Title CLINICAL PHARMACOLOGY OF ATRACURIUM (BW 33A) IN ADOLESCENTS ANESTHETIZED WITH HALOTHANE

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Atracurium (BW 33A) is a bisquaternary non-depolarizing neuromuscular blocking agent with short to intermediate duration with no cumulative properties. It has minimal cardiovascular effects. The neuromuscular and cardiovascular effects have been studied in adults and the drug has proven to be safe (1,2). Prior to utilization of atracurium in children, we elected to evaluate it in adolescents to determine its neuromuscular and cardiovascular effects, and determine its safety.

Method. The study was approved by the Subcommittee on Human Studies, Committee on Research of our institution. Parental consent was obtained. Eighteen ASA Class I male adolescents (11-17 yrs) were studied. Their mean (±SE) age was 13.6 ± 0.5 years. They were anesthetized with halothane, N_2O and O_2. Anesthesia was maintained with 1-2.0% inspired halothane. Ventilation was assisted or controlled to maintain an end expired $PaCO_2$ of 40 torr.

After the establishment of steady state anesthesia, the ulnar nerve was supramaximally stimulated via surface electrodes. Repetitive train-of-four (2Hz for 2 sec repeated every 10 sec) responses of thumb adductors were recorded. In the first 10 patients, atracurium was given incrementally at a dose of 0.1 mg/kg or 0.05 mg/kg until more than 95% depression of the twitch height was obtained. In 8 patients atracurium was given as a bolus (0.4 mg/kg). The cardiovascular changes were obtained in the absence of stimulation. The twitch height was allowed to recover spontaneously until 25% of control. If the surgical procedure warranted, incremental doses of atracurium (0.1 mg/kg) were given and the neuromuscular response was followed. If no further muscle relaxation was required, no additional drug was given and the recovery of the twitch was followed. When necessary, residual neuromuscular block was antagonized with atropine and neostigmine.

In 7 patients, routine urine analysis, blood CBC, serum electrolytes, creatinine, and SGOT was obtained preoperatively and 2 days postoperatively.

Results. In 9 of 10 patients who received incremental doses of atracurium, a total dose of 0.23 ± 0.02 mg/kg (mean ± SE) administered in 9.2 ± 0.4 min produced 98.7 ± 1.0% depression of the twitch. In these patients the twitch recovered to 25% of control in 18.2 ± 0.7 min, from 25-50% in an additional 5.9 ± 0.5 min, from 50-75% in 6.4 ± 1.0 min and 75-95% in 7.2 ± 1.2 min. The calculated ED_{50} and ED_{95} was 0.13 mg/kg and 0.22 mg/kg respectively. One patient was markedly resistant to atracurium; in this patient a dose of 0.6 mg/kg produced 91% depression of the twitch.

A dose of 0.4 mg/kg produced satisfactory conditions of intubation in 8 of the patients studied. This dose abolished the twitch response in all patients in 2.1 ± 0.2 min without any significant change in heart rate and blood pressure. Mild flushing of the face and the chest was detected in 3 patients. The twitch recovered to 25% in 34.2 ± 2.6 min and the time elapsed from the injection of the drug to 95% recovery was 54.7 ± 4.7 min.

No significant change occurred between preop and postop urine analysis, blood CBC, serum electrolytes, creatinine, and SGOT.

Discussion. Atracurium was found to be a safe muscle relaxant for adolescents anesthetized with halothane. Neuromuscular depression caused by a mean cumulative dose of 0.23 mg/kg lasted 40 minutes. A bolus dose of 0.4 mg/kg produced satisfactory conditions for intubation whereas the neuromuscular effects of this dose lasted 55 min. This drug did not cause any appreciable cardiovascular changes. We found that atracurium can be used satisfactorily for provision of muscular relaxation in adolescents and that it can be repeatedly given for continuation of muscular relaxation. Its neuromuscular effects can be satisfactorily antagonized with neostigmine.

References

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