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Title: HALOTHANE AND ETHRANE EFFECTS ON THE CORONARY CIRCULATION

Authors: D.C. Sawyer, D.V.M., Ph.D., S.W. Ely, Ph.D. and J.B. Scott, Ph.D.

Affiliation: Departments of Small Animal Surgery and Medicine and Physiology, College of Veterinary Medicine, Michigan State University, East Lansing, Michigan 48824

Introduction. A recent study in our laboratory conducted in the dog demonstrated that the direct local effect of halothane is to produce vasodilation of the vasculature supplied by the right coronary artery (RCA). However, when the vapor is administered systemically, reflex baroreceptor stimulation in conjunction with depressed cardiac metabolism partially or completely antagonizes the local action of halothane. Since the RCA provides only 15% of the total coronary flow in the dog, these studies were conducted in an animal model more representative of man. Thus, we now report the effects produced by local and systemically administered halothane and ethrane on the right coronary circulation of the pig.

Methods. Poland China pigs (35-45kg) were anesthetized with thiamylal Na and 66% nitrous oxide, and ventilated to maintain acid-base and pH values within the normal range. In seven animals, femoral vessels were isolated and following sternotomy, an extracorporal constant pressure perfusion circuit was interposed between a femoral artery (FA) and the RCA. Right ventricular pressure was recorded and dP/dt derived with an integrated amplifier. Halothane and ethrane were separately introduced into the ventilatory mixture, end-tidal concentrations held constant for steady state conditions and values recorded as systemic (syst.) effects (Tables 1 and 2). In five of these animals, coronary perfusion pressure was decreased from control levels (107±10) to the mean arterial pressure produced by halothane (53±5 torr) Table 1,C. In five of these animals, a coronary perfusion circuit containing an isolated porcine donor lung was interposed between the FA and RCA. The donor lung was used to deliver halothane and ethrane directly into blood perfusing the RCA and the values recorded as "local" effects.

Results and Discussion. These studies demonstrate that the local action of halothane and ethrane is to produce coronary vasodilation with a subsequent increase in flow during constant pressure perfusion. This dilation occurred in the face of no change (ethrane) or a reduction in myocardial activity (halothane) as judged by a fall in dP/dt and hence at a time when cardiac oxygen consumption was apparently unchanged or reduced. Thus the dilation is most likely mediated via a direct action of these vapors on vascular smooth muscle and not secondary to their effects on the myocardium. Both halothane or ethrane administered systemically produced large reductions in systemic pressure but no significant change (P>0.05) in coronary resistance suggesting that the local coronary vasodilator effects were effectively antagonized by an indirect effect(s). When coronary perfusion pressure was decreased to the existing systemic pressure during halothane, there was a dramatic fall in flow which resulted from a reduction in perfusion pressure. Resistance was not affected. The indirect antagonism of the direct local dilator action of halothane and ethrane is most likely mediated via reflex activation of the sympathetic nervous system due to hypotension. This may be abetted by a concomitant fall in myocardial $\dot{V}O_2$. The former is supported by studies in the dog heart which show that systemically administered halothane during alpha blockade produces a decrease in right coronary resistance. In conclusion, it would appear that in a coronary circulation like that of man, halothane and ethrane are not detrimental to coronary flow and may, in fact, be beneficial as long as perfusion pressure is maintained in the anesthetized patient. However, even under these conditions halothane reduces dP/dt, and thus may depress myocardial contractility. This is apparently a direct effect that is not antagonized by increased coronary flow or augmented sympathetic activity.

Table 1 - Halothane

	Right Cornary Artery		Right Vent.	Syst.
	Vascular Res. (CRU)	Flow ml/min/ 100g	dP/dt	Mean Art. Press.
Local cont. A .8%	2.00±.42 ↓1.52±.28*	↑80±22 ↑100±26*	↓1383±53 1042±42*	↓97±5 92±4*
Syst. cont. B .5%	1.28±.24 1.12±.20	103±15 121±19	↓1250±116 ↓657±90*	↓87±7 ↓51±4*
Syst. cont. C .5%	1.35±.34 1.21±.29	94±21 ↓43±10*	↓1140±112 ↓620±97*	↓88±10 ↓53±5*

* $p < .05$ $\bar{x} \pm SE$ cont. = control

(A&B coronary perfusion pressures held constant; C coronary perfusion pressure lowered during halothane to systemic pressures.)

Table 2 - Ethrane

	Right Coronary Artery		Right Vent.	Syst.
	Vascular Res. (CRU)	Flow ml/min/ 100g	dP/dt	Mean Art. Press.
Local cont. 2.0%	↓1.8±.44 ↓1.20±.28*	↑93±36 ↑131±45*	1137±80 962±126	85±5 84±8
Syst. cont. 1.5%	1.16±.12 0.99±.12	106±14 128±23	↓912±133 ↓637±137*	85±5 ↓53±3*

* $p < .05$ $\bar{x} = SE$ cont. = control