TITLE: EVALUATION OF ACUTE CARDIOVASCULAR EFFECTS OF ESMOLOL IN THE DOG--AWAKE AND ANESTHETIZED WITH HALOTHANE AND ENFLURANE.

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Introduction. Esmolol is a new cardioselective β-adrenergic antagonist characterized by an ultra-short duration of action.[1] Beta-blockade has been employed to attenuate undesirable reflex sympathetic tachycardia and hypertension associated with laryngoscopy, tracheal intubation and surgical manipulation.[2] However, the current β-blockers may not be desirable for this purpose because of their long duration of action. The ultra-short duration of esmolol may overcome this drawback. Since esmolol will be employed perioperatively in conjunction with inhalational agents, the potential interaction of esmolol and the inhalational anesthetics required investigation. The current random crossover study was undertaken to evaluate the hemodynamic effects of intravenous infusions of esmolol in dogs anesthetized with halothane and enflurane and in the awake state.

Methods. Six, male, mongrel dogs with an average weight of 19.4 kg were used. On experimental day 1, dogs were randomly assigned to one of the inhalational anesthetics. On experimental days 2 and 3, dogs were randomly allocated to either awake or the remaining inhalational agent. On day 1, all animals had indwelling catheters placed in the inferior vena cava, abdominal aorta and cephalic vein and an introducer (to allow floatation of a modified pulmonary artery thermodilution catheter) in the external jugular vein. In the anesthetized dogs, control readings were not begun until at least 90 minutes after induction and tracheal intubation. Infusions of 100, 300, 500 and 1000 μg/kg/min of esmolol were administered in stepwise fashion by infusion pump, the dosage being increased every 60 minutes. End-expired concentration of inhalational agent was monitored frequently by gas chromatography and kept stable at 1.53 (± 0.03) % for halothane and 2.20 (± 0.05) % for enflurane. Verification of β-blockade was obtained using 0.25 μg/kg isoproterenol challenge administered during the first control period and 20 minutes into the 100 μg/kg/min infusion period. Systolic (SAP), mean (MAP), and diastolic arterial, central systemic venous, pulmonary artery and capillary occlusion pressures, lead II EKG intervals, heart rate (HR), respiratory rate, thermodilution cardiac output, arterial blood gases, pH, Na^+, K^+ and body temperature were recorded throughout the experiment. Infusion of esmolol was increased at 60 minute intervals and discontinued when MAP was depressed by at least 30% of the pre-esmolol value.

Results. Table 1 shows the mean change in HR, SAP and MAP produced by isoproterenol prior to and following the infusion of 100 μg/kg/min of esmolol. Esmolol was able to significantly attenuate the increase in heart rate produced by isoproterenol. Following esmolol infusion, isoproterenol produced a significantly greater decrease in SAP in all groups.

		$HR_{(beats/min)}$	$SAP_{(torr)}$	$MAP_{(torr)}$
AWK	Control	44.6 ± 6.6	9.0 ± 1.9	- 3.8 ± 2.7
	Esmolol	24.4 ± 7.4*	- 5.6 ± 3.3*	-10.0 ± 2.8
HALO	Control	40.2 ± 4.4	- 5.6 ± 5.6	-15.4 ± 3.3
	Esmolol	8.2 ± 2.9*	-21.6 ± 3.7*	-22.0 ± 4.2
ENFL	Control	48.0 ± 4.5	- 0.8 ± 6.0	-21.0 ± 3.5
	Esmolol	21.4 ± 4.7*	-27.8 ± 3.7*	-32.8 ± 2.6*
* Indicates significant difference from previous control mean ($p < 0.05$)				

TABLE 1. Change (mean ± SEM) in HR, SAP and MAP following isoproterenol before and after esmolol infusion.

Table 2 shows the mean percentage change in SAP and MAP between the control values and the value observed when the experiment was terminated because either a greater than 30% reduction in MAP occurred or the 1000 μg/kg/min infusion was completed. The fall in SAP and MAP was greater ($p < 0.05$) in the halothane and enflurane animals than in the awake dogs.

	$SAP_{(\Delta\ \%)}$	$MAP_{(\Delta\ \%)}$
AWAKE	- 4.5 ± 6.0	6.9 ± 5.2
HALOTHANE	-42.1 ± 4.4	-41.7 ± 5.0
ENFLURANE	-43.8 ± 9.5	-44.7 ± 9.9

TABLE 2. Percentage change in SAP and MAP following esmolol infusion in awake and anesthetized dogs.

Discussion. The results confirm that esmolol is a beta-adrenergic antagonist with a rapid onset and short duration of action.[3] This study demonstrates that the hemodynamic effects of esmolol are more pronounced in the anesthetized animal than in the awake state. Even at doses of 100 μg/kg/min. Esmolol reliably reduced the chronotropic effects of isoproterenol in both awake and anesthetized dogs. In summary, esmolol may prove to be a useful β-receptor antagonist during the perioperative period but caution is suggested in the selection of an appropriate dose when it is used in combination with halothane or enflurane anesthesia.

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