TITLE: EFFECTS OF HALOTHANE AND ISOFLURANE ON DIAPHRAGMATIC MICROCIRCULATION IN THE RATS

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Halothane (HAL) produced a marked impairement in diaphragmatic function,[1] whereas isoflurane (ISO) had only minor effects.[2] This discrepancy could result from different effects at the microcirculatory level. The aim of this study was to assess diaphragmatic arteriolar diameters during HAL and ISO anesthesia.

Twenty five rats mechanically ventilated were studied. After a midline laparotomy, the diaphragm was transilluminated and arterioles were visualized using a microscope which was connected to a video tape recorder. The arteriolar network exhibited 3 to 4 successive bifurcations from the point where the first order arteriole entered the muscle. The arteriolar branches of second (A2), third (A3) and fourth (A4) order were studied. After baseline measurements, rats were allocated into 2 groups accordingly to HAL (n = 13) or ISO (n = 12) progressive (0.5, 0.75 and 1 MAC) exposure. Each MAC level was administered for a 15 min period. Systolic arterial blood pressure (SAP) was continuously recorded. Statistics were performed with ANOVA and Wilcoxon rank sum test.

Changes in SAP and vessel diameters during the study are summarized in tables 1 and 2 respectively (mean ± SD).

Table 1. SAP (mm Hg)

	Control	0.5 MAC	0.75 MAC	1 MAC
SAP (ISO)	123±3	123±3	101±3*+	93±4*+
SAP (HAL)	129±3	93±8+	82±8+	76±9+

Table 2. Arteriolar diameters (% of control)

	0.5 MAC		0.75 MAC		1 MAC	
	HAL	ISO	HAL	ISO	HAL	ISO
A2	109±26	86±14	102±23	90±20	89±26	86±19
A3	82±31	91±20	79±27	91±23	74±29	97±26
A4	90±15	75±24	18±37+	72±42*	20±34+	89±17*

* $p < 0.05$ vs other group, + $p < 0.05$ vs control

HAL at clinical concentration markedly decreased diaphragmatic arteriolar precapillar (A4) perfusion whereas ISO had no deleterious effects. Two mechanisms may explain HAL effects: 1) a reduction in diaphragmtic blood flow related to the induced decrease in SAP; 2) a direct effect on arteriolar vascular resistances. These findings support the fact that microvascular alteration under HAL may be responsable for the reduced diaphragmatic strength.[1]

References
1. J Appl Physiol 63:1757-1762, 1987
2. Anesthesiology 70:118-122, 1989

TITLE: REMOVAL OF EPITHELIUM DOES NOT AFFECT THE RESPONSE OF ISOLATED CANINE AIRWAYS TO HALOTHANE

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Introduction: Airway epithelium can modulate the responses of airway smooth muscle to bronchoconstrictor and bronchodilator agents (1). The purpose of this study was to determine whether airway epithelium modulates the relaxing effect of halothane on canine airways in vitro.

Methods: Paired canine 2nd or 3rd order bronchial rings from 10 mongrel dogs were studied. The epithelium was removed from one ring of each pair by gentle rubbing using a cotton swab. The rings were mounted in organ chambers filled with physiologic salt solution (37°C) aerated with 94% O_2 and 6% CO_2. Cumulative dose-response curves of isometric tension responses to acetylcholine (ACH, 10^{-8} to 10^{-3} M) and 5-hydroxytryptamine (5HT, 10^{-8} to 10^{-5} M) were obtained in the absence and presence of 1 MAC halothane and in the absence or presence of epithelium.

Results: In the absence of halothane (control), epithelium removal significantly decreased the ED50 (log molar concentration of agonist necessary to produce 50% of max. contraction) for ACH and the ED30 for 5HT, indicating an increased sensitivity to these agonists. Halothane significantly increased the ED50 and ED30 values in rings both with and without epithelium, indicating that halothane decreased sensitivity to these agonists. The changes in the ED50 and ED30 values caused by halothane were not significantly different in the presence or absence of epithelium.

Discussion: Epithelium removal increased the sensitivity of canine airway smooth muscle to muscarinic and serotoninergic agonists. Although halothane decreased the sensitivity of canine bronchi to contractile agonists, consistent with its clinical effects in relieving bronchospasm, this effect does not appear to be mediated by the airway epithelium in isolated canine bronchi. This finding suggests that the bronchodilating effect of halothane may not be altered in subjects with injured airway epithelium (asthmatics).

Table: **Effect of halothane on canine airway smooth muscle contraction in the presence (epi) and absence (no epi) of halothane or epithelium**

Agent†	Control		1 MAC halothane	
	epi	no epi	epi	no epi
ACh (ED50)	-5.0	-5.4#	-4.7*	-5.2*#
5TH (ED30)	-6.5	-6.8#	-6.1*	-6.4*#

*Significantly different ($p < 0.05$; paired t-test) from rings not exposed to halothane. #Significantly different ($p < 0.05$; paired t-test) from rings with epithelium. †n = 5 dogs (20 bronchial rings) for each agent.

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Reference:
1. Vanhoutte PM. Epithelium-derived relaxing factor(s) and bronchial reactivity. Am. Rev. Resp. Dis. 138: S24-S30, 1988.