ISOFLURANE INDUCES CORONARY STEAL COMPARED TO ENFLURANE IN A DOG MODEL OF CRITICAL CORONARY STENOSIS

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INTRODUCTION: Isoflurane has been identified as a possible inducer of coronary steal.Despite numerous investigations the coronary circulatory effects of isoflurane remain controversial[1,2]. We developed a dog model of critical coronary stenosis to determine the effects of isoflurane and enflurane in producing redistribution of coronary blood flow. By excluding changes in coronary flow mediated by systemic hemodynamics, we attempted to quantitate coronary flow redistribution attributable to the anesthetic effect on the coronary circulation.

METHOD: 21 mongrel dogs were anesthetized with enflurane (N=10) or isoflurane (N=11) and ventilated with 100% oxygen after institutional approval was obtained. All animals received a narcotic base of morphine 2-3 mg/kg. The hearts were paced at 140/minute. A critical coronary stenosis was created between the first and second diagonal branch of the proximal left anterior descending coronary artery by means of a micrometer driven occluder. Abolition of reactive hyperemia to a 20 second coronary occlusion confirmed the creation of a critical stenosis. Myocardial blood flow was measured by radioactive microspheres. Coronary blood flow measurements were obtained after creation of the critical stenosis at 0% anesthetic, 1 MAC end tidal anesthetic with phenylephrine (NEO) infusion to maintain baseline arterial pressure and 1 MAC anesthetic without phenylephrine permitting arterial pressure to fall more than 30%below baseline arterial pressure. The results were analyzed by analysis of variance and linear regression.

RESULTS:

Table I Regional Microsphere Blood Flow Ratios

ENFLURANE

	NORMAL		ISCHEMIC ZONE	
MAC	ENDO	EPI	ENDO	EPI
0	0.95±.05	.96±.04	1.02±.10	1.1±.13
1	0.93±05	.98±.04	0.90±.08	0.99±.09
1+NEO	0.87±.07	.88±.05	0.97±.12	0.96±.14

ISOFLURANE

	NORMAL		ISCHEMIC ZONE	
MAC	ENDO	EPI	ENDO	EPI
0	1.1±.05*	.98±.03	0.82±.03*	0.89±.05*
1	0.93±.03*	.98±.03	0.71±.04*	0.80±.04*
1+NEO	0.99±.05	1.14±.10*	1.01±.11*	1.14±1.10

Endocardium=Endo; Epicardium=Epi
Mean ± SEM
*p<.05

CONCLUSIONS: We conclude that in this dog model of critical coronary stenosis that Isoflurane compared to enflurane at equipotent doses produces a much larger decrement in flow to the ischemic region. However, this reduced flow in the ischemic zone is readily restored by normalizing arterial blood pressure with phenylephrine infusion.

REFERENCES:

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Title: **HEART RATE DEPENDENT EFFECTS OF VOLATILE ANESTHETICS ON THE CARDIAC SARCOPLASMIC RETICULUM**

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Different actions of halothane (HAL) and isoflurane (ISO) on the cardiac sarcoplasmic reticulum (SR) and the transsarcolemmal influx of calcium seem to be responsible for their negative inotropic effect (1,2). Recently it has been shown through the use of rapidly cooling contracture (RCC) - a method to investigate the calcium content of the SR (3) - that ISO has a stronger action on the SR than HAL (4,5). Since calcium loading of the SR and its contribution to force of contraction (FC) is largely influenced by the heart rate (HR) (6), we investigated the effects of HAL and ISO on RCC of isolated heart muscles driven at a low and a high HR. The results were compared with the effect of ryanodine (RYA), a selective SR blocking agent, and that of verapamil (VER), a transsarcolemmal calcium blocker.

Guinea pig papillary heart muscles were electrically driven at HRs of 1 Hz or 3 Hz (isometric conditions). Temperature of the modified tyrode solution (calcium 2.5 mM) was 35 °C. Stimulation was stopped every 20 min and RCC was elicited. RCC was performed by continuous flow of pre-cooled solution through the organ chamber (flow rate 20 ml/s), resulting in a temperature of 5 °C. Tension of RCC was 65% of the FC prior to it at 1 Hz and 93 % of FC at 3 Hz. Drugs were given on a single exposure basis after the second RCC (control-RCC) for an exposure time of 20 min until the test-RCC was elicited. MAC for rodents (1 MAC = 1 vol% HAL = 1.4 vol% ISO) were used for comparative concentrations. For both HR series each concentration was tested on six preparations.

The results are summarized in table 1. RYA depressed RCC stronger at a HR of 3 Hz than at 1 Hz. In contrast, VER had a slightly weaker effect on RCC at the higher HR. HAL had properties similar to VER, i.e. it suppressed RCC less at the higher HR. ISO suppressed RCC at both HRs and each concentration completely.

Table 1: RCC tension (% of control)

RYA	1.0 nM	3.0 nM	10 nM	HAL	0.25 %	0.5 %	1.0 %
1 Hz	106 ± 21	75 ± 14	< 1	1 Hz	74 ± 11	44 ± 8	33 ± 12
3 Hz	60 ± 13	18 ± 7*	4 ± 2	3 Hz	80 ± 12	71 ± 8*	40 ± 7
VER	**0.1 µM**	**0.3 µM**	**1.0 µM**	**ISO**	**0.35 %**	**0.7 %**	**1.4 %**
1 Hz	91 ± 5	81 ± 10	56 ± 4	1 Hz	< 1	< 1	< 1
3 Hz	99 ± 18	87 ± 6	81 ± 4*	3 Hz	< 1	< 1	< 1

means ± SEM, * p < 0.05 - 3 Hz vs. 1 Hz

These results suggest that volatile anesthetics have a substantial effect on the SR, either by inhibiting it directly or limiting the supply of calcium to the SR. While HAL might act primarily by limiting the calcium supply to the SR, ISO seems to suppress the SR directly. The effect of ISO on RCC awaits further evaluation.

References: 1. Anesth Analg 66:29, 1987. 2. Anesthesiology 64:620, 1986. 3. J Gen Physiol 88:437, 1986. 4. Am J Physiol 257:H1804, 1989. 5. Anaesthesist 39 (Suppl.):110, 1990. 6. Pflügers Arch 364:203, 1976.