Title: THE DOSE-RESPONSE RELATIONSHIP OF MIVACURIUM UNDER BALANCED OR ENFLURANE ANESTHESIA

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Introduction. Mivacurium chloride is a nondepolarizing neuromuscular blocking agent (NBA) with a shorter duration of action than currently available agents. Since the action of other NBAs is potentiated by volatile anesthetic agents we would expect that the same is true for mivacurium. To examine this we compared the dose-response relationship of mivacurium under anesthesia based on nitrous oxide and fentanyl (balanced) to that under anesthesia based on nitrous oxide and enflurane.

Methods. Approval was obtained from our Committee for Human Research and 72 patients were studied. Premedication was with midazalom 0.02-0.05 $mg \cdot kg^{-1}$ iv. Anesthesia was induced with thiopental 2-6 $mg \cdot kg^{-1}$ iv; patients in the balanced group (n=36), received, in addition, fentanyl 5-10 $\mu g \cdot kg^{-1}$ iv, while the remaining 36 received enflurane (0.9-1.2% end-tidal concentration). Thereafter, anesthesia was maintained with nitrous oxide 60-70% (end-tidal) and supplemental boluses of fentanyl or pentothal. Esophageal temperature was maintained at 35-37 ^{o}C and end-tidal CO_2 tension between 30 and 40 mmHg. Supramaximal stimuli of 0.2 msec duration, were applied in a train-of-four sequence, repeated at 15 s intervals, to the ulnar nerve at the wrist and the the mechanical evoked response of the adductor pollicis muscle to the first stimulus (T1) in each train measured. When anesthetic conditions and T1 were stable, each patient received a predetermined, rapidly administered iv bolus of mivacurium. In the balanced anesthesia group, 4 doses, 30, 40, 50 or 70 $\mu g \cdot kg^{-1}$, were administered to 9 patients each. In the enflurane group, doses were 15, 20, 30 and 40 $\mu g \cdot kg^{-1}$. The response (R_{max}) was the maximum depression of T1 expressed as a percentage of the control response and the duration was the interval from injection until T1 recovered to 90% of control (Dur_{90}). The dose-response relationship was calculated by log-probit linear regression analysis. In each anesthesia group linear regression was used to compare R_{max} to Dur_{90}. The regression lines were for each anesthesia group were compared and differences were considered significant at $P < 0.05$.

Results. The dose-response regression line for the enflurane group was displaced significantly to the left of the line for the balanced group, (fig. 1). The mean ED50 and ED95 (doses producing 50% and 90% depression of T1, respectively) values were 38 and 69 $\mu g \cdot kg^{-1}$ under balanced anesthesia and 26 and 53 $\mu g \cdot kg^{-1}$ under enflurane anesthesia. The regression line for R_{max} vs Dur_{90} under enflurane was displaced significantly to the left of the line under balanced anesthesia (fig. 2), which indicates that the action of mivacurium is prolonged under enflurane anesthesia.

Discussion. The ED95 which we determined under balanced anesthesia falls within the range of values (58-90 $\mu g \cdot kg^{-1}$) reported by other investigators.[1,2,3] The range probably reflects differences in study design, patient populations and normal biological variation. Isoflurane has a similar effect to enflurane on the dose response relationship of mivacurium.[3] This is consistent with the effect these volatile agents have on the action of other NBAs. Priming doses of 30 $\mu g \cdot kg^{-1}$ have been used, under balanced anesthesia, to facilitate rapid endotracheal intubation with mivacurium.[4] In our study this dose produced depression of twitch response of greater than 40% in 4 out of nine patients, which suggests that this is perhaps an excessively large priming dose. In conclusion, when compared with balanced anesthesia, enflurane both potentiates and prolongs the neuromuscular blocking action of mivacurium chloride.

Figure 1. Dose-response relationship of mivacurium under balanced (• ____) and enflurane anesthesia (Δ ----). X-axis is dose of mivacurium; y-axis is maximum depression of T1 twitch tension (R_{max}).

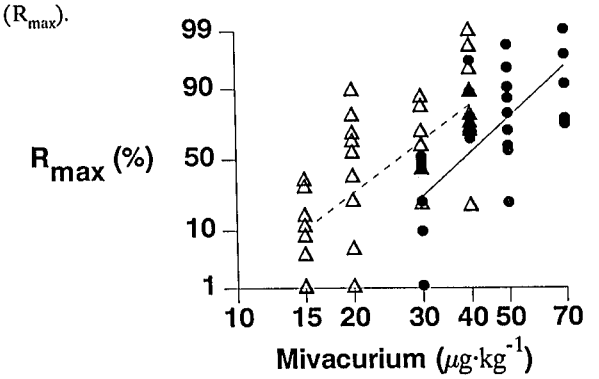
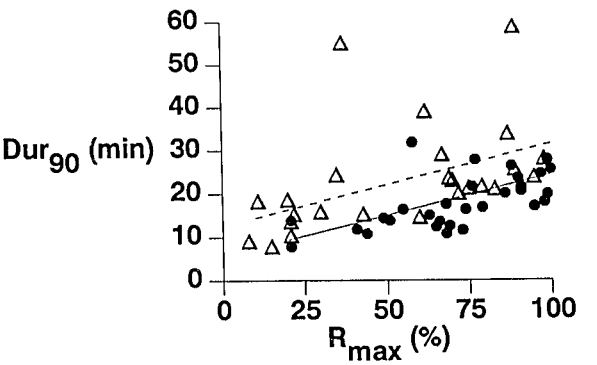


Figure 2. Relationship between maximum depression of T1 twitch tension (R_{max}) and time from injection until recovery of T1 to 90% (Dur_{90}), following mivacurium, under balanced (• ____) and enflurane anesthesia (Δ ----).



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