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TITLE: THE DURATION OF ACTION OF MIVACURIUM-INDUCED NEUROMUSCULAR BLOCK IN PATIENTS HOMOZYGOUS FOR THE ATYPICAL PLASMA CHOLINESTERASE GENE

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The elimination of mivacurium is dependent on the patients' plasma cholinesterase (pChe) activity[1]. Earlier studies have shown an inverse correlation between the duration of action of mivacurium and pChe activity in patients with normal genotype[2]. In patients heterozygous for the atypical gene mivacurium-induced block following 0.2 mg kg^{-1} has been found to be approximately 50% prolonged[3]. Four patients homozygous for the atypical pChe gene[4] were given mivacurium 0.03 mg kg^{-1} (ED_{10}) during narcotic anesthesia. The response to train-of-four (TOF) nerve stimulation was recorded using a Myograph 2000.

Results: Time to 100% block was 3.0-4.6 minutes. The mean (range) time to reappearance of the first response to TOF stimulation was 62 (26-128) minutes. The neuromuscular block was antagonized with neostigmine preceded by atropine at 45-50 and 70% twitch height recovery, and the time to 90% twitch height recovery was 8-12 and 4 minutes, respectively.

The magnitude of block and the duration of action of mivacurium 0.03 mg kg^{-1} was significantly increased in patients homozygous for the atypical gene compared to genotypically normal patients.

In conclusion, patients with homozygous occurrence of the atypical plasma cholinesterase gene are extremely sensitive to mivacurium, but once recovery has begun reversal of the neuromuscular block with neostigmine is safe and effective.

References

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A775

TITLE: DOSE-RESPONSE RELATIONSHIP OF MIVACURIUM CHLORIDE (MIVACRON®) IN INFANTS DURING NITROUS OXIDE-HALOTHANE ANESTHESIA

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INTRODUCTION: Mivacurium is a new nondepolarizing neuromuscular blocker with relatively short duration of action. We determined the dose-response relationship of this drug in infants 2 through 6 months of age during halothane-nitrous oxide anesthesia.

METHODS: After IRB approval and with written, informed consent from a parent, 26 ASA I-II infants undergoing elective surgical procedures were studied. No premedication was administered. Inhalation induction was performed with 70% N_2O and up to 3% inspired halothane. An intravenous catheter was placed. Blood for measurement of pseudocholinesterase activity and dibucaine inhibition with propionylthiocholine as substrate was obtained. Ten $\mu g \cdot kg^{-1}$ of atropine and 1 $\mu g \cdot kg^{-1}$ of fentanyl were administered and the end-tidal halothane was adjusted to 1.0%. The ulnar nerve was stimulated supramaximally using cutaneous electrodes on the forearm with train-of-four stimuli (2 Hz for 2 sec at 10-sec intervals). The compound electromyogram of the adductor pollicis was recorded using a Datex NMT monitor.

Eight patients received 50 $\mu g \cdot kg^{-1}$, 9 patients received 40 $\mu g \cdot kg^{-1}$, and 9 received 60 $\mu g \cdot kg^{-1}$ of mivacurium as a bolus into a rapidly running IV. The maximum percent block produced by a given dose of mivacurium was transformed to a probit value. Linear regression of log-dose and probit of response was performed. The mean ± SEM are reported.

RESULTS: Two patients were omitted from data analysis because of abnormal pseudocholinesterase activity (PA). Both patients received 60 $\mu g \cdot kg^{-1}$. One had PA of 8.8 IU/ml (normal range 2.5-7.1) with normal inhibition by dibucaine, and developed 82% blockade. The other had PA of 5.1 with 60% inhibition by dibucaine (normal range 77-83% inhibition), and developed 76% blockade. The mean age, height, weight, and body surface area of the 24 infants were 4.5 ± 0.3 months, 62.5 ± 0.8 cm, 7.1 ± 0.2 kg, and 0.37 ± 0.01 m^2. The ED_{50} and ED_{95} were 46 and 74 $\mu g \cdot kg^{-1}$ or 870 and 1397 $\mu g \cdot m^{-2}$, respectively. The slope of the log dose-probit regression was 7.9; R=0.5. Blood was obtained from 19 patients. The mean PA was 5.5 ± 0.2 IU/ml, and percent inhibition by dibucaine was 80.9 ± 1.3.

DISCUSSION: In children (2-12 yr) the ED_{50} of mivacurium was 52 and the ED_{95} was 89 $\mu g \cdot kg^{-1}$ during anesthesia with 0.8% end-tidal halothane (1). It may be that infants are somewhat more sensitive than children to a $\mu g \cdot kg^{-1}$ bolus of this drug. When dose is referenced to surface area, the age-related difference in effect is magnified; ED_{50} in infants is 870 $\mu g \cdot m^{-2}$ whereas ED_{50} of children is about 1400 $\mu g \cdot m^{-2}$. In this regard mivacurium appears to be similar to atracurium (2).

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