Title: CEREBRAL ISCHEMIC THRESHOLDS DURING HALOTHANE/N_2O AND ISOFLURANE/N_2O ANESTHESIA

Authors: Jei-Gang Zhou, Micheal M. Todd, David S. Warner

Affiliation: Departments of Anesthesia and Surgery (Neurosurgery), University of Iowa College of Medicine, Iowa City, Iowa 52242

Introduction. Messick et al. have reported that patients undergoing carotid endarterectomy who were anesthetized with isoflurane (Isof)/N_2O had a lower "critical cerebral blood flow" (i.e. CBF below which EEG evidence of ischemia appears) than patients breathing halothane (Halo)/N_2O(1). Also, Michenfelder et al. showed a lower incidence of EEG changes during carotid occlusion with Isof/N_2O vs Halo/N_2O(2). However, both studies were clinical and retrospective. To better examine this question, we determined CBF values associated with EEG-demonstrated cerebral ischemia in rats anesthetized with these two volatile agents (VA) in the presence of N_2O.

Method. Fasted Spraque-Dawley rats were initially anesthetized with Halo or Isof, tracheostomized, and ventilated to normocarbia with ≈1 MAC concentrations of the agent (in 70% N_2O) during the placement of arterial(2) and venous(1) catheters. Both carotid arteries were exposed in the neck, and a silk tie passed loosely around each. The animals were turned prone, their heads fixed into a stereotactic frame, and the skull exposed. Four screw electrodes were placed into the skull (2 frontal, 2 occipital, one pair over each hemisphere) and connected to a Grass recorder [to provide a paper record of the raw EEG trace] and to a Tracor Northern Nomad [to permit real-time display of a color density spectral array (CDSA) and 3 derived parameters: total power (TP), spectral edge frequency (SEF), and the ratio of power in the 1-6Hz band to that in the 8-26Hz band (PBR). Two small burr holes were then drilled (3mm lateral and posterior to the bregma) to allow placement of two 250μm diameter platinum needles, that were used to measure left (L) and right (R) hemispheric cortical CBF (H_2 clearance). Mixed expired VA concentrations were reduced to 0.7 MAC (N_2O unchanged) and the animals rested for 30 min. One of the arterial catheters was connected to a pressure controlled reservoir partially filled with blood. The animal was then heparinized, and the reservoir used to adjust mean arterial pressure (MAP) to ≈100mmHg. When stable, normocarbia (PaCO2≈40), normoxia, and normothermia were verified, and "Baseline" CBF and EEG recorded. The L carotid artery was then occluded, and the EEG observed for 5 min. If assymetry appeared in either the raw trace, CDSA, TP, SEF, or PBR, the animal was discarded. If not, CBF was again recorded ("occluded"), and the animals then entered into one of 2 groups. In Grp 1, MAP was reduced (by adjusting the pressure in the reservoir) over ≈10 min to 60 mmHg and held there while EEG and CBF were recorded ("low BP"). In Grp 2, MAP was gradually reduced until any of the 5 EEG parameters became assymetric, at which point CBF was measured. CBF data were examined by a 3-way ANOVA and a Neuman-Keuls test. In Grp 1, the incidence of EEG ischemia was assessed by Chi-Square.

Results. In Grp 1, only 1/9 animals breathing Isof/N_2O developed EEG evidence of ischemia, compared with 8/10 animals in the Halo/N_2O group (p=0.011). However, while there were L-R differences in CBF at the time of ischemic change, the observed CBF differences between anesthetics at 60 mmHg did not achieve significance (Table 1). In Grp 2, Isof/N_2O animals first developed ischemic EEG changes at a MAP = 46 ± 10 mmHg, compared with 64 ± 4 mmHg in the Halo/N_2O group (p=0.0014). However, there were no anesthetic differences between L-sided CBF values at the time of ischemia (Table 2).

Discussion. There were clear differences between Halo/N_2O and Isof/N_2O anesthesia. At a MAP = 60 mmHg (Grp 1), 80% of Halo/N_2O animals developed ischemic EEG changes, compared with only 11% of Isof/N_2O rats. In the threshold study (Grp 2), Halo/N_2O animals developed EEG changes at a significantly higher MAP than with Isof/N_2O. However, these differences were not reflected by CBF, with the "critical CBF" being identical for the two agents. These results suggest that differences in the effects of Halo/N_2O and Isof/N_2O on autoregulatory limits may be the most important factor in determining ischemic thresholds(3).

References. (1) Messick et al. Anesthesiology 66:344-9, 1987. (2) Michenfelder JD et al. Anesthesiology 67:336-40, 1987. (3) Todd MM, Drummond JC. Anesthesiology 60:276-82, 1984.

Table 1. Group 1

Anesthetic	Side	"Baseline"	"Occluded"	"Low BP"
Isof/N_2O	R	81 ± 21	87 ± 19	61 ± 23
	L	74 ± 16	61 ± 16*	36 ± 17*
Halo/N_2O	R	66 ± 16	70 ± 23	47 ± 3
	L	73 ± 19	47 ± 16*	24 ± 11*

Table 2. Group 2

Anesthetic	Side	"Baseline"	"Occluded"	"Low BP"
Isof/N_2O	R	84 ± 43	73 ± 12	45 ± 10
	L	88 ± 18	58 ± 10*	24 ± 7*
Halo/N_2O	R	94 ± 32	76 ± 22	41 ± 15
	L	92 ± 40	64 ± 35*	28 ± 15*

Legend. CBF values (ml/100gm/min, mean±SD) for the two groups. L and R refer to hemispheres. * = significant differences between L and R. There were no anesthetic related CBF differences (either group).