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Title: THIOPENTAL POTENTIATION OF EPINEPHRINE SENSITIZATION WITH HALOTHANE

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Introduction. While the induction of anesthesia with halothane is relatively fast and pleasant, there is an excitement stage accompanied by the release of catecholamines that is removed or obtunded by intravenous induction agents. It is therefore common to induce anesthesia with thiopental in both man and experimental animals. MacCannell and Dresel have shown that thiopental potentiates sensitization to epinephrine in cyclopropane-anesthetized dogs (1). Moreover, the duration of this effect of thiopental far outlasted the expected anesthetic effect following a single induction dose of 20 mg/kg iv. Characteristic ventricular arrhythmias were produced with the same dose of epinephrine up to 5 hours following the administration of thiopental. The effect of thiopental on epinephrine sensitization with clinically used halogenated hydrocarbons has not been reported. We report here the effect of thiopental on epinephrine sensitization with halothane.

Materials and Methods. Healthy mongrel dogs (N=16) were anesthetized on separate occasions one week apart (randomized) with halothane (1.09 percent end-tidal) or the same level of halothane preceded by an induction dose of thiopental (20mg/kg iv). Dogs were mechanically ventilated with oxygen (FiO_2=1.0) and the end-tidal CO_2 level kept between 35 and 40 torr. Rectal temperature was maintained between 37 and 38°C. Catheter high right atrial and His bundle electrocardiograms (ECG) were simultaneously displayed and recorded along with surface Lead II of the ECG and femoral arterial pressure. Graded, 5 minute infusions of epinephrine were administered beginning with a dose of 0.25 mcg/kg/min. This dose was increased logarithmically until ventricular arrhythmias appeared. A time interval of 10 or more minutes elapsed between infusions. During this time heart rate and blood pressure returned to their control values. The dose of epinephrine needed to produce supraventricular arrhythmias (SVA), A-V dissociation (AVD), minimal ventricular arrhythmias (VAmin) and maximal ventricular arrhythmias (VAmax) was expressed as mcg/kg/min x infusion duration in min=mcg/kg. VAmin were ventricular premature beats or bigeminy. VAmax were multifocal ventricular beats or ventricular tachycardia. Paired comparisons (Student's t) for the effect of thiopental on SVA, AVD, VAmin and VAmax were made on dogs which exhibited these rhythm disturbances on both anesthetic occasions.

Results. Thiopental reduced the dose of epinephrine needed to produce VAmin and VAmax, but had no significant ($p < 0.05$) effect on the dose for SVA or AVD (Table 1). The sequence for arrhythmia development with increasing dose of epinephrine was SVA, AVD, VAmin, and VAmax. Blood pressure increases accompanying ventricular arrhythmias with epinephrine were similar for dogs anesthetized with halothane or halothane-thiopental. Finally, with three dogs, the sensitizing dose to epinephrine (VAmin) was the same at 4-5 hours as 1-2 hours following thiopental.

Discussion. The results of this study indicate that thiopental potentiates ventricular, but not supraventricular sensitization to epinephrine during halothane anesthesia in dogs. This interaction has not been documented in man for any of the hydrocarbon anesthetics despite the widespread use of thiopental as an induction agent. The appearance of supraventricular arrhythmias and A-V dissociation prior to sensitization is noteworthy. With the exception of a single report (2), arrhythmias preceding ventricular sensitization have not been characterized or the dose of epinephrine needed to produce them determined. Thus, while sensitization has usually been equated with ventricular arrhythmias, the clinician should recognize that sensitization is a hierarchy of arrhythmias beginning with the most benign supraventricular and leading to the most severe ventricular rhythm disturbances.

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References.

1. MacCannell KL, Dresel PE: Potentiation by thiopental of cyclopropane-adrenaline cardiac arrhythmias. Can J Physiol Pharmacol 42:627-639, 1964.
2. Puerto BA, Wong KC, Puerto AX et al: Epinephrine-induced dysrhythmias: Comparison during anaesthesia with narcotics and with halogenated inhalation agents in dogs. Can Anaesth Soc J 26:263-268, 1979.

TABLE 1. EPINEPHRINE-SENSITIZING DOSE (mcg/kg)

	SVA	AVD	VAmin	VAmax
HALOTHANE	0.97 (0.89)	2.79 (1.37)	3.49 (1.39)	5.76 (2.32)
HALOTHANE-THIOPENTAL	1.31 (1.11)	2.16 (1.14)	2.05* (1.17)	2.93* (1.71)
NO. DOGS	8	5	8	11

* $p < .05$ Halothane-thiopental vs. halothane