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HEMODYNAMICS AND OXYGEN UPTAKE BELOW AND ABOVE OCCLUSION OF THE THORACIC AORTA IN DOGS: EFFECTS OF DEXMEDETOMIDINE

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Crossclamping of the thoracic aorta is associated with decreases in blood flow and oxygen consumption in tissues below aortic occlusion; above the occlusion, blood flow increases but paradoxically oxygen uptake decreases.[1] The present study tested the hypothesis that dexmedetomidine, an α_2 adrenergic agonist, modifies adrenergically mediated circulatory disorders possibly developing above the aortic clamp, and subsequently improves tissue oxygen supply above aortic occlusion.

Methods. Sternotomy was performed in dogs anesthetized with halothane. After heparinization, the inferior vena cava was transected above the diaphragm and the appropriate cannulating electromagnetic probe was inserted. Cardiac output was measured by pulmonary artery catheter and thermodilution. Catheters were also placed in the carotid and femoral arteries and both caval veins.

The animals were divided into three groups: control group (group C), and two groups (D3 and D30) treated with 2 doses of dexmedetomidine (3 µg/kg, 30 µg/kg, respectively) prior to aortic crossclamping.

Results. Crossclamping of the thoracic aorta was associated with an expected increase in mean arterial pressure (MAP) and a decrease in cardiac index (CI) in all 3 groups. An increase in MAP was greater in groups C and D3 than in group D30. CI was the lowest in group D30 and the highest in group C. Filling pressures were unchanged in group C and significantly increased in animals treated with dexmedetomidine in a dose-related fashion. Oxygen uptake and blood flow through the lower part of the body dramatically decreased (to 20% of preclamp values) without differences between the groups. Oxygen uptake in the upper part of the body, contrary to the control group, increased in D3 and D30 groups in a dose-related fashion (3- and 6-fold increase, respectively) without an increase in the flow. Concentration of lactate in the superior vena caval blood increased almost 3-fold in control group and did not change significantly in either dexmedetomidine treated groups; lactate concentration in the inferior caval blood increased in all 3 groups, but this increase was significantly greater in control than in D3 and D30 groups.

Discussion and Conclusions. 1) Dexmedetomidine administration was associated with a lack of increase in myocardial contractility in response to aortic crossclamping which was reflected in greater decreases in CI and increases in filling pressures during aortic crossclamping in animals treated with dexmedetomidine. 2) Dexmedetomidine administration was associated with an increase in oxygen uptake (without an increase in flow) and a decrease in lactate production in tissues above crossclamping suggesting an improvement in microcirculation and oxygen delivery to the tissues. 3) Dexmedetomidine therapy did not affect the decrease in blood flow and oxygen consumption below aortic occlusion; however, it did decrease lactate production by the ischemic tissues below the occlusion. This suggests that dexmedetomidine might decrease oxygen demand, providing protection from hypoxic insult.

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TITLE: INHIBITION OF Na/Ca EXCHANGE IN HEART CELLS BY ENFLURANE, ISOFLURANE AND HALOTHANE

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Na/Ca exchange in sarcolemmal vesicles is relatively insensitive to general anesthetics: an inhibition of 50% by 10% enflurane has been reported briefly[1]. Recently we found evidence that Ca influx into Na-loaded cells by Na/Ca exchange was inhibited by octanol, with a potency much greater than we expected[2] on the basis of the vesicle work with enflurane. We did, however, also find a four-fold enhancement of octanol potency by the presence of physiological levels of extracellular Na. Since Na/Ca exchange in vesicles is measured in the absence of extravesicular Na, we surmised that this could have resulted in a relative insensitivity of the exchanger to enflurane. Since the volatile anesthetics in common clinical use have a significant negative inotropic effect on the myocardium, we have examined the influence of enflurane, isoflurane and halothane on Na/Ca exchange in isolated heart cells in the presence of physiological levels of Na.

Adult heart cells were isolated from female retired breeder rats and incubated in a Krebs Henseleit medium without Ca or Mg, plus 0.1mM EDTA, for 10 min. We have previously found these conditions to cause complete equilibration of monovalent ions across the sarcolemma via the Ca channel[3], resulting in complete Na loading. After 10min Mg was restored, ouabain (1mM) was added, and cells were stored on ice until use. Ca uptake by Na/Ca exchange was measured in a closed chamber at 37°without an airspace in which cell suspension was mixed with buffer plus ouabain and a 15 MAC stock solution of anesthetic. Anesthetic concentration was also monitored by gas chromatography of headspace extracts of anesthetic-buffer mixtures under similar conditions. Ca uptake was initiated by adding Ca (1mM) containing isotopic Ca. An aliquot (0.5ml) was removed after 2 min and centrifuged as previously[2]. The zero uptake baseline was determined from Ca uptake by ATP-depleted cells, as before, and subtracted from all values.

Control uptake rate of Ca by Na/Ca exchange under these conditions was 2.07 +/- 0.46 nmol/mg/min. All anesthetics inhibited this uptake, with the dose dependence shown in Fig 1. Concentrations of anesthetic required to inhibit 50% were 1.5 MAC (2.6%) for enflurane, 2.7 MAC (3.1%)for isoflurane, and 4.1 MAC (3.1%) for halothane. These results show that at physiological Na . concentrations enflurane does indeed inhibit Na/Ca exchange with a potency fourfold greater than previously observed[1]. The inhibition is stronger than that by isoflurane or halothane at equivalent anesthetic concentrations. The inhibition by enflurane is likely to be significant at clinical concentrations of the anesthetic.

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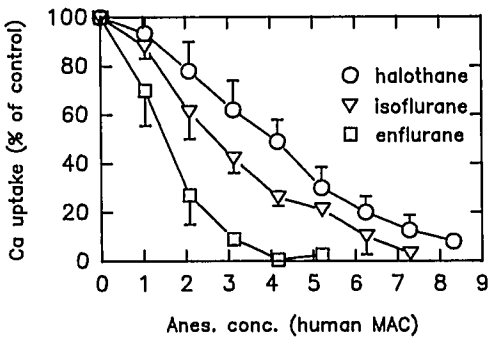

Fig 1