Title: HEPATIC OXYGEN SUPPLY DURING HALOTHANE OR ISOFLURANE ANESTHESIA IN GUINEA PIGS

Authors: S. Gelman, M.D., Ph.D., and D. Hursh, M.D.,

Affiliation: Department of Anesthesiology, The University of Alabama at Birmingham, Birmingham, AL 35294

**Introduction:** It has been suggested that similar changes in mean arterial pressure (MAP) and oxygen content in arterial blood during halothane or isoflurane anesthesia in guinea pigs are accompanied by similar changes in hepatic oxygen supply.[1] This study was designed to test this hypothesis. If the hypothesis is confirmed, the speculations that the differences in hepatotoxicity between halothane or isoflurane treated guinea pigs are related to metabolic biotransformation of halothane would be indirectly supported.[1] On the other hand, if the hypothesis is rejected and halothane anesthesia is accompanied by more severe hepatic oxygen deprivation than isoflurane anesthesia, then the observed hepatic injury during halothane, but not isoflurane anesthesia,[1] may be explained by the hypoxic hypothesis, namely that hepatic oxygen deprivation per se might be responsible for halothane induced hepatic damage.

**Methods:** Twenty-seven guinea pigs were randomly assigned to three equal groups: a control group, and animals anesthetized with halothane or isoflurane to decrease MAP by 50%. The control group was exposed to 40% oxygen in nitrogen without endotracheal intubation for one hour. Halothane or isoflurane was administered in 40% oxygen in nitrogen via an endotracheal tube, also for one hour. Surgical preparation performed under isoflurane anesthesia in a chamber and then via a mask consisted of cannulation of the left ventricle via the left carotid artery and the distal aorta via the femoral artery. Then, a laparotomy was performed and a 20 gauge catheter was placed into the portal vein. All incisions were closed. The catheters were externalized and fixed. After complete recovery from anesthesia, arterial and portal venous blood samples were obtained for measurements of pH, gas tensions, and oxygen content. Approximately 150,000-200,000 15 μm spheres labeled with $^{95}Nb$ or $^{113}Sn$ were injected into the left ventricle (Stage I, awake state). Later, hepatic arterial blood flow (HABF) and portal blood flow (PBF) were calculated. A second set of microspheres was injected during anesthesia with halothane or isoflurane (titrated to decrease MAP by 50%) and again, a second time, during the awake state in the control group. Hepatic oxygen delivery ($HDO_2$) was calculated using values of arterial and portal venous blood oxygen content, HABF, and PBF.

**Results:** (Table) Concentrations of 0.95 ± 0.11% inspired halothane and 1.22 ± 0.17% inspired isoflurane were needed to produce a 50% decrease in MAP. During control observations, HABF was found to be extremely low (0.04 $ml \cdot min^{-1} \cdot g^{-1}$) and represented approximately only 2% of total hepatic blood flow (THBF) while in other species it represents 20-30% of THBF.[2] Equal degrees of arterial hypotension during halothane and isoflurane anesthesia were accompanied by a decrease in HABF during halothane, but not during isoflurane anesthesia. PBF decreased in both groups of observations; however, the decrease was more prominent during halothane than during isoflurane anesthesia. These observations resulted in a 65% reduction in hepatic oxygen supply during halothane and only a 34% decrease in hepatic oxygen supply during isoflurane anesthesia.

**Discussion:** Since HABF is unusually low in guniea pigs, it appears that the guinea pig model may be suitable for studying some hypoxic mechanisms of liver injury, but it does not seem to be suitable for examining hepatic circulatory responses to anesthetics or other insults.

The posed hypothesis is rejected: similar degrees of halothane- or isoflurane-induced arterial hypotension are associated with different degrees of hepatic oxygen deprivation ($HDO_2$ was much lower during halothane than isoflurane anesthesia). The significant reduction in both HABF and PBF during halothane anesthesia may be responsible for the hepatic injury observed in the guinea pig model.

**Table**

Hepatic Oxygen Delivery in Guinea Pigs Anesthetized with Halothane and Isoflurane Expressed as Percent of Baseline (Awake) Values

| Variable | Control (No Anesthesia) | Halothane | Isoflurane |
|---|---|---|---|
| MAP | 94.4±2.06 | 53.4±2.31* | 51.3±2.09* |
| CO | 91.1±3.81 | 48.4±6.59* | 78.3±5.90*+ |
| HABF | 109.5±21.16 | 63.0±4.28* | 93.8±5.74+ |
| PBF | 94.2±2.51 | 42.8±4.00* | 77.3±2.48*+ |
| $HDO_2$ | 90.7±2.71 | 35.1±3.01* | 65.8±3.45*+ |

Mean ± SE. MAP = mean arterial pressure (mmHg); CO = cardiac output ($ml \cdot min^{-1}$); HABF, PBF = hepatic arterial blood flow, portal blood flow, respectively ($ml \cdot min^{-1} \cdot g^{-1}$); $HDO_2$ = hepatic oxygen delivery ($ml\ O_2 \cdot min^{-1} \cdot g^{-1}$). * $p < 0.05$ versus control; + $p < 0.05$ vs halothane.

**References:**

1. Lunam CA, Cousins MJ, Hall P: Guinea pig model of halothane associated hepatotoxicity in the absence of enzyme induction and hypoxia. J Pharmacol Exp Ther 232:802-809, 1985
2. Richardson PDI, Withrington PG: Liver blood flow. I. Intrinsic and nervous control of liver blood flow. Gastroenterology 81:159-173, 1981