TITLE: A COMPARISON OF THE INTRINSIC CEREBRAL VASODILATING POTENCIES OF HALOTHANE AND ISOFLURANE IN THE NEW ZEALAND WHITE RABBIT

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Isoflurane (I) has been shown to cause lesser increases in cerebral blood flow (CBF) than halothane (H) in several species[1,2]. I has also been shown to cause a greater reduction in the cerebral metabolic rate for oxygen ($CMRO_2$) than equi-potent concentrations of H[2]. The authors speculated that it might be this difference in the effects of H and I on $CMRO_2$ rather than a difference in their intrinsic (direct) cerebral vasodilating potencies which accounts for their disparate effects on CBF. To investigate this possibility, the CBF effects of H and I were compared during administration of a background anesthetic (deep barbiturate) designed to produce maximum antecedent suppression of $CMRO_2$ and thereby to preclude major additional volatile agent (VA) induced change in $CMRO_2$.

Methods: Ten NZW rabbits were anesthetized with H, intubated and ventilated with 1-1.25% H and 60% N_2O in O_2. Immediately after placement of arterial and venous lines, H was discontinued and pentobarbital (PB) was given IV as a loading dose ($60 mg.kg^{-1}$ over 45-60 mins) followed by an infusion ($30 mg.kg^{-1}.hr^{-1}$). N_2O was replaced with 60% N_2. Temperature (servo-controlled to 37° C), EKG, EEG, blood pressure (BP), CVP, ICP (needle in cisterna magna), end-tidal (ET) CO_2 and ET-VA concentrations (infrared analyzers) were monitored continuously. CBF was determined intermittently by hydrogen clearance in frontal and parietal cortex and in the dorsal hippocampus using platinum needles placed stereotacticly via small burr holes. In seven rabbits, a limited craniectomy was performed and a 23 gauge needle was placed non-occlusively in the confluence of the sinuses (CS). $CMRO_2$ was calculated as the product of arterio-CS O_2 content difference x CBF (mean of 3 structures). Mean BP was maintained (phenylephrine infusion) between 65-70mmHg and $PaCO_2$ between 38-42mmHg throughout the study. After 90 mins of PB infusion, CBF and $CMRO_2$ were determined. H or I (alternating basis) was then introduced and, after 15 minutes at an ET concentration of 0.75 MAC, CBF/$CMRO_2$ determination was repeated. The VA was then omitted and after a 60 min "washout", a third CBF/CMRO2 study was performed. Thereafter, the second VA was introduced and a final CBF/$CMRO_2$ determination was made.

Results: The EEG was isoelectric at all times subsequent to the PB loading dose. The direction and relative magnitude of CBF changes in individual structures were similar and CBF results are expressed as the average of the three values. CBF during the two control states (PB only) prior to administration of H and I was not different (see Table). CBF was increased by a significant ($p<.001$, paired t) and similar amount during administration of both H and I (see Table). The doses of phenylephrine required to support BP were not different during either the control states or during administration of H and I. The $CMRO_2$ was not significantly different during the four study phases.

Discussion: In a previous study[3] performed in rabbits during anesthesia with N_2O and morphine, 1.0 MAC H produced an increase in CBF while 1.0 MAC I resulted in no significant change. $CMRO_2$ was not measured in that study, however in a similar feline study[2] the pattern of CBF response to H and I was comparable and was associated with a significantly greater depression of $CMRO_2$ during I. By contrast, in the present study performed during barbiturate induced EEG isoelectricity (a state which prevented significant VA-induced depression of $CMRO_2$) substantial and identical increases in CBF occurred during the administration of both H and I. These results suggest that the intrinsic (direct) vasodilating effects of H and I may be very similar. Furthermore, they are consistent with the suggestion that the lesser cerebral vasodilating effects of I observed in several models may reflect a greater offsetting "coupled" reduction in CBF occurring during the administration of I.

References: 1) FL Murphy, EM Kennell, RE Johnstone et al. The effects of enflurane, I and H on CBF and metabolism in man. ASA Abstracts, 1974, p 61.

2) MM Todd, JC Drummond. A comparison of the cerebrovascular and metabolic effects of H and I in the cat. Anesthesiology, in press, 1984.

3) MS Scheller, MM Todd, JC Drummond. The effects of H and I on CBF at various levels of PaCO2 in the rabbit. Unpublished data.

	PB	PB+I	PB	PB+H
CBF ($ml.100gm^{-1}.min^{-1}$)	24.0±9.3	58.9±38.8	27.4±12.6	59.1±35.5
$CMRO_2$ ($ml.100gm^{-1}.min^{-1}$)	1.69±.39	1.47±.65	1.65±.57	1.66±.36
PHENYLEPHRINE ($\mu g.kg^{-1}.min^{-1}$)	1.73±1.2	4.35±1.9	1.83±0.9	4.53±2.7

Table. CBF, $CMRO_2$ and phenylephrine infusion rate before (PB) and during administration of 0.75 MAC isoflurane (PB+I) and halothane (PB+H). Statistical comparison in text.