Title: COMPARISON OF EDROPHONIUM AND NEOSTIGMINE ANTAGONISM OF ATRACURIUM INDUCED NEUROMUSCULAR BLOCKADE IN INFANTS AND CHILDREN

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Introduction. Complete antagonism of neuromuscular blockade is essential for safe recovery from balanced anesthesia. The pharmacokinetics of anticholinesterases may vary with age.[1,2] There are few studies to evaluate the clinical neuromuscular antagonism of pediatric patients.[3] Therefore, we designed this study to reveal possible differences in the efficacy of antagonism and in cardiovascular adverse effects between edrophonium and neostigmine in infants and children. Atracurium was chosen as the neuromuscular blocking agent because the rate of spontaneous recovery from atracurium-induced block is largely unrelated to age.[4]

Methods. The study protocol was approved by the institutional ethical committee and an informed consent was given by the parents.

Eighty ASA I pediatric surgical patients were selected to the study on the basis of their age. Five groups of 16 patients were formed: 0-3 months, 3-12 months, 3-6 years, 6-11 years and 11-16 years old. Premedication was with either flunitrazepam or methohexital, and the anesthesia was effected by fentanyl, thiopental, and 70% N_2O in O_2. Atracurium was given for intubation and maintenance of 90-95% neuromuscular block (NMB) monitored with thenar EMG responses to train-of-four stimulation of the ulnar nerve (NMT 221, Puritan-Bennett). In those cases where halothane was used it was stopped at least 30 min before the end of surgery. After surgery, at the time of 90% NMB patients were randomly given either edrophonium, 1 mg/kg, with atropine, 10 µg/kg, or neostigmine, 50 µg/kg, with atropin, 20 µg/kg. NMB, train-of-four (TOF) ratio, non-invasive blood pressure, and heart rate were registered at one minute intervals from zero to 15 minutes after administration of the antagonist. Analysis of variance followed by Tukey's test were used for comparison of results in the different study groups.

Results. The initial recovery from NMB and of TOF-ratio was more rapid in all age groups after edrophonium than after neostigmine. After 6 min, the recovery from NMB was comparable after both antagonists and in all age groups. Although TOF-ratio recovered initially more rapidly with edrophonium than with neostigmine, neostigmine was more effective later during time of follow-up (Fig. 1). In infants, TOF-ratio recovered faster than in children, regardless of the antagonist (Fig. 1).

There were no age-related differences in the blood pressure or heart rate response to antagonism. An initial rise and a subsequent fall in blood pressure occurred consistently in all groups, but pressure rise appeared to last longer with edrophonium than with neostigmine. After an initial rise in heart rate, there was a significantly greater fall in all neostigmine groups when compared to edrophonium groups (Fig.2).

Discussion. The results do not indicate marked differences between edrophonium and neostigmine antagonism of atracurium-induced neuromuscular block in any pediatric age group. We do not attach clinical significance to the more rapid initial recovery of TOF-ratio after edrophonium. Moreover, in older children, the recovery subsequently becomes slower than that observed after neostigmine. The 20-25% deceleration in heart rate was observed in all age groups after neostigmine despite a higher dose of atropine. In some patients, this may cause clinically significant bradycardia, which is not seen after edrophonium. Therefore, we consider edrophonium and neostigmine, when administered with an anticholinergic, to be equally safe and effective in infants and children.

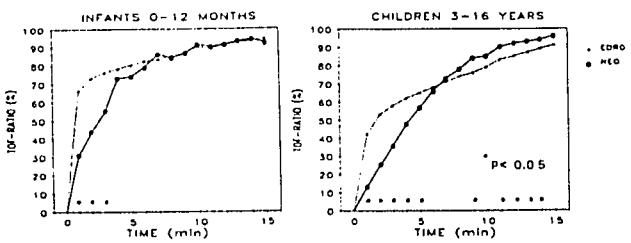

Figure 1. Train-of-four antagonism in infants and children.

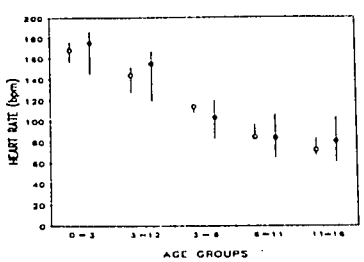

Figure 2. Average minimum and maximum heart rates (vertical lines). Symbols as in Figure 1. The circles show heart rate before antagonization.

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