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The Effects of Sevoflurane, Halothane, Enflurane, and Isoflurane on Hepatic Blood Flow and Oxygenation in Chronically Instrumented Greyhound Dogs

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Inhalational anesthetics produce differential effects on hepatic blood flow and oxygenation that may impact hepatocellular function and drug clearance. In this investigation, the effects of sevoflurane on hepatic blood flow and oxygenation were compared with those of enflurane, halothane, and isoflurane in ten chronically instrumented greyhound dogs. Each dog randomly received enflurane, halothane, isoflurane, and sevoflurane, each at 1.0, 1.5, and 2.0 MAC concentrations. Mean arterial blood pressure and cardiac output decreased in a dose-dependent fashion during all four anesthetics studied. Heart rate increased compared to control during enflurane, isoflurane, and sevoflurane anesthesia and did not change during halothane anesthesia. Hepatic arterial blood flow and portal venous blood flow were measured by chronically implanted electromagnetic flow probes. Hepatic O_2 delivery and consumption were calculated after hepatic arterial, portal venous, and hepatic venous blood gas analysis. Hepatic arterial blood flow was maintained with sevoflurane and isoflurane. Halothane and enflurane reduced hepatic arterial blood flow during all anesthetic levels compared to control ($P < 0.05$), with marked reductions occurring with 1.5 and 2.0 MAC halothane concomitant with an increase in hepatic arterial vascular resistance. Portal venous blood flow was reduced with isoflurane and sevoflurane at 1.5 and 2.0 MAC. A somewhat greater reduction in portal venous blood flow occurred during 2.0 MAC sevoflurane ($P < 0.05$ compared to control and 1.0 MAC values for sevoflurane). Enflurane reduced portal venous blood flow at 1.0, 1.5, and 2.0 MAC compared to control. Halothane produced the greatest reduction in portal venous blood flow ($P < 0.05$ compared to sevoflurane). Hepatic O_2 delivery during 1.5 and 2.0 MAC halothane exposure was reduced compared to results obtained with sevoflurane and isoflurane ($P < 0.05$). Hepatic O_2 extraction showed no significant increase at any anesthetic MAC level other than 2.0 MAC for halothane and sevoflurane. Increases in O_2 extraction were due to large reductions in O_2 delivery with halothane and a moderate reduction in O_2 delivery with sevoflurane not accompanied by a further reduction in O_2 consumption. The authors conclude that sevoflurane at concentrations less than 2.0 MAC preserves hepatic arterial blood flow, total hepatic O_2 delivery, and the O_2 delivery-to-consumption ratio. Halothane produces the greatest reductions in hepatic arterial and portal venous blood flow. (Key words: Anesthetics, volatile: sevoflurane; halothane; enflurane, isoflurane. Liver: blood flow; oxygen consumption. Arteries: hepatic. Veins: portal.)

SEVOFLURANE is a halogenated volatile anesthetic that is nonpungent and possesses a low blood–gas solubility coefficient, providing rapid induction and emergence[1,2] compared to that of other currently used inhalation anesthetic agents. Sevoflurane is currently undergoing clinical evaluation in the United States and is approved for clinical use in Japan. The cardiovascular effects of sevoflurane appear to be comparable to those of isoflurane[3,**]; however, the effect of this agent on hepatic perfusion and oxygenation has not been well studied.

Alterations in hepatic blood flow and O_2 delivery may have an impact on hepatocellular damage and various liver functions, including drug metabolism. In this study we used chronically instrumented greyhound dogs to compare alterations in hepatic blood flow and oxygenation caused by halothane, enflurane, isoflurane, and sevoflurane. The use of chronically instrumented animals allows comparison of all agents in each animal and avoids changes in hepatic blood flow, which may occur with surgical trauma in more acute experimental preparations.

Materials and Methods

Ten healthy greyhound dogs (28–30 kg) were used for study after approval from the Tucson Veterans Administration Institutional Animal Care and Use Committee had been obtained.

Surgical Preparation

Following induction of anesthesia with sodium thiopental (4–6 $mg \cdot kg^{-1}$) and tracheal intubation and the establishment of maintenance anesthesia with isoflurane,

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** Kazama T, Ikeda K: The comparative cardiovascular effects of sevoflurane, halothane and isoflurane. Japanese Journal of Anesthesia 2:63–68, 1988.

a midline laparotomy was performed for insertion of chronic electromagnetic flow probes (Carolina Medical Electronics, King, NC) around the common hepatic artery (10 or 12 mm ID) and the portal vein (35 or 40 mm ID) for best fit. Care was taken during dissection to preserve surrounding neurovascular structures. Heparin-coated polyurethane catheters (89 cm length; Arrow International Inc., Reading PA) were inserted into the portal vein, abdominal aorta (*via* the femoral artery), and hepatic vein (surgically below the diaphragm) for monitoring of pressure and blood sampling. Following abdominal closure, catheters and flow probe wires were passed subcutaneously and exteriorized to the animal's back.

A 7.5-Fr pulmonary artery catheter (Baxter Healthcare Corp., Irvine, CA) was inserted *via* the right external jugular vein into the distal pulmonary artery and tunneled subcutaneously to the animal's back. All vascular catheters were protected in the pouch of a specially designed animal jacket. The electromagnetic flow probe terminals were protected with metal caps on the animal's back. During the surgical procedure lactated Ringer's solution was infused (8–10 $ml \cdot kg^{-1} \cdot h^{-1}$). Postoperative analgesia was provided during the first 24 h with fentanyl citrate infusion and subsequent use of pentazocine as required on the 2nd day of recovery. Intravenous fluids were given during the first 24 h and antibiotic prophylaxis accomplished using cefazolin sodium. Animals were allowed to recover for 5–7 days prior to experimentation. All animals were ambulatory on the 1st day after surgery and were tolerating oral intake well by the 2nd day.

Experimental Protocol

With the animals in a quiet state, control measurements were taken for body temperature, arterial pressure, heart rate, cardiac output, pulmonary capillary wedge pressure, and hepatic venous pressure. Blood samples were obtained for hematocrit and arterial, hepatic venous, and portal venous blood gas analysis (Nova Biomedical Stat Profile 3, Waltham, MA). Hepatic arterial blood flow (HABF) and portal venous blood flow (PVBF) measurements (model FM701D electromagnetic flow meter, Carolina Medical Electronics) were obtained with the animal resting quietly on its side.

After control measurements, animals received in random fashion halothane, enflurane, isoflurane, or sevoflurane each on a subsequent experimental day with 2 days allowed between investigations. Anesthesia was delivered using a semiclosed anesthetic circuit containing soda lime CO_2 absorbent. Each animal was evaluated during anesthesia with the four anesthetic agents using equivalent concentrations for 1.0, 1.5, and 2.0 MAC for each agent. For each anesthetic agent evaluated, the order of concentration was randomized during each experimental procedure.

Animals were deprived of food and water the night before each experiment. Intravenous fluids in the form of 0.9 N saline were administered as 16 $ml \cdot kg^{-1}$ prior to anesthesia and then 3 $ml \cdot kg \cdot {}^{-1}h^{-1}$ during anesthesia. After inhalation induction *via* mask using the appropriate anesthetic agent and after tracheal intubation, the lungs ventilated with 70% nitrogen (2.5 $l \cdot min^{-1}$) and 30% O_2 (750 $ml \cdot min^{-1}$) with the ventilatory rate adjusted to maintain arterial CO_2 tension at 35–40 mmHg as determined by blood gas analysis. For each anesthetic MAC level evaluated, end-tidal anesthetic concentration (Datex Puritan-Bennett Anesthetic Agent Monitor 222, Wilmington, MA) was equilibrated for 30 min before repeat experimental measurements were obtained. End-tidal sevoflurane, enflurane, halothane, and isoflurane measurements were obtained with an infrared anesthetic agent monitor (Datex) that was calibrated using the appropriate anesthetic gas standard samples (Scott Medical Products, Plumsteadville, PA). Anesthetic concentrations evaluated in each animal were as follows: halothane 0.9, 1.3, and 1.8%; enflurane 1.7, 2.5, and 3.4%; isoflurane 1.3, 1.95, and 2.6%; and sevoflurane 2.3, 3.4, and 4.6%. These percentages represent 1.0, 1.5, and 2.0 equivalent MAC value concentrations respectively for each agent.

When end-tidal anesthetic concentration had been maintained for 30 min at each MAC value, hemodynamic measurements and blood sampling were repeated using a protocol as outlined previously for control measurements. During anesthetic delivery, all measurements were recorded while the animals were positioned laterally in a manner similar to the preanesthetic period.

Calculations

Total hepatic blood flow was the sum of HABF and PVBF in $ml \cdot min^{-1} \cdot 100\ g^{-1}$. Blood O_2 content was calculated as: 1.34 × hemoglobin × O_2 saturation + 0.003 × P_{O_2}. Total hepatic O_2 delivery per 100 g liver was calculated as portal venous O_2 delivery + hepatic arterial O_2 delivery, where portal venous O_2 delivery = portal venous O_2 content × PVBF/100 g and hepatic arterial O_2 delivery = hepatic arterial O_2 content × HABF/100 g. Hepatic O_2 consumption in $ml \cdot min \cdot 100\ g^{-1}$ (HVO_2) was calculated as

([portal venous O_2 content × portal venous flow]
+ [hepatic arterial O_2 content × hepatic arterial flow]
− [hepatic venous O_2 content] × [hepatic arterial flow
+ portal venous flow)/100.

Hepatic oxygen extraction (%)

$$= \frac{\text{hepatic } O_2 \text{ consumption}}{\text{hepatic artery} + \text{portal venous } O_2 \text{ supply}} \times 100$$

The data were analyzed for comparison of values obtained for each anesthetic agent at various MAC values and for comparison between anesthetic agents at comparable MAC values. Two-way analysis of variance and Duncan multiple-range testing were used, with significance defined as $P < 0.05$. All data are expressed as mean ± standard errors of the mean.

Results

Changes in mean arterial pressure, heart rate, and cardiac output are summarized in table 1. Enflurane decreased mean arterial pressure compared to control during 1.0 MAC exposure. All four anesthetics decreased mean arterial pressure compared to control with exposure to 1.5 and 2.0 MAC concentrations. Heart rate increased compared to control during enflurane, isoflurane, and sevoflurane anesthesia. Heart rate at comparable MAC values did not differ with these three agents. Heart rate did not change compared to control during halothane anesthesia. Cardiac output decreased in a dose-dependent fashion with all anesthetic agents evaluated. Cardiac output at 2.0 MAC-equivalent exposure during halothane anesthesia was lower when compared to values obtained with isoflurane only. Enflurane produced a decreased cardiac output when compared to isoflurane during 1.5 MAC anesthetic exposure.

Hepatic blood flow and oxygenation variables during control and anesthetized conditions are summarized in tables 2, 3, and 4. HABF was maintained with sevoflurane and isoflurane at all MAC levels studied when compared to control. Enflurane and halothane caused a decrease in HABF compared to the control state. Halothane caused the greatest decrease in HABF; values obtained during 1.5 and 2.0 MAC exposure were less than those for sevoflurane or isoflurane at MAC-equivalent values (table 2). PVBF decreased with all anesthetic agents evaluated at higher MAC (1.5 and 2.0) values compared to control. Halothane decreased PVBF during 1.0 and 1.5 MAC exposure when compared to sevoflurane at equianesthetic concentrations (table 2).

Total hepatic blood flow showed a decline with increasing anesthetic concentration for all agents. Enflurane decreased total hepatic blood flow to a greater extent than did sevoflurane only at the 1.0 MAC level. Sevoflurane and isoflurane did not differ in their effect on total hepatic blood flow. Halothane, in contrast to sevoflurane and isoflurane, caused a dramatic decrease in total hepatic blood flow, particularly during 1.5 and 2.0 MAC exposure (table 2).

The observed changes in hepatic blood flow produced corresponding changes in hepatic O_2 delivery, with halothane producing the greatest reduction in O_2 delivery (tables 3 and 4).

Hepatic O_2 extraction was relatively well maintained or decreased with all anesthetic agents during 1.0 and 1.5 MAC anesthetic exposure other than enflurane, which tended to increase O_2 extraction in a dose-dependent fashion. O_2 extraction values during enflurane anesthesia were not, however, significantly different from control, due to a larger standard error. Halothane at 2.0 MAC produced an increase in O_2 extraction compared to the 1.5 MAC value, largely because of reduced O_2 delivery.

TABLE 1. Systemic Hemodynamic Variables During Control and Halothane, Enflurane, Isoflurane, and Sevoflurane, Anesthesia

Anesthetic (MAC)	Cardiac Output ($l \cdot min^{-1}$)	Mean Arterial Pressure (mmHg)	Heart Rate (beats per min)
Sevoflurane			
Control	7.4 ± 0.4	105 ± 4	84 ± 4
1.0	5.5 ± 0.2*	94.7 ± 5.3	107 ± 5*
1.5	4.8 ± 0.3*	77.2 ± 3.6*	101 ± 3*
2.0	3.9 ± 0.3*†	63.7 ± 4.2*†	96 ± 3*
Isoflurane			
Control	7.5 ± 0.4	113 ± 4	85 ± 4
1.0	5.8 ± 0.3*	96.6 ± 7.1	115 ± 7*
1.5	5.4 ± 0.3*	86.7 ± 2.9*	106 ± 4*
2.0	4.7 ± 0.4*†	75.4 ± 8.2*†	106 ± 5*
Enflurane			
Control	7.5 ± 0.5	106 ± 7	89 ± 6
1.0	4.9 ± 0.4*	89.4 ± 5.2*	107 ± 5*
1.5	4.2 ± 0.2*‡	73.2 ± 4.7*†	104 ± 6
2.0	3.8 ± 0.3*	60.0 ± 4.9*†	103 ± 3*
Halothane			
Control	7.8 ± 0.6	106 ± 7.4	84 ± 5
1.0	5.3 ± 0.5*	90.6 ± 7.5	90 ± 6
1.5	4.6 ± 0.4*	78.6 ± 6.8*	90 ± 6
2.0	3.3 ± 0.3*†‡	63.6 ± 4.0*†	92 ± 5

* Differs from control ($P < 0.05$).
† Differs from 1.0 MAC value ($P < 0.05$).
‡ Differs from isoflurane at comparable MAC values ($P < 0.05$).

TABLE 2. Liver Circulation and Hepatic Arterial Vascular Resistance during Control and Halothane, Enflurane, Isolfurane, and Sevoflurane Anesthesia

Anesthetic (MAC)	Hepatic Arterial Blood Flow (ml·min^{-1}·100 g^{-1})	Portal Venous Blood Flow (ml·min^{-1}·100 g^{-1})	Total Hepatic Blood Flow (ml·min^{-1}·100 g^{-1})	Hepatic Arterial Vascular Resistance (mmHg·min·ml^{-1})
Sevoflurane				
Control	26.3 ± 3.2	115 ± 6	141 ± 11	0.77 ± 0.12
1.0	24.5 ± 3.4	97 ± 7	122 ± 9	0.76 ± 0.11
1.5	26.1 ± 3.2	79 ± 7*	104 ± 6*	0.56 ± 0.08
2.0	24.7 ± 4.0	69 ± 3*†	92 ± 5*†	0.50 ± 0.08
Isoflurane				
Control	25.7 ± 2.4	107 ± 6	133 ± 6	0.79 ± 0.10
1.0	23.8 ± 2.3	85 ± 6	108 ± 7*	0.80 ± 0.18
1.5	21.7 ± 1.7	75 ± 4*	97 ± 5*	0.65 ± 0.08
2.0	21.0 ± 2.8	74 ± 7*	96 ± 6*	0.70 ± 0.17
Enflurane				
Control	26.4 ± 2.8	115 ± 5	142 ± 8	0.79 ± 0.17
1.0	17.2 ± 1.7*	70 ± 5*‡	86 ± 5*§	0.94 ± 0.14
1.5	16.3 ± 1.8*‡	72 ± 4*	83 ± 5*	0.85 ± 0.18
2.0	16.1 ± 2.7*	63 ± 6*	75 ± 6*§	0.78 ± 0.19
Halothane				
Control	25.0 ± 2.4	110 ± 6	134 ± 7	0.83 ± 0.18
1.0	16.8 ± 2.2*	67 ± 5*‡	84 ± 7*§	0.97 ± 0.12
1.5	13.1 ± 0.6*§	62 ± 4*‡	75 ± 4*§	0.97 ± 0.07‡
2.0	9.9 ± 1.1*§	49 ± 4*§	59 ± 4*§	1.08 ± 0.12‡

* Differs from control ($P < 0.05$).
† Differs from 1.0 MAC value ($P < 0.05$).
‡ Differs from sevoflurane at comparable MAC values ($P < 0.05$).
§ Differs from isoflurane and sevoflurane at comparable MAC values ($P < 0.05$).

Halothane produced the greatest reduction in hepatic O_2 consumption compared to control values of the four agents evaluated. During 2.0 MAC exposure, sevoflurane increased O_2 extraction, which differed from O_2 extraction values at 1.0 MAC but not control. This appeared to be due to further-reduced O_2 delivery (largely due to reduced PVBF) that was not balanced by a concomitant reduction in O_2 demand.

TABLE 3. Hepatic Vascular Oxygen Content, Hepatic Arterial and Portal Venous Oxygen Delivery during Control and Halothane, Enflurane, Isoflurane, and Sevoflurane Anesthesia

Anesthetic (MAC)	Hepatic Arterial O_2 Content (ml/100 ml)	Hepatic Vein O_2 Content (ml/100 ml)	Portal Vein O_2 Content (ml/100 ml)	Hepatic Arterial O_2 Delivery (ml·min^{-1}·100 g^{-1})	Portal Venous O_2 Delivery (ml·min^{-1}·100 g^{-1})
Sevoflurane					
Control	19.91 ± 0.73	14.25 ± 0.70	16.92 ± 0.65	5.32 ± 0.12	19.3 ± 0.3
1.0	18.28 ± 0.75	13.17 ± 0.92	15.93 ± 0.79	4.53 ± 0.12	15.5 ± 0.2
1.5	18.22 ± 0.81	12.92 ± 0.75	15.77 ± 0.89	4.68 ± 0.12	12.3 ± 0.1
2.0	18.44 ± 0.60	12.17 ± 0.98	15.31 ± 0.88	3.88 ± 0.13	11.3 ± 0.1
Isoflurane					
Control	20.93 ± 0.50	15.90 ± 1.10	18.56 ± 0.57	5.43 ± 0.80	19.9 ± 1.3
1.0	19.27 ± 0.68	14.54 ± 0.57	16.76 ± 0.76	4.50 ± 0.37	13.9 ± 0.9*
1.5	18.65 ± 0.93	13.79 ± 0.91	16.70 ± 1.00	3.99 ± 0.29	12.5 ± 0.9*
2.0	18.60 ± 1.06	13.96 ± 0.98	16.59 ± 1.31	4.12 ± 0.55	12.2 ± 1.3*
Enflurane					
Control	20.81 ± 0.41	15.15 ± 1.17	18.19 ± 0.58	5.39 ± 0.96	20.4 ± 1.4
1.0	18.19 ± 0.73	13.59 ± 0.88	15.84 ± 0.93	3.09 ± 0.35*	10.4 ± 0.9*
1.5	18.79 ± 0.75	14.04 ± 0.73	16.27 ± 0.85	2.62 ± 0.31*†	11.2 ± 0.5*
2.0	18.55 ± 1.06	14.79 ± 1.53	16.00 ± 1.45	2.43 ± 0.70*†	10.2 ± 1.1*
Halothane					
Control	20.51 ± 0.42	14.55 ± 0.86	18.01 ± 0.58	4.98 ± 0.65	20.2 ± 1.6
1.0	18.21 ± 0.89	13.00 ± 1.06	15.78 ± 1.14	3.11 ± 0.54*‡	10.4 ± 1.2*
1.5	18.21 ± 0.77	13.25 ± 1.07	16.20 ± 0.96	2.49 ± 0.24*§	9.8 ± 0.6*
2.0	18.31 ± 1.06	11.49 ± 1.17	15.28 ± 1.64	1.64 ± 0.11*§	8.0 ± 1.7*

* Differs from control ($P < 0.05$).
† Differs from sevoflurane at comparable MAC values ($P < 0.05$).
‡ Differs from 2.0 MAC value ($P < 0.05$).
§ Differs from isoflurane and sevoflurane at comparable MAC values ($P < 0.05$).

TABLE 4. Hepatic Oxygen Delivery, Consumption, and Extraction during Control and Halothane, Enflurane, Isoflurane, and Sevoflurane Anesthesia

Anesthetic (MAC)	Total Hepatic O_2 Delivery ($ml \cdot min^{-1} \cdot 100\ g^{-1}$)	Total Hepatic O_2 Consumption ($ml \cdot min^{-1} \cdot 100\ g^{-1}$)	O_2 Extraction (%)
Sevoflurane			
Control	38.0 ± 2.3	7.09 ± 0.59	19.22 ± 1.10
1.0	32.7 ± 2.1	5.04 ± 0.57*	17.23 ± 1.97
1.5	29.4 ± 2.4*	6.19 ± 1.04	23.78 ± 2.61
2.0	26.8 ± 1.9*	6.10 ± 0.56	27.96 ± 1.93*†
Isoflurane			
Control	37.5 ± 4.0	6.59 ± 1.20	21.79 ± 3.45
1.0	30.2 ± 1.9	5.46 ± 0.92	18.07 ± 2.20
1.5	27.8 ± 2.1*	5.25 ± 0.59	19.78 ± 1.85
2.0	27.7 ± 3.7	5.09 ± 0.46	23.96 ± 3.24
Enflurane			
Control	45.5 ± 7.1	9.04 ± 0.86	19.98 ± 0.72
1.0	26.1 ± 4.2*	7.05 ± 0.74	27.03 ± 3.39
1.5	24.6 ± 1.8*	7.28 ± 0.68	28.42 ± 2.86
2.0	21.1 ± 3.6*	5.89 ± 0.98	31.09 ± 7.52
Halothane			
Control	42.6 ± 3.0	8.60 ± 1.53	22.54 ± 2.35
1.0	24.4 ± 2.2*	3.73 ± 0.28*	20.13 ± 2.19
1.5	25.4 ± 1.4*	3.20 ± 0.33*	16.80 ± 1.33
2.0	18.6 ± 3.2*	4.15 ± 0.65*	27.10 ± 1.82‡

* Differs from control ($P < 0.05$).
† Differs from 1.0 MAC value ($P < 0.05$).
‡ Differs from 1.5 MAC value ($P < 0.05$).

The hepatic arterial vascular resistance at 1.5 and 2.0 MAC concentration of halothane were greater than corresponding values for sevoflurane (table 2) ($P < 0.05$).

Discussion

The results of this investigation indicate that sevoflurane produces only moderate changes in hepatic perfusion, particularly during exposure to concentrations less than 2.0 MAC, and that these changes are similar to those produced during isoflurane anesthesia.

In our investigation, several features of study design were important. First, a single breed of dog was used, and each animal was evaluated during all four anesthetic agents. Second, we studied anesthetic effects on hepatic perfusion in chronically instrumented animals. This should allow evaluation of anesthetic influence devoid of changes in hepatic blood flow that can occur with surgical trauma.[4] In addition, awake control measurements were possible without necessity for "barbiturate" control, as has been used in two previous investigations.[5,6]

The results of our study are similar in several respects to those obtained in other investigations. Yu *et al.*†† compared sevoflurane and halothane effects on hepatic circulation in conjunction with hepatic lobectomy. They found that hepatic blood flow, particularly HABF, was better maintained during sevoflurane than during halothane. Another investigation using chronically instrumented dogs[7] showed that sevoflurane increased HABF compared to the awake state.

Isoflurane in several investigations has been associated with good maintenance of HABF.[8,9] Our investigation produced comparable results. Two previous investigations[10,11] have suggested that isoflurane may actually increase HABF. Reasons for these differing results are unclear. Radioactive labeled microspheres were used to measure blood flows in the studies showing increased HABF with isoflurane, whereas our study used electromagnetic flow probes. The study in dogs by Gelman *et al.*[10] allowed 1 week for recovery; however, a laparotomy was not performed during their investigation. Our recovery time after surgery prior to investigation was 5–7 days. It is unclear what recovery time in these animals may be required to prevent any influence of the previous surgical procedure on hepatic perfusion. However, the order of anesthetic to which each animal was exposed was randomized in our investigation, and each animal was evaluated under the influence of all four agents. Therefore, results obtained in this study for comparison between agents should accurately reflect differential effects.

Hepatic blood flow decreases with the institution of positive pressure ventilation. During control measurements, the dogs breathed spontaneously whereas during the anesthetized condition, controlled ventilation was maintained, which may have produced a percentage of the reductions in hepatic blood flow observed during anesthetized states compared to control.

Hepatic O_2 extraction neither changed significantly nor decreased except during exposure to 2.0 MAC sevoflurane and halothane. Halothane produced an increase in O_2 extraction due to a dramatic decline in total hepatic O_2 delivery. Sevoflurane reduced O_2 delivery at 2.0 MAC; this reduction was not counterbalanced by a further reduction in O_2 consumption. The explanation for this result with sevoflurane is at present unclear. In the study by Yu *et al.*,†† hepatic O_2 consumption during sevoflurane and halothane anesthesia was evaluated. They found no difference in O_2 consumption between agents. However, a single anesthetic level (1.5 MAC) was evaluated for each agent, and thus their data does not differ from our results: our reduction in O_2 delivery-to-consumption ratio occurred only with the highest concentration (2.0 MAC) of sevoflurane exposure.

Halothane decreased total hepatic flow, and particularly HABF, to a greater extent than did the other inhalational agents. Halothane reduced HABF with an increase in HAVR that has been noted in previous investigations.[5,10]

†† Yu B, Miyazaki T, Matsumato N, Hori T: Effects of sevoflurane vs halothane anesthesia combined with hepatolobectomy on liver circulation and oxygen metabolism in the dog. Hiroshima Journal of Anesthesia 25:85–89, 1989.

Normally, a decrease in PVBF is reciprocally compensated by an increase in HABF both in animals[12,13] and in humans.[14] This mechanism appears to be relatively well preserved with isoflurane and altered to the greatest extent with halothane anesthesia.[10]

In summary, our results suggest that sevoflurane is capable of maintaining hepatic blood flow (particularly HABF) and O_2 delivery; these effects are comparable to those produced by isoflurane with 1.0 and 1.5 MAC anesthesia. Halothane produces more marked reductions than enflurane, isoflurane or sevoflurane in total hepatic blood flow, largely because of dramatic decreases in HABF.

References

1. Holaday DA, Smith FR: Clinical characteristics and biotransformation of sevoflurane in healthy human volunteers. ANESTHESIOLOGY 54:100–106, 1981
2. Manohar M, Parks CM: Porcine systemic regional organ blood flow during 1.0 and 1.5 minimum areolar concentrations of sevoflurane anesthesia without and with 50% nitrous oxide. J Pharmacol Exp Ther 231:640–648, 1984
3. Bernard J, Wouters PF, Doursont M, Florence B, Chelly, JE, Merin, RG: Effects of sevoflurane and isoflurane on cardiac and coronary dynamics in chronically instrumented dogs. ANESTHESIOLOGY 72:659–662, 1990
4. Gelman SI: Disturbances in hepatic blood flow during anesthesia and surgery. Arch Surg 111:881–883, 1976
5. Hughes RL, Campbell D, Fitch W: Effects of enflurane and halothane on liver blood flow and oxygen consumption in the greyhound. Br J Anaesth 52:1079–1086, 1980
6. Gelman S, Dillard E, Bradley EL: Hepatic circulation during surgical stress and anesthesia with halothane, isoflurane or fentanyl. Anesth Analg 66:936–943, 1987
7. Wouters P, Doursont M, Kashimoto S, Lawrence C, Merin RG, Chelly JE: Sevoflurane preserved hepatic arterial blood flow in dogs (abstract). ANESTHESIOLOGY 71:A306, 1989
8. Conzen PF, Hobbhahn J, Goetz AE, Habazettl H, Granetzny T, Peter K, Brendel W: Splanchnic oxygen consumption and hepatic surface oxygen tensions during isoflurane anesthesia. ANESTHESIOLOGY 69:643–651, 1988
9. Lundeen G, Manohar M, Parks C: Systemic distribution of blood flow in swine while awake and during 1.0 and 1.5 MAC anesthesia with or without 50% nitrous oxide. Anesth Analg 62: 499–512, 1983
10. Gelman S, Fowler KC, Smith LR: Liver circulation and function during isoflurane and halothane anesthesia. ANESTHESIOLOGY 61:726–730, 1984
11. Matsumoto H, Mizukami S, Hagaska H, Aikawa K, Hori T: Effects of isoflurane on hepatic circulation and oxygen metabolism in dogs under hypoxia (abstract). Anesth Analg 68:S321, 1989
12. Lautt WW, Legare DJ: The use of 8-phenyltheophylline as a competitive antagonist of adenosine and an inhibitor of the intrinsic regulatory mechanism of the hepatic artery. Can J Physiol Pharmacol 63:717–721, 1985
13. Lautt WW, Greenway CV: Conceptual review of the hepatic vascular bed. Hepatology 5:952–963, 1987
14. Doi R, Inoue K, Kogire M, Sumi S, Takori K, Suzuki T, Tobe T: Simultaneous measurement of hepatic arterial and portal venous flows by transit time ultrasonic volume flowmetry. Surg Gynecol Obstet 167:65–69, 1988