EXPERIMENTAL CIRCULATION IV — CEREBRAL CIRCULATION

A541

TITLE: HALOTHANE EXHIBITS AGONIST SPECIFICITY IN ATTENUATING CANINE CEREBRAL ARTERY CONTRACTIONS

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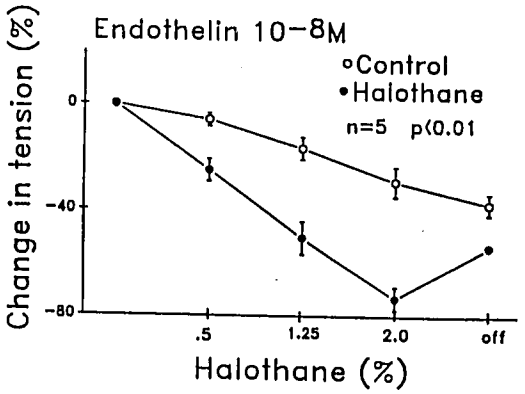
The effects of anesthetics on contractile responses of conductance arteries supplying vital organs is of clinical importance. Halothane has been shown to attenuate contractions of coronary arteries from a number of species including humans. The current study was performed to determine if halothane also inhibited contractions of cerebral arteries from dogs.

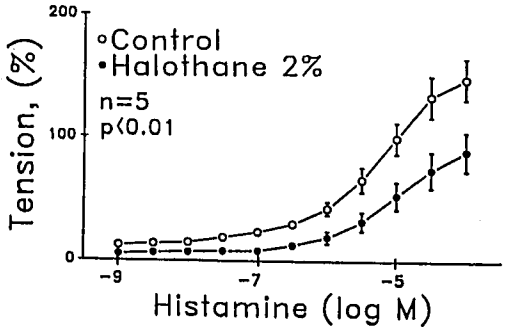
Isometric tension was measured in rings (with and without endothelium) cut from the middle cerebral arteries obtained from the brains of 36 dogs and suspended in organ chambers in the presence and absence of halothane (0.5 to 2.0%). They were stimulated with either K^+, endothelin, histamine, prostaglandin U46619, serotonin or the phorbol ester PDBU-agonists that activate contractions by a range of cellular mechanisms.

Results indicated that halothane inhibited contractions evoked by the Ca^{2+} mobilizing agonists endothelin, histamine, U46619 and serotonin. Effects were more marked in the absence of endothelium. Halothane had no effect on K^+ (voltage operated Ca^{2+} influx) or PDBU (protein kinase C activation) evoked contractions.

In conclusion, halothane attenuated canine cerebral artery contractions and exhibited agonist specificity with a more pronounced effect on receptor activated contractions.



Effects of halothane on sustained contractions evoked by endothelin (vessels without endothelium).



Effects of halothane on contractions evoked by increasing doses of histamine (vessels without endothelium).

A542

TITLE: Cerebral microvascular effects of fentanyl, sufentanil, and alfentanil in piglets.

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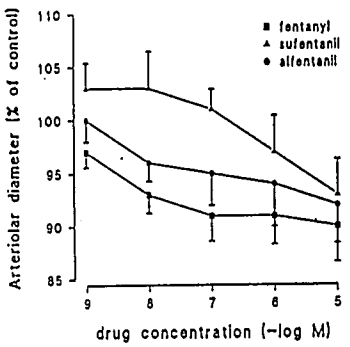
Despite having similar molecular structures, fentanyl, sufentanil, and alfentanil appear to have different effects on cerebral vasculature. Studies[1,2] have shown that fentanyl decreases or does not change cerebral blood flow (CBF), while sufentanil and alfentanil may increase or decrease CBF. Interpretation of these studies, however, is confounded by methodological differences. Our study aimed to determine the effect of fentanyl, sufentanil, and alfentanil on cerebral microvasculature in situ in piglets.
Methods: In 11 halothane anesthetized piglets aged 3-6 days a closed cranial window[3] was placed over the parietal lobe. Pial arteriolar luminal diameter was measured by intravital microscopy. After preparation, halothane was equilibrated to 0.5-0.7%. Dose response curves to fentanyl, sufentanil, and alfentanil were carried out as follows. Artificial cerebrospinal fluid (CSF) was suffused over the cortical surface, and vessel diameter was measured (control). Increasing concentrations of opiate (10^{-5} to 10^{-9} M in CSF) were similarly suffused and arteriolar diameter measured. Values are mean ± SEM. Data was analyzed by ANOVA. Significance is $P < 0.05$.
Results: Mean arterial blood pressure (61 ± 3 mmHg), pH (7.41 ± .02), pCO_2 (40 ± 1 torr) and pO_2 (117 ± 7 torr) were constant during the dose-response studies. As concentration increased from 10^{-9}M to 10^{-5}M, both fentanyl and alfentanil significantly decreased arteriolar diameter (Figure). Sufentanil increased arteriolar diameter between 10^{-9} and 10^{-7}M, but at ≥ 10^{-6}M, diameter significantly decreased. The maximum constrictions for fentanyl, alfentanil, and sufentanil were similar. The dose response was blocked by 10^{-5}M naloxone.
Conclusions: Pial arterioles are important cerebral vascular resistance (CVR) vessels. Our results suggest that fentanyl and alfentanil decrease CBF by increasing CVR, while sufentanil may either increase or decrease CBF depending on dosage. At clinically relevant drug concentrations (10^{-8} - 10^{-9}M), though, fentanyl may be preferable to sufentanil and alfentanil as arteriolar diameter is the smallest among the three.
References: 1. Anesthesiology 66:524, 1987. 2. Anesth & Analg 70:138, 1990. 3. Circ. Res. 62:1019, 1988.



Effect of fentanyl, sufentanil, and alfentanil on a cerebral arteriolar diameter. Control diameter=122 ± 7 um