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ALTERED RELEASE AND METABOLISM OF NOREPINEPHRINE IN SUPERFUSED CANINE SAPHENOUS VEINS IN THE PRESENCE OF HALOTHANE AND/OR HYPOXIA. GS Kamath, M.D., DK Rorie, M.D., Ph.D., GM Tyce, Ph.D. Anesthesiology Dept., Mayo Clinic, Rochester, MN 55905.

AIM: The aims of the studies were to examine the effects of hypoxia and halothane on the release and disposition of norepinephrine (NE) in canine saphenous vein. METHODS: Segments of vein were cleaned of perivascular tissue and cut into helical strips. The strips were suspended and superfused at 2 ml/min with Krebs-Ringer solution containing corticosterone ($4x10^{-5}M$) and desipramine ($10^{-6}M$). The tissues were allowed to equilibrate for 60 min at 37°C. Four samples of superfusate were then collected at 10-min intervals. The first sample was collected at basal conditions after which the tissues were stimulated at 2 Hz. Two poststimulation collections were made. The tissues were then allowed to rest for 60 min, and the identical sampling and stimulation repeated. In the first half of each study tissues were aerated with 95% O_2 and 5% CO_2. Three of the four tissues studied simultaneously were then subjected to either halothane (1 or 2 MAC) in 95% O_2 + 5% CO_2, hypoxia (5% O_2), or halothane in the presence of hypoxia. The time control tissues were aerated with 95% O_2-5% CO_2 throughout. NE and 3,4-dihydroxyphenylglycol (DOPEG) were quantified in superfusate by high-performance liquid chromatography using electrochemical detection. DOPEG is an index of neuronal reuptake and monoamine oxidase (MAO) activity. Five experiments each were carried out with 1 or 2 MAC halothane. RESULTS: The results were expressed as percentage change in NE or DOPEG in the second half of the experiment compared to the corresponding collection periods in the first half:

Percentage change in DOPEG efflux (mean±SE)

	Basal	Stimulation	Poststim.
Control	-20.1±5.1	-20.9±3.9	-18.4±5.8
Halothane	-52.7±2.5*	-52.7±2.8*	-51.7±3.5*
Hypoxia	-62.9±1.4*	-56.8±4.5*	-61.6±5.5*
Hal.+ Hypox.	-84.5±0.9*	-81.1±2.2*	-79.9±3.8*

Percentage change in NE release (mean±SE)

	Basal	Stimulation	Poststim.
Control	- 9.0±4.7	+ 1.0±1.5	- 1.7±4.4
Halothane	-13.1±4.9	- 8.5±0.8*	- 8.1±2.9*
Hypoxia	-14.9±3.3	+16.8±1.4*	+22.3±3.1*
Hal.+ Hypox.	-14.2±3.1	- 7.4±0.6*	-2.4±3.1

* Significantly different from control (P<0.05).

Statistical analyses were performed with ANOVA followed by Student's t-test with $P < 0.05$ considered significant. Halothane (1 MAC) in the presence of hypoxia reduced the efflux of DOPEG significantly greater than either treatment alone during all collection periods. The effects of 2 MAC halothane on DOPEG efflux were quantitatively similar to those of 1 MAC; however, the reduction in evoked NE release (-14.8±1.2) exceeded that seen with 1 MAC. Hypoxia-induced increase in NE efflux was eliminated in the presence of halothane (1 or 2 MAC). DISCUSSION: While both halothane and hypoxia reduced the efflux of DOPEG, halothane decreased while hypoxia increased evoked NE release. DOPEG efflux was markedly reduced in the presence of both. We postulate that halothane and hypoxia reduce DOPEG efflux by different mechanisms. These results suggest that the prime action of hypoxia is to inhibit MAO, thereby increasing the intraneuronal availability of NE, while the prime effects of halothane are to decrease synthesis or inhibit release of NE. REFERENCES: Anesthesiology 61:337-384, 1984; Anesth Analg 63:1059-1064, 1984.

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TITLE: INTERACTION OF DEXMEDETOMIDINE AND INTRAVENOUS ANESTHETIC AGENTS IN CHRONICALLY INSTRUMENTED DOGS

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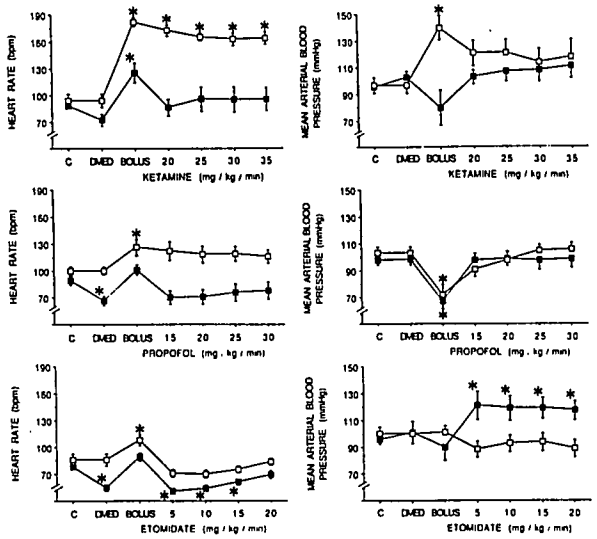
Alpha$_2$ agonists provide analgesia, sedation, and attenuation of autonomic nervous system reflexes. These agents may be useful as premedicants for general anesthesia. This study was designed to examine hemodynamic interactions between the alpha$_2$ agonist, dexmedetomidine (DMED) and three commonly used intravenous anesthetic agents with markedly different hemodynamic profiles. After institutional Animal Care Committee approval, chronically instrumented dogs received IV induction doses of etomidate, propofol, or ketamine followed by continuous infusions of each drug at four different doses for 15 min intervals. Six separate groups (n=10 each) with and without pretreatment with oral DMED (20 µg/kg) were completed. Heart rate, arterial pressure, left ventricular pressure and dP/dt, segment shortening, cardiac output and coronary blood flow were continuously recorded.

DMED caused a significant ($p<0.05$*) decline in heart rate and rate-pressure product as compared to control (c) in all groups. DMED abolished or reversed the increase in heart rate, rate-pressure product, cardiac output, dP/dt and segment shortening observed during induction of anesthesia with ketamine and etomidate. After pretreatment with DMED, continuous infusion of ketamine did not cause increased heart rate or rate-pressure product and decreased dP/dt_{50} and cardiac output. Infusion of etomidate increased arterial pressure and decreased cardiac output after DMED. DMED decreased heart rate and rate-pressure product during anesthesia with propofol, but did not significantly affect other hemodynamic variables (see Fig; ■ DMED; □ Placebo).



This study demonstrates that oral DMED given one hour prior to IV induction with etomidate, propofol, or ketamine may blunt the rise in heart rate and rate-pressure product observed with these anesthetics. Whereas this may provide beneficial actions in certain patients, caution should be used in other patients when an increase or maintenance of sympathetic tone during induction of anesthesia with ketamine or etomidate is desirable.

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