INFLUENCE OF HALOTHANE ON THE TRAIN-OF-FOUR FADE AFTER ATRACURIUM IN CHILDREN

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SUMMARY
The influence of halothane was studied on train-of-four fade during spontaneous recovery from neuromuscular block produced by atracurium in 42 children undergoing routine surgical procedures under general anaesthesia. The ulnar nerve was stimulated at the wrist, and compound electromyographic responses were recorded from the adductor pollicis brevis, using a Relaxograph. One group of children was anaesthetized with nitrous oxide and 1% halothane (end-tidal concentration) in oxygen; in the other group nitrous oxide and fentanyl in oxygen was used (control group). Halothane was found to increase the train-of-four fade during the recovery phase compared with control. It is possible that presynaptic and postsynaptic cholinoceptors differ in their sensitivity to the depressant action of halothane.

KEY WORDS

It has been shown recently that muscle relaxation produced by volatile anaesthetic agents is caused by action on the neuromuscular junction [1].

There is evidence that atracurium impairs neuromuscular transmission at presynaptic and at postsynaptic sites at the motor end-plate [2, 3]. Bowman suggested that single twitch depression and train-of-four (TOF) fade are separate effects of neuromuscular blocking drugs, the former being a result of postjunctional block, and the latter resulting mainly from action at the prejunctional receptors [4].

This study was designed to investigate the effect of halothane on TOF fade produced by atracurium.

METHODS AND RESULTS
After approval was given by the local Ethics Committee, 42 children, ASA physical status I and II, requiring muscle relaxation for surgical procedures were studied. All were free from neuromuscular, renal and hepatic disease; none was taking drugs known to interfere with neuromuscular transmission. Children in group I (n = 19; age 5.2 (sd 1.3) yr, weight 18.1 (4.2) kg) were anaesthetized with 60% nitrous oxide and halothane in oxygen and those in group II (control group: n = 23; age 6.0 (3.4) yr; weight 21.1 (7.8) kg) were anaesthetized with 60% nitrous oxide and fentanyl in oxygen.

Premedication consisted of atropine 0.02 mg kg⁻¹ and pethidine 1 mg kg⁻¹, given i.m. 30 min before induction of anaesthesia. In the first group, anaesthesia was induced and maintained with 60% nitrous oxide and 1% halothane (end-tidal concentration, measured using Servo-gas monitor, Siemens-Elema) in oxygen. In the control group, anaesthesia was induced using thiopentone 5 mg kg⁻¹ i.v. and maintained with 60% nitrous oxide and fentanyl 4–6 μg kg⁻¹ in oxygen, as required. Atracurium (bolus or two incremental doses) was given after induction of anaesthesia to produce 95–100% block of neuromuscular transmission and facilitate tracheal intubation. The lungs were ventilated artificially to an end-tidal Pco₂ of 4.7–6 kPa (Datex Capnograph).

Spontaneous recovery of neuromuscular transmission was allowed.

Neuromuscular transmission was studied using a Relaxograph (Datex). The ulnar nerve was stimulated at the wrist via two surface electrodes. Train-of-four stimulation, 2 Hz for 2 s, every
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20 s, was applied. The compound electromyogram was measured from the adductor pollicis brevis via two surface electrodes. The ratio between the height of the first twitch (T1) before and after atracurium (T1:control (%)) and the ratio between the height of the fourth and the first twitch in the same train (TOF ratio) were analysed.

Comparison of TOF fade was made during nitrous oxide and halothane in oxygen and during nitrous oxide and fentanyl in oxygen anaesthesia. The T1:control and TOF ratios during spontaneous recovery, expressed as percent of appropriate baseline values, were transformed to logit values, which were plotted subsequently against natural logarithm of time. The slope of the line was calculated by regression analysis, and the difference of the regression coefficient was compared, using standard tests for statistical significance.

When the degree of fade was compared at a T1:control of 25 %, the TOF ratio in children in the halothane group did not differ from that in the control group (11 % vs 14 %); at a T1:control of 50 %, the TOF ratio was 21 % in the halothane group and 35 % in control subjects; at a T1:control of 75 %, the TOF ratios were 44 % and 63 %, respectively. The regression coefficient for the TOF ratio during the recovery phase in the halothane group was significantly different from control (P < 0.05).

COMMENT

After a bolus dose of a neuromuscular blocking agent, and after a redistribution phase of four to five half-lives, the elimination phase of the drug begins, when pseudoequilibrium exists between plasma and tissue concentrations. Under these circumstances, there is a constant and reliable relationship between the absolute values of T1:control and TOF ratios. Halothane was found to influence this relationship; the TOF ratio during anaesthesia with nitrous oxide and 1 % halothane in oxygen was significantly smaller than that of controls. There is recent evidence [3] that the site for synergism of volatile anaesthetics and non-depolarizing neuromuscular blocking agents is at a receptor (or receptors) within the neuromuscular junction.

Although there is no proof, it is possible that a site other than postsynaptic (possibly presynaptic) may be responsible for fade during high frequency stimulation (tetanic or train-of-four). Bowman suggested that the prejunction receptors are isoreceptors of postsynaptic cholinocceptors which serve to mediate mobilization of reserve transmitter to the readily releasable pool within the axoplasm [4]. It is believed that these prejunctional receptors function as a positive feedback control system that maintains availability of acetylcholine when demand is high. Fade during high frequency stimulation may represent the action of neuromuscular blocking drugs at sites other than postsynaptic receptors, probably prejunctional cholinocceptors. The results of this study suggest that this receptor may be influenced also by halothane.

REFERENCES