TITLE: ISOFLURANE AND HALOTHANE AND RESPONSES OF CULTURED PIG CORONARY ARTERY ENDOTHELIAL CELLS

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The vascular endothelium has a major role in regulating coronary artery tone. It does so by synthesizing and releasing relaxing and contracting factors, including endothelium-dependent relaxing factor and endothelin. Their formation is induced by agonists and is associated with cellular second messengers and Ca^{2+} entry. In this study cultured porcine endothelial cells were used to ask: do isoflurane and halothane (a) affect cytosolic Ca^{2+} and agonist-induced changes in Ca^{2+} measured using the fluorescent indicator Indo-1?, (b) affect inositol phosphate formation (inositol phosphates are cell second messengers).

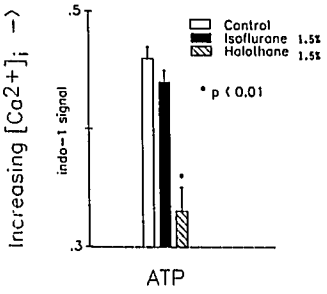
Pig coronary artery endothelial cells were cultured and studied in the presence and absence of either isoflurane or halothane (1.5%) using two protocols: (a) cells were loaded with Indo-1/AM. Cytosolic Ca^{2+} responses to the anesthetics alone and to the anesthetics plus ATP 10^{-4}M were measured in individual cells at 300-600 cells.sec^{-1} using a flow cytometer; (b) cells were labeled with ^{3}H-inositol and inositol phosphate formation evoked by angiotensin II 10^{-6}M measured using resin columns and a scintillation counter.

Preincubation with halothane for 20 minutes minimally depressed cytosolic Ca^{2+} (signal ratio 153±1 before versus 146±1 after halothane, $p<0.05$). Halothane attenuated increase in cytosolic Ca^{2+} evoked by ATP. Isoflurane had no effect. Inositol phosphate formation increased with isoflurane.

In this experiment halothane inhibited increase in cytosolic Ca^{2+} while isoflurane had a minimal effect. These preliminary results suggest that in cultured pig endothelial cells the anesthetics may differ in their effects on inositol lipid hydrolysis.

Inositol phosphates . counts.min^{-1} x10^{3}

angio II	angio II + hal	angio II + iso
26±4	27±5	33±5



TITLE: PROLONGATION OF PERMISSIBLE HYPOTHERMIC CIRCULATORY ARREST TIME IN DOGS.

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Profound hypothermic circulatory arrest (PHCA) is commonly employed during complex intracardiac repairs and for aortic arch replacements. Despite accumulating clinical experience, the safe duration of PHCA is still controversial and circulatory arrest (CA) periods exceeding 60 minutes are known to threaten central nervous system (CNS) integrity. Since complex procedures may require longer CA duration, a study was undertaken to explore the feasibility of extending the safe duration of CA by means of two periods of PHCA separated by a period of reperfusion.

Fourteen mongrel dogs (15-25Kg) were anesthetized, mechanically ventilated with 50% oxygen in air and cooled to 10°C on cardiopulmonary bypass (CPB) with their head packed in ice bags. Two groups of animals were studied. Ten dogs underwent two 45 minute periods of CA separated by 15 minutes of reperfusion at 10°C (total 105 minutes). Four control dogs were maintained at 10°c on CPB for 105 minutes. Thereafter, both animal groups were rewarmed to 33°C and weaned from CPB and mechanical ventilation. On the seventh PO day, all animals were anesthetized and underwent in situ perfusion fixation of the brain with intraaortic infusion of paraformaldehyde. Following hematoxylin and eosin staining, an average of 32 sections per brain of the cerebrum, cerebellum and brain stem were analyzed by one neuropathologist in "blinded" fashion.

All animals survived. On the first postoperative (PO) day, animals of both groups were awake, could stand, drink and feed. None manifested any overt neurologic deficit during the first PO week. There was no discernible neuropathological difference between experimental and control brains. Histology was remarkably normal in both groups with only scattered dark neurons, presumably artifactual, seen in the hippocampus and cortex but not in other areas.

Despite anedoctal clinical reports, no formal investigation has been conducted to study the effects of two separate periods of PHCA. This study, in which no overt neurologic dysfunction or abnormal brain histology were observed after 90 minutes of CA separated by 15 minutes of reperfusion, suggests the clinical feasibility of this approach in extending the permissible period of PHCA.

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