TITLE: ATRACURIUM INDUCED NEUROMUSCULAR BLOCK IS PROLONGED IN HEPATIC VASCULAR OCCLUSION

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INTRODUCTION. The pharmacokinetics of atracurium were reported not to be altered by impaired hepatic function in patients due to its unusual metabolism[1,2]. The present study was undertaken to evaluate the neuromuscular block induced by single intravenous dose of atracurium in monkeys with total hepatic vascular occlusion.

METHOD. Five adult monkeys (Macaca Cyclopis Swinhoe) weighing 5 to 8 kg were anesthetized with methohexital 10-15 mg/kg intramuscularly and one intravenous infusion line was then inserted in the right limb. Intravenous fluid of dextrose 5% in water was infused at 5 ml/kg/hr. The trachea was intubated without the use of muscle relaxant and anesthesia was maintained with halothane 0.5% in oxygen. The end-tidal CO_2 and halothane concentration were monitored and recorded with Datex Normocap CO_2 monitor and Datex anesthetic gas monitor. Ventilation was controlled with mechanical ventilator to keep end-tidal PCO_2 at 30-40 mmHg and body temperature was maintained at 35-37°C with thermoblanket. An arterial catheter was placed into anterior tibial artery for recording blood pressure and for frequent blood gas studies and arterial PH was controlled at 7.30-7.40. The ulnar nerve in left wrist was stimulated with Grass S-44 nerve stimulator using single stimuli at 0.2 Hz with 0.1 msec. duration, at supramaximal voltage. Force of left thumb adduction was recorded by a Grass FT-03 force displacement transducer ECG, arterial pressure and twitch depression were recorded simultaneously on a 4 channel polygraph. After a stable anesthetic plane was established, a single I.V. bolus injection of atracurium 0.3 mg/kg was given and thumb adduction twitch height was continuously recorded. The degree of maximal twitch depression, onset time from injection to 90% depression, duration from injection to 25% twitch recovery and recovery time from 25% to 75% twitch recovery were measured to serve as control. Two hours after full recovery of twitch, a median laporotomy was done and the portal tract including hepatic artery, portal vein and common bile duct were isolated and ligated with a looping tourniquet. Two minutes after the hepatic occlusion, an I.V. bolus dose of atracurium 0.3 mg/kg was given and the thumb twitch was continuously recorded in the similar manner as during the control period. Frequent arterial blood gas were taken and $NaHCO_3$ was given to maintain the PH between 7.30-7.40. Portal ligature was released after 75% twitch recovery to allow hepatic revascularization to avoid fatality. For statistical comparison, Wilcoxon-Rank test was used and $p<0.05$ was considered significant.

RESULT. As shown in Table I, the maximal twitch depression and the onset time from injection to 90% depression were quite similar between control and hepatic occlusion conditions. However, the duration of twitch depression and recovery time were significantly prolonged with hepatic occlusion ($p<0.05$). Heart rate and arterial blood pressure were well maintained in all the animals under both conditions and all the monkeys recovered from this experimental procedure without mortality.

DISCUSSION. Ward and Neill studied the pharmacokinetics of atracurium in normal patients and in six patients with acute hepatic and renal failure and found that the pharmacokinetic variables did not differ for the two groups. However, the characteristics of the neuromuscular block was not measured in their study. In our primate animal model when the portal-hepatic circulation was totally occluded, the duration of atracurium-induced neuromuscular block was significantly prolonged. This seem to indicate that hepatic enzymatic activity plays a more important role in the metabolism of atracurium than previously reported. Perhaps such a difference could be due to the fact that in our study total hepatic occlusion instead of hepatic dysfunction was achieved. Farman, et al[3] using a continuous infusion of atracurium in adult patients undergoing liver transplantation reported that atracurium requirements were less during the anhepatic period and greater after hepatic revascularization. Therefore, caution should be exercised when atracurium is used in patients with severe hepatic failure.

REFERENCES.

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3. Farman JV, Turner JM, et al: Atracurium in liver transplantation. Br. J. Anaesth. 58:96S-102S, 1986.

TABLE I

The neuromuscular effect of atracurium (0.3 mg/kg) during hepatic exclusion in primate (n=5)

	Control	Hepatic vascular exclusion
Maximal twitch depression	94 ± 2%	95 ± 2%
Onset time (min) (inj. to 90% depression)	3.8 ± 0.3	3.0 ± 0.1
Duration of time (min) (inj. to 25% recovery)	20 ± 3	32 ± 2.5*
Recovery time (min) (25%-75% recovery)	5 ± 0.5	8 ± 1.2*

*P < 0.05 Values are mean = S.E.M.