Title: QUANTITATIVE COMPARISON OF CEREBRAL BLOOD VOLUME IN RATS RECEIVING HALOTHANE OR ISOFLURANE

Authors: J.J. Katz, M.D., M.M. Todd, M.D., D.S. Warner, M.D.

Institution: Neuroanesthesia Research Group, Department of Anesthesia, University of Iowa, College of Medicine, Iowa City, Iowa 52242

Introduction. Volatile anesthetics are are known to increase cerebral blood flow (CBF). This may be of importance in patients with reduced intracranial compliance, because an increase in cerebral blood flow may be associated with an increase in cerebral blood volume (CBV), which may in turn lead to an elevation in intracranial pressure (ICP). However, little information exists concerning the effects of volatile agents on CBV. The current study was thus designed to quantitate CBV in rats receiving 1MAC doses of isoflurane and halothane.

Methods. Sprague Dawley rats (300-400gm) were anesthetized with either isoflurane or halothane, tracheostomized and mechanically ventilated with 40%O_2/balance N_2. Vascular catheters were placed and succinylcholine (3mg) and heparin (100IU) were given. PaCO2 (38-42 mmHg), PaO2 (>80 mmHg) and temperature (36.5-38.5 C) were controlled, and mean arterial pressure (MAP) was kept above 85 mmHg with autologous blood infusion. The head was then placed in a stereotactic frame, the scalp reflected, and a 17mm diameter funnel was secured to the exposed skull. Following surgical preparation, mean expired anesthetic concentrations were reduced to 1 MAC (isoflurane = 1.4%, halothane = 1.0%), and maintained for an added 45 min stabilization period. CBV was then measured using a modification of the method of Everett et al.(1). 10μCi ^{14}C labeled Dextran (M.W. >70 000) were injected i.v. Five minutes later a 250μl arterial blood sample was drawn. Immediately thereafter, the circulation was arrested with i.v. KCl while the brain was simultaneously frozen in-situ with liquid N_2 poured into the funnel. The skull and dural sinus were removed and the still frozen right hemisphere extracted intact and placed in a pre-weighed scintillation vial. Blood samples and brain were solubilized, neutralized and ^{14}C activity measured by liquid scintillation. Counts per minute (cpm) were converted to disintergrations per minute (dpm) by equations derived from internally standardized controls. CBV(ml/100g of brain) was calculated as [dpm/mg brain]/[dpm/μl blood] X100. Values were compared by unpaired t-testing, with significance assumed for $p<0.05$. [This methodology has recently been validated in our laboratory by demonstrating the expected CBV response to increased PaCO2.]

Results. No significant differences were present between the groups for physiologic values (MAP, $PaCO_2$, PaO_2, pH or temperature). Similarly there were no differences in CBV between halothane and isoflurane anesthetized animals.

Discussion. As noted, there are very few studies examining the effects of anesthetics on CBV. Artru measured the relative changes in CBV produced by volatile agents administered in the presence of N_2O(2,3). While he found no differences, the method used did not provide absolute values and may have substantial errors. Archer et al, using PET scanning, examined the changes in canine CBV produced by $PaCO_2$ during isoflurane anesthesia but provided no comparative information regarding the volatile agents(4). The current study, therefore, appears to be the first comparative, quantitative measurement of absolute CBV during the administration of these two volatile agents.

Halothane is generally believed to be a more potent vasodilator than isoflurane. It thus might be expected to result in greater CBV values than isoflurane. However, the fact that no CBV differences were found may be related to the recent observation by Hansen et al, in which halothane and isoflurane were noted to have very different effects on cortical CBF but to have identical effects on hemispheric flow in rats(5). This would suggest that hemispheric CBF and CBV are closely related. Furthermore, since CBV is a major determinant of ICP, our results raise the possibility that the ICP effects of these two drugs may be very similar, a conclusion that is consistent with the findings of Scheller et al.(6).

References. 1) Everett NB, et al. Circ Res 4: 419, 1958. 2) Artru A. Anesthesiology 58: 533, 1983. 3) Artru A. Anesthesiology 60:575, 1984. 4) Archer D, et al. Anesthesiology 65:A323, 1986. 5) Hansen TD, et al. Anesthesiology 67: A574, 1987. 6) Scheller MS, et al. Anesthesiology 67:507, 1987.

Table. MAP $PaCO_2$ and CBV: ISOFLURANE vs HALOTHANE

	Isoflurane (n=10)	Halothane (n=10)	P value
MAP (mmHg)	104 ± 14	108 ± 11	0.54
$PaCO_2$ (mmHg)	38 ± 2	37 ± 2	0.36
CBV (ml/100gm)	3.61 ± 0.52	3.67 ± 0.48	0.78

All values are mean ± SD