Title: ISOFLURANE EFFECT ON ISOLATED CANINE CEREBRAL VASCULAR SEGMENTS IS NOT ENDOTHELIUM-DEPENDENT

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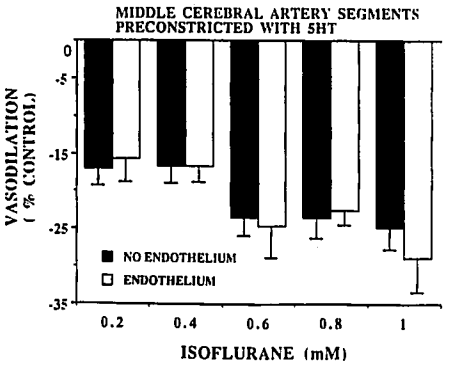
A number of studies[1-3] suggested that volatile agents (isoflurane, halothane) exert an endothelium-dependent relaxation in different vessels (aortic, coronary, femoral, and carotid arteries). The purpose of this study was to examine isoflurane's effect on isolated canine middle cerebral artery (MCA) segments and to determine whether these effects are endothelium dependent.

Canine MCA segments (N=250) were randomly allocated into 2 groups. In Group I, 50% of the vessels were stripped of endothelium before suspension in the baths. In Group II, 50% of the vessels were exposed to N^G-monomethyl-L-arginine (LnMMA) (300 μM) to inhibit endothelium dependent responses.[4] All the vessel segments were suspended in temperature controlled baths (37°C) containing a modified Krebs solution equilibrated with PCO_2 6.5% and O_2 93.5% to maintain pH at 7.38-7.42 and PCO_2 35-40 mmHg. The vessels (pre constricted with ED_{50} dose of 5HT (2×10^{-7}M) were exposed to a range of isoflurane concentrations. Endothelium-dependent responses were verified by exposing the preconstricted vessels to bradykinin (2×10^{-9}M). The results were statistically analyzed using 2-way ANOVA. A p value of 0.05 or less was considered statistically significant. Data were expressed as mean ± SEM. A dose dependent vasodilatation during isoflurane occurred in all the vessels (i.e. LnMMA, non LnMMA, stripped and non stripped vessels). There was no significant difference in the isoflurane induced vasodilatation that occurred between the stripped and the non-stripped vessels or between the LnMMA and non-LnMMA vessels (see graph). Contrary to previous studies, our results indicated that although isoflurane caused a significant dose dependent relaxation of MCA, this response was not endothelium-dependent.



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Title: HALOTHANE ATTENUATES MESENTERIC VENOCONSTRICTION IN RESPONSE TO GRADED HYPERCAPNEA

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The neural control of venous tone in the splanchnic bed contributes significantly to the regulation of total venous capacitance. Previously, it was shown that 0.5 and 1% inhaled halothane attenuates baroreflex mediated mesenteric venoconstriction[1] as well as the venoconstriction, hypertension and bradycardia resulting from activation of peripheral chemoreceptors by graded hypoxia.[2] The objective of the present study was to determine if 1% inhaled halothane also modulates the centrally-initiated reflex venoconstriction produced by graded hypercapnea.

Alpha chloralose anesthetized rabbits (1-1.5 kg) were surgically prepared with a tracheotomy for controlled ventilation, a femoral venous cannula for infusion and a femoral arterial cannula for measurement of heart rate and blood pressure. A 13 cm loop of terminal ileum was externalized through a midline laparotomy and superfused with physiologic salt solution (37°C). The mesentery was transilluminated, and the diameters of small mesenteric veins (500-800 μm) were measured continuously by videomicroscopy. Intravenous pressures were measured simultaneously at the same site *via* glass micropipettes using a servo-null system.

Reflex venoconstriction in response to sequentially administered 40 sec intervals of 20%, 25% and 30% $FiCO_2$ was significantly reduced by 1% inhaled halothane (See Figure).

Percent changes were analyzed by repeated measure multiple analysis of variance following normalization by arc sign transformations. Superfusion of the mesenteric vein with 15 μg of tetrodotoxin abolished this reflex constriction without affecting intravenous pressure or producing systemic hemodynamic changes thus confirming a neurally mediated mechanism.

Inhaled halothane impairs neurally mediated hypercapnea induced mesenteric venoconstriction as well as the baroreflex and hypoxia induced venoconstriction observed previously.

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References:

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