Title: CEREBRAL EFFECTS OF ATRACURIUM

Authors: W. L. Lanier, M.D.; J. H. Milde; and J. D. Michenfelder, M.D.

Affiliation: Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota 55905

Introduction: The cerebral effects of atracurium, a new medium-duration nondepolarizing neuromuscular blocking drug, are unknown. Laudanosine, a degradation product of atracurium, has been shown to induce seizures in dogs.[1] The following study was performed to evaluate the effect of atracurium on cerebral metabolic rate (CMR) and blood flow (CBF), intracranial pressure (ICP), and the electroencephalogram (EEG).

Methods: Twelve mongrel dogs were anesthetized with halothane in oxygen and nitrogen. Temperature, blood pressure, PaO_2, and $PaCO_2$ were maintained within normal range. Direct measurement of CBF and calculation of CMR were performed using previously described methods.[2] Six dogs (Group A) were maintained at 0.86% expired halothane (1 MAC). After control measurements, dogs were given in sequence at 30 min intervals: atracurium 0.5 mg/kg, neostigmine 0.07 mg/kg plus glycopyrrolate 0.0125 mg/kg, atracurium 1.0 mg/kg, and atracurium 2.5 mg/kg. Group B dogs received tetracaine spinal anesthesia and expired halothane was adjusted to that concentration which was just sufficient to produce an EEG sleep pattern. This varied from 0.55 to 0.75% expired halothane. After control measurements, dogs were given atracurium 1.0 mg/kg and 2.5 mg/kg in sequence at 30 min intervals. At the completion of atracurium administration in groups A and B, dogs were hyperventilated and intense auditory stimulation was provided in an attempt to ellicit seizures.

Results: There were no consistent changes in CBF, CMR, ICP, or EEG in group A dogs in response to low-dose atracurium, its reversal with neostigmine, or to high dose atracurium. EEG evidence of arousal occurred in one dog following a cumulative atracurium dose of 4.0 mg/kg. In group B dogs EEG evidence of arousal occurred in 6 of 6 dogs. Arousal occurred following cumulative atracurium doses of 1.0 mg/kg in 5 dogs and 3.5 mg/kg in one dog. The EEG never returned to control levels of anesthetic depth after arousal was noted. When the period of maximum EEG arousal was compared to the previous 5 minute measurement period or the measurement period in which the EEG last resembled the control sleep EEG, CMR increased in 5 of 6 dogs. However, as a group, changes in CMR, CBF or ICP after atracurium administration never achieved significance at the $p < .05$ level by an analysis of variance or paired t-test (Figure). Seizure activity was not seen in either group A or B.

Discussion: Augmentation of anesthetic depth following nondepolarizing neuromuscular blockade has previously been reported.[3-4] However, CNS stimulation by atracurium is unique among nondepolarizing neuromuscular blocking drugs. Atracurium consistently produces delayed EEG arousal at halothane concentration less than one MAC. This effect was abolished in 5 of 6 dogs by anesthetic concentrations of halothane. We assume the arousal after atracurium is independent of neuromuscular blockade and is secondary to the metabolite laudanosine, a known CNS stimulant.

References:

1. Mercier J, Mercier E: Action de quelques alcaloides secondairess de l'opium sur l'electrocorticogramme du chien. C R Soc Biol 149:760-762, 1955.
2. Michenfelder JD, Messick JM Jr, Theye RA: Simultaneous cerebral blood flow measured by direct and indirect methods. J Surg Res 8:475-481, 1968.
3. Forbes AR, Cohen NH, Eger EI II: Pancuronium reduces halothane requirement in man. Anesth Analg 58:497-499, 1979.
4. Hodes R: Electrocortical synchronigation resulting from reduced proprioceptive drive caused by neuromuscular blocking agents. Electroenceph Clin Neurophysiol 14:220-232, 1962.