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TITLE : ACUTE CARDIOVASCULAR TOXICITY OF LIDOCAINE, BUPIVICAINE AND ETIDOCAINE IN ANESTHETIZED, VENTILATED DOGS

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Recent clinical reports^{1,2} concerning sudden cardiac arrest after inadvertent intravascular injections of clinical doses of bupivacaine and etidocaine have called attention to the need for more precise information concerning the toxicity of local anesthetics. The threshold of CNS toxicity in animals³ and man has been established. However, speculation that bupivacaine and etidocaine may cause cardiovascular collapse coincidentally with the onset of CNS seizures and without antecedent hypoxia indicates the necessity to define the cardiovascular toxicity of these local anesthetics. This requires prevention of toxic CNS effects and subsequent hypoxia from seizures.

This study was undertaken to determine the dose-response for cardiac toxicity for lidocaine, bupivacaine and etidocaine. Anesthetized and artificially ventilated dogs were utilized so that CNS toxicity and hypoxia secondary to seizures would not interfere with cardiac response.

Methods. Adult mongrel dogs of either sex were anesthetized and maintained with intravenous pentobarbital. After intubation ventilation was maintained with a Harvard animal ventilator and oxygen enriched air. Arterial blood gases were sampled and the animals were maintained at normal CO₂, O₂ and pH. Two venous cutdowns, an arterial line, a Swan-Ganz catheter, EKG, rectal temperature probe and heating blanket were utilized. Arterial BP, heart rate, P-A pressure, cardiac output, and arterial and venous local anesthetic levels were determined.

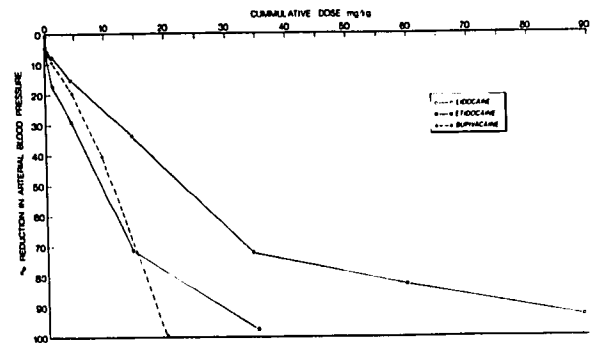
Five animals were studied in each group. After a control period each dog received increasing dosages of intravenous local anesthetic at 30 minute intervals. Heart rate, BP, mean arterial BP, cardiac output, stroke volume, systemic vascular resistance, P-A pressure, mean P-A pressure and pulmonary vascular resistance were determined.

Results.

	cummulative lethal dose(mg/kg) *
Lidocaine	76.3 ± 15.1
Etidocaine	40.4 ± 6.0
Bupivacaine	20.4 ± 2.4

*(mean ± S.E.)

The following figure indicates % decrease in mean arterial BP from pre drug control as the cummulative dose (mg/kg) increases.



Deterioration of other hemodynamic parameters with increasing dose of local anesthetic produces figures similar to the example presented above.

Conclusion. The in vivo cardiovascular toxicity of lidocaine, bupivacaine and etidocaine seem to parallel their intrinsic anesthetic potency. Comparison of the cardiotoxic dose in dogs to human clinical dosage suggests that cardiovascular collapse due to cardiotoxic effects of local anesthetics alone is unlikely.

References.

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3. Munson ES, et al: Etidocaine, Bupivacaine and Lidocaine Seizure Thresholds in Monkeys. *Anesthesiology* 42:471-478, 1975