muscle relaxant. Data were statistically evaluated using an analysis of variance for repeated measures.

No differences existed in the three groups in demographic characteristics or in the use of ß-receptor blocking drugs. Mean blood pressure was comparable in all groups and did not change significantly. A significant increase in mean heart rate occurred in the patients receiving pancuronium, but not in the remaining two groups (Figure).



A one-to-one mixture of pancuronium and vecuronium is commonly used during cardiac operations to achieve neuromuscular blockade with both rapid onset and long duration. Our results show that this combination does not have a significant chronotropic effect. In this respect, the mixture is similar to vecuronium alone, but differs significantly from pancuronium, which frequently causes tachycardia.

Reference: 1. Anesthesiology 36:612-615, 1972

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Title: Human Dose Response of ORG 9426 under Isoflurane General Anesthesia

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The single bolus dose response of ORG 9426 was evaluated in 72 adult human subjects during isoflurane general anesthesia. Patients were given a dose of 120, 160, 200, or 240 μg/kg of ORG 9426 after establishing a measured steady state expired isoflurane concentration between 0.5% and 1.5%. Neuromuscular blockade was continuously monitored using the ulnar evoked EMG. ED_{95}, determined by the log probit method, was 268 μg/kg, ED_{90} was 251 μg/kg, and ED_{50} was 144 μg/kg (Figure 1). No cardiovascular side effects were noted at any of these doses. The duration of 75 μg/kg and 100 μg/kg repeat doses was 14.6 ± 6.0 and 17.8 ± 6.3 minutes respectively, and no cumulative effect was apparent after as many as 5 doses. The onset time (T1 decreased to 20%) was 1.9 ± 1.0 minute at 240 μg/kg, comparable to much larger[1] relative doses of vecuronium (6xED_{90}). The average time to peak effect was 4.6 ± 1.4 minutes, which did not vary with dose. The duration (injection until T1 returned to 25%) was 23.3 ± 8.8 minutes and the recovery index (T1 increased from 25 - 75%) was 15.4 ± 8.9 minutes using 300 μg/kg. We conclude that ORG 9426 is an effective short acting non-depolarizing muscle relaxant of relatively low potency which has significantly different pharmacodynamic characteristics than currently available agents and that it deserves further evaluation in humans.

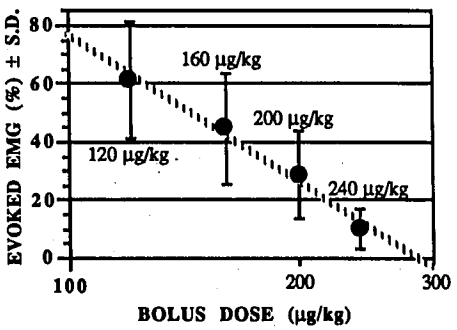

Figure 1) ORG 9426 Average Dose Response with Isoflurane

1) Ginsberg B, Glass PSA, Quill TJ, Shaffron D, Ossey KD: Onset and Duration of Neuromuscular Blockade Following High dose vecuronium administration. Anesthesiology 1989; 71:201-205