A780

TITLE: EFFECT OF ATRACURIUM ON SYMPATHETIC NERVE ACTIVITY

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Hypotension caused by high dose atracurium has been attributed to its histamine release. It has been attempted to eliminate this side effect by administering H1 and H2 blockers (1,2). However, depressant effect of atracurium on the sympathetic nervous system in atracurium induced hypotension should not be ignored. The purpose of this study was to investigate the effects of atracurium and histamine on renal sympathetic activity (RSNA) in bilaterally vagotomized and baroreceptor-denervated dogs.

Fourteen mongrel dogs were anesthetized with α-chloralose, intubated and mechanically ventilated with oxygen, and the left femoral artery was cannulated for mean arterial pressure (MAP) recording. After bilateral sino-aortic denervation (SAD)and vagotomy, the left kidney was exposed through a left flank incision. The renal sympathetic nerves were isolated and placed on a bipolar silver electrode for recording RSNA. Sodium nitroprusside (5-10μg/kg) and phenylephrine (2-4μg/kg) were administered to confirm the effectiveness of denervation with no change in RSNA and heart rate. Seven dogs were given histamine (1μg/kg) intravenously, and the remaining dogs received atracurium (1.5mg/kg). In both groups, MAP and RSNA were recorded continuously.

During the procedure, arterial blood gases were maintained within normal ranges. Histamine decreased blood pressure significantly at 1 min with a quick recovery, but RSNA was not affected (Fig.1). Atracurium significantly depressed both MAP at 5 min and RSNA at 5 and 30 min (Fig.2).

Since animals were totally denervated, the primary reduction of MAP should not have affected the RSNA as observed during histamine injection. Therefore, depression of RSNA by atracurium must result from direct inhibition of the vasomotor center or sympathetic nervous system, including sympathetic ganglia. Thus, our results indicate that atracurium can cause hypotension not only by histamine release but also by direct sympathetic nerve depression.

Statistical analysis: ANOVA followed by Duncan's Method

References: (1) Life Sci 44:347-53,1989
(2) Anesth Analg 67:1089-92,1988

Fig. 1

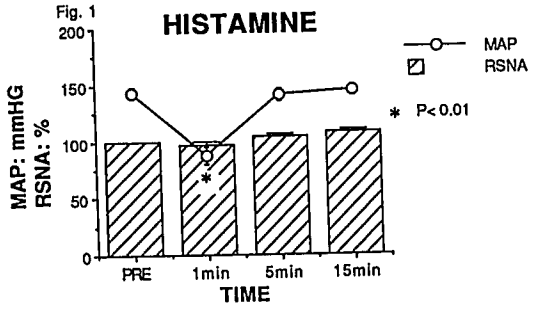
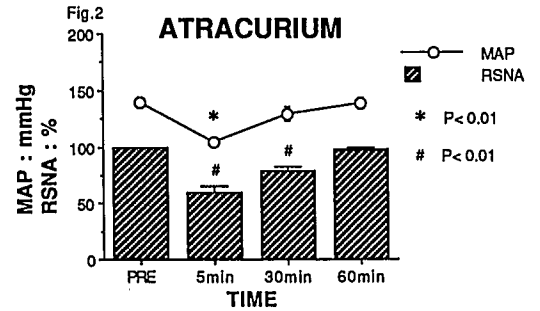


Fig.2



A781

TITLE EVALUATION OF PROCONVULSANT EFFECT OF LAUDANOSINE IN RENAL TRANSPLANT RECIPIENT.

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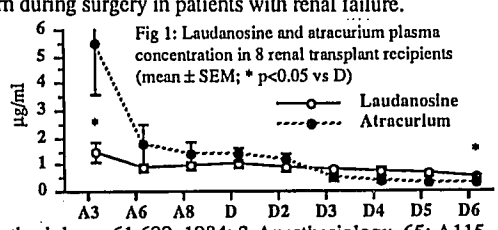
Introduction: Laudanosine (L), a major breakdown product of atracurium (A), is both renally excreted and metabolized by the liver.[1] Thus there is concern on the possible accumulation of L in anephric patients. L has been shown to induce epileptiform activity in plasma concentrations of 5 μg/ml in rabbits and 17 μg/ml in dogs.[2,3] In cats, L plasma concentrations between 10 and 100 μg/ml were not associated with EEG seizure activity.[4] This large interspecies variation makes it impossible to make extrapolation to man. Meanwhile chronic infusion of A to 6 renally impaired patients in an intensive care unit was associated with L concentrations up to 5.1 μg/ml with no evidence of cerebral excitation,[5] no specific correlates of CNS activity and plasma L concentrations have been reported in humans. The aim of this study was to determine the plasma concentrations of L resulting from A infusion during renal transplantation and to determine if EEG seizure activity can be detected under these conditions.

Methods: 16 adults undergoing cadaveric renal transplant entered this open study which was approved by Institutional Ethic Committee and written informed consent was obtained in each case. All had been dialysed within 6 hours of surgery and were free from cardiac or hepatic dysfunction, uncontrolled hypertension, allergic and epileptic history. No premedication was given. Anesthesia consisted of propofol (2 mg/kg followed by an infusion of 100 μg/kg/min), fentanyl (5-10 μg/kg) and 50% N_2O in O_2. 8 patients received A (200 μg/kg followed by an infusion of 5 μg/kg/min) and 8, paired on age, weight and sex received vecuronium (V) (40 μg/kg followed by an infusion of 10 μg/kg/min). $FECO_2$ and esophageal temperature were kept within normal range. Neuromuscular blockade was assessed using TOF stimulation at 0.1 Hz of the ulnar nerve and recording the force generated in the adductor pollicis. The first response in the TOF sequence (T1) was maintained below 25% of control with increments of A (5 mg) or V (0.5 mg) without changing the infusion rate. EEG monitoring was obtained by scalp electrodes placed bilaterally at frontal, parietal, and occipital positions with reference electrodes at the cheek. EEG tracing was recorded over 20 min periods at the following times: before anesthesia (A1), onset-time from A or V injection to maximal T1 block (A3), 1 and 2 hours after onset-time (A6 and A8), release of the arterial clamps on the transplanted kidney (D), end of A or V infusion (D2) and 1, 2, 4 and 8 hours after D2 (D3, D4, D5 and D6). At the beginning of each EEG recording, blood samples were collected for estimation of plasma L and A in the A group. Immediately after collection the samples were centrifugated for 1 min; 1 ml of the plasma was mixed with 4 ml of 0.005 M sulphuric acid and frozen (-80°C) until later analysis by specific HLPC assay.[6] Statistics were carried out by ANOVA, Chi-square test and Wilcoxon test where appropriate.

Results: The 2 groups were similar with regard to demographic and biochemical data, treatment and duration of surgery. pH and $PaCO_2$ were maintained within physiological range (7.31-7.45 and 4.6-5.3 KPa respectively). In both groups neither clinical evidence of cerebral excitation nor EEG seizure activity were noticed. Plasma L and A concentrations in A group are displayed in figure 1.

Conclusion: In this little group of renal transplant recipients, maximum L plasma concentration gave a range of 0.6-2.72 μg/ml, substantially below concentrations required to cause adverse CNS effects in animals.These results definitely confirm that L is of little concern during surgery in patients with renal failure.



1-Anesthesiology, 61:699, 1984; 2-Anesthesiology, 65: A115, 1986; 3-Anesthesiology, 65: 56, 1986; 4-Br J Anaesth, 58: 14S, 1986; 5-Br J Anaesth, 59:211, 1987; 6-J Chromatogr, 343: 431, 1985.