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Title: CEREBRAL AND CIRCULATORY EFFECTS OF HIGH-DOSE BUPIVACAINE AND ETIDOCAINE

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Since resuscitation following inadvertent IV injection of bupivacaine(B) or etidocaine(E) is said to be difficult,[1] we studied their cardiovascular effects beyond the convulsive threshold. Intubated cats (n=27) anesthetized with halothane, and with arterial and venous catheters in place, had extradural recording electrodes driven into the skull, and ECG electrodes inserted in the extremities. On completion of surgery the animal was given gallamine and ventilated one hour with 50% N_2O. End-expired CO_2 was adjusted for an arterial pCO_2 around 33 torr and pH 7.40, corrected with $NaHCO_3$ as needed. N_2O was then discontinued, the animal ventilated with O_2-enriched air, and the first arterial blood for B or E assay drawn. Control polygraph tracings were taken and stored in parallel on magnetic tape. Next, B or E dissolved in saline was pumped IV at a constant rate of 1 mg/kg/min. The infusion was halted, and another blood sample collected, with the onset of synchronous high-voltage epileptiform discharges in the EEG. This determined the first convulsant dose (CD_{100}) of local anesthetic. About one hour later, when the EEG, ECG, and BP had returned to near control, infusion was restarted and continued until either the EEG became flat (14 cats) or triple the first convulsant dose had been given (10 cats) or the animal died (3 cats).

Results: Within a minute of infusion (1 mg/kg) of B or E, amplitude of the QRS complex increased. After about 3 minutes (3 mg/kg; 60 to 75% of the CD_{100}), the EEG changed from fast low voltage to slow high amplitude waves, and 10-Hz spindles began to appear. After 4 or 5 minutes (4-5 mg/kg total), small random spikes appeared, especially in temporal leads, and fast activity disappeared completely. These pre-convulsant changes were similar for both B and E. At this time, odd and irregular ECG irregularities appeared unpredictably, though mean BP generally remained stable. With the onset of seizures after 5-7 minutes, BP and end-expired CO_2 rose sharply, the QRS complex widened and the P-wave disappeared. Electrical convulsions stopped in 7 to 10 minutes, and sinus rhythm returned soon thereafter.

At the start of the second infusion, EEG, ECG and BP had returned to near control levels. Though somewhat less, the second convulsant dose did not differ significantly from the first (Table), though the blood levels were higher. Most (24/27) cats tolerated 3 to 4.5 times the convulsant dose of B or E, even though cardiac rhythm and rate were chaotic and the BP was below 60 torr. The EEG became flat after 3.1 times the CD_{100} of B and after 3.5 times the CD_{100} of E. However, in cats whose BP did not fall below 60 torr, electrical convulsions persisted, and continued for at least 30 minutes after the end of infusion. Diazepam (0.5 mg IV) halted seizures within 2 minutes in 4 of 6 cats; the other 2 cats required up to 4 mg diazepam.

Convulsant Doses (CD_{100}) and Plasma Levels

	1st CD_{100} (mg/kg)	Level (μg/ml)	2nd CD_{100}* (mg/kg)	Level (μg/ml)
B(12)	5.4	3.05**	4.6	6.39**
E(15)	6.5	6.57	5.4	11.59

* Convulsant dose 1 to 1.2 hours after the first
** Data from 6 cats

Discussion: Earlier we showed that B-induced convulsions are about 90% fatal if animals are left untreated.[2] The present work shows that though B and E severely compromised cardiac rhythmicity and circulation, adequate ventilation and support of fluid and acid-base balance prevented death from massive doses. Also, unlike earlier reports,[3] we observed characteristic EEG changes from subconvulsant doses of B or E. Others[4] also found that well-ventilated dogs survived repeated procaine seizures, whereas most of their untreated dogs died. And cats given IV procaine or lidocaine "benefited from artificial respiration".[5] Within the limits of extrapolation to man, we conclude that B- or E-induced convulsions are potentially lethal complications. Merely providing support of ventilation can assure survival from severalfold the convulsant dose.

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References.

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