

The Cerebral and Systemic Hemodynamic and Metabolic Effects of Desflurane-induced Hypotension in Dogs

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The cerebral and systemic hemodynamic and metabolic effects of hypotension induced with desflurane were examined in 11 dogs. During a steady-state baseline period under 1 MAC desflurane (7.2%), the following were measured or derived: arterial, pulmonary artery, and pulmonary artery occlusion pressures; arterial, mixed venous, and sagittal sinus blood gases; cardiac index and cerebral blood flow (CBF); whole-body and cerebral O₂ consumption; systemic and cerebral vascular resistance; intracranial pressure; and blood glucose and lactate concentrations. After the baseline period, hypotension to a mean arterial pressure (MAP) of 50 mmHg was produced by 15.5% (2.2 MAC), and hypotension to an MAP of 40 mmHg was produced by 17.1% (2.4 MAC) for 1 h. During this hypotensive period all measurements were taken at 5- or 15-min intervals. At the end of the hypotensive period, brain biopsy specimens were taken for measurement of cerebral concentrations of ATP, phosphocreatine, and lactate to determine whether there was any metabolic evidence of cerebral ischemia. Desflurane-induced hypotension produced a significant, 40-50% decrease in cardiac index with a significant change in systemic vascular resistance at the lower blood pressure, but produced little change in heart rate. Even though whole-body O₂ consumption did not decrease, adequate peripheral perfusion was maintained with the lower cardiac output, as evidenced by lack of accumulation of blood lactate. Induced hypotension caused a significant, 50 (at MAP = 50 mmHg) to 64% (at MAP = 40 mmHg) decrease in cerebral perfusion pressure, accompanied by a significant, 36 (at MAP = 50 mmHg) to 60% (at MAP = 40 mmHg) decrease in CBF. The concentration of desflurane necessary to produce these levels of hypotension significantly decreased cerebral O₂ consumption (CMR_{O₂}) 19-21%, to 2.7-2.5 ml · min⁻¹ · 100 g⁻¹. The cerebral metabolite concentrations of high-energy phosphates taken at the end of the hypotensive period were within the range of normal canine values for our laboratory, although there was a moderate increase in lactate concentration. This indicates that the CBF, though decreased, was able to provide adequate cerebral perfusion to meet the demands of CMR_{O₂}, even during the period of profound hypotension. (Key words: Anesthetic technique: hypotension, induced. Anesthetics, volatile: desflurane. Blood pressure: drug effects. Brain: blood flow; electroencephalography; intracranial pressure; metabolism; oxygen consumption. Heart: cardiac output. Metabolism: ATP; lactate; metabolites; oxygen consumption; phosphocreatine.)

THE CHARACTERISTICS OF AN IDEAL hypotensive agent include ease of administration, known predictability, efficacy, and reliability; a rapid onset of action and rapid elimination with return to normotensive blood pressure levels when hypotension is no longer needed; compatibility

with anesthetic agents; lack of toxic side effects; maintenance of adequate peripheral perfusion of all tissues at low levels of blood pressure; and absence of tachyphylaxis, rebound hypertension when the agent is discontinued, and reflex tachycardia. Currently, the most common clinically used hypotensive agents are nitroprusside¹ and isoflurane.² Isoflurane fulfills most of the criteria for an ideal hypotensive agent. A potent systemic vasodilator, isoflurane in concentrations of 2-3% (≈2 MAC) can produce profound hypotension by decreasing systemic vascular resistance while maintaining cardiac output and peripheral perfusion. At these concentrations, isoflurane maintains cerebral blood flow (CBF) while significantly decreasing cerebral metabolism, and thereby assures adequate perfusion to the brain.³

Desflurane, difluoromethyl 1-fluoro,2,2,2-trifluoroethyl ether, is a potent inhalation anesthetic currently being investigated for possible clinical use. The cardiovascular effects of desflurane⁴⁻⁹ have been reported to be similar to those of isoflurane. In swine,⁴ desflurane produces a dose-dependent decrease in mean arterial pressure (MAP) and systemic vascular resistance (SVR) and a lesser decrease in cardiac output and no significant change in heart rate. These cardiovascular changes indicate that desflurane may decrease MAP while maintaining adequate peripheral perfusion. For this reason, desflurane may be useful agent for inducing hypotension intraoperatively when hypotension is required to reduce blood loss or provide a clear operative field for more definitive surgery. It was the purpose of the current study to determine the cardiovascular and cerebrovascular effects of desflurane-induced hypotension.

Materials and Methods

With approval of the Animal Care and Use Committee of the Mayo Clinic, 11 unmedicated adult, fasting mongrel dogs weighing 11.3-17.5 kg were studied. Anesthesia was induced with halothane and O₂ in an airtight chamber. Once anesthetized, the animals were removed from the chamber and given pancuronium 0.1 mg · kg⁻¹ intravenously (iv) to facilitate tracheal intubation. Anesthesia was maintained with 1.2 MAC desflurane (8.6%), delivered by a DM 5000 vaporizer modified by Ohmeda through a low-flow closed circuit. N₂ and O₂ were adjusted to maintain arterial O₂ tension (Pa_{O₂}) at approximately 140-160 mmHg. Ventilation with a Harvard® pump was con-

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trolled to maintain normocapnia (arterial CO_2 tension $[\text{Pa}_{\text{CO}_2}] = 38 \pm 2$ mmHg).

Cannulae were placed *via* cutdown into the left femoral artery for pressure measurements and blood sampling, into the left external jugular vein for blood return from the direct CBF measurements,¹⁰ and percutaneously into a peripheral vein for the administration of maintenance fluid (normal saline at $5\text{--}10$ ml \cdot kg⁻¹ \cdot h⁻¹) and drugs as needed. A flow-directed balloon catheter was floated into a pulmonary artery *via* cutdown of the right external jugular vein; this was used for measurements of right atrial pressure (RAP), pulmonary arterial pressure (PAP), and pressure in the left atrium by balloon occlusion of the pulmonary artery (pulmonary arterial occlusion pressure [PAOP]), blood sampling, and measurement of cardiac output by thermodilution.

A two-lead electrocardiogram (ECG) was recorded from needle electrodes placed in the forelimbs. A pulmonary artery catheter thermistor measured core temperature, and a parietal epidural thermistor measured brain temperature, which was maintained near 37° C with heating blankets and lamps. Intracranial pressure (ICP) was recorded continuously with an epidural fiberoptic device (model P-1500, Ladd Research Industries). A four-lead electroencephalogram (EEG) continuously monitored neuronal function from bifrontal and biparietal disc electrodes, which were cemented to the skull to minimize muscle artifact.

After anticoagulation (with heparin $300\text{--}400$ IU \cdot kg⁻¹ iv) the sagittal sinus was exposed, isolated, and cannulated as previously described¹¹⁻¹² for direct measurement of CBF by a square-wave electromagnetic flowmeter (model EP 300 API, Carolina Medical Electronics).¹³ Blood sampling from this catheter was used for calculation of the cerebral metabolic rate for O_2 (CMR_{O_2}). Thereafter, the cranium was closed rigidly by sealing the cranial openings with Surgicel® and Super Line® adhesive (Rawn Co.) to allow measurement of ICP.

Arterial, sagittal sinus, and mixed venous blood gases were measured with standard electrodes (model 1303, Instrumentation Laboratories). Blood O_2 contents were calculated from measurements of hemoglobin (Hb) and oxyhemoglobin saturation (model 282, Instrumentation Laboratories) and O_2 tension.¹⁴ The CMR_{O_2} was calculated as the product of CBF and the difference between arterial and sagittal sinus blood O_2 content, and total body O_2 consumption (\dot{V}_{O_2}) was calculated as the product of the cardiac index ([CI] cardiac output/body surface area) and the difference between arterial and mixed venous blood O_2 content. Cerebral perfusion pressure (CPP) was calculated as the difference between MAP at the head level and ICP. Cerebrovascular resistance (CVR) was calculated as the quotient of CPP and CBF. SVR was calculated as the quotient of $\text{MAP} - \text{RAP}$ and CI. Blood glucose and blood lactate were measured with a mem-

brane-bound enzyme (glucose oxidase or lactate oxidase) technique (model 23A, Yellow Springs Instrument Co.).

Continuous monitoring included MAP, PAP, EEG, ECG, heart rate, temperature, CBF, and ICP. Intermittent measurements included arterial and sagittal sinus blood O_2 saturation and Hb, for calculation of CMR_{O_2} (measured every 5 min). Arterial blood gas tensions, mixed venous O_2 saturation, and CI for calculation of \dot{V}_{O_2} , PAOP, blood glucose and lactate concentrations, and end-tidal desflurane and CO_2 concentrations were measured by an infrared analyzer (Datex, Puritan-Bennett, model 254) every 15 min.

After completion of the surgical preparation, the desflurane concentration was decreased to 1 MAC (7.2%). After a 10-min equilibration period to achieve a steady state, baseline measurements were obtained over a 30-min period. The inspired concentration of desflurane then was increased in six dogs to reduce MAP (with the pressure transducer zeroed at the heart level) to 50 mmHg and in the other five dogs to reduce MAP to 40 mmHg. The selected MAP was maintained for 1 h by adjusting the inspired desflurane concentration. During hypotension, measurement of the variables were taken at the same intervals as for the baseline measurements.

At the end of the hour, the dura overlying the cerebral cortex was exposed and incised, and bilateral cortical biopsies were taken¹⁵⁻¹⁶ for measurement of adenosine triphosphate (ATP), adenosine diphosphate (ADP), adenosine monophosphate (AMP), phosphocreatine, glucose, lactate, and pyruvate.¹⁷ The energy charge was calculated from the concentrations of the adenine nucleotide pool.¹⁸ To determine whether there was any evidence of cerebral ischemia, the concentrations of the cerebral metabolites were compared to normal canine values obtained in our laboratory from dogs anesthetized with 1 MAC halothane, isoflurane, or spinal anesthesia.

Means were calculated for the values measured for each variable during the 30-min baseline period at 1 MAC desflurane for each dog and for the values measured for each variable during the hypotensive period. Student's *t* test for paired data was used to compare mean baseline values with mean hypotensive values for each variable in each group. Student's *t* test for unpaired data was used to compare mean hypotensive values obtained at a MAP of 50 mmHg with hypotensive values obtained at an MAP of 40 mmHg.

Results

The method for inducing hypotension was to gradually increase the inspired desflurane concentration until the target MAP was achieved. A MAP of 50 mmHg was achieved within 14.5 ± 2.7 min (mean \pm SE) with a mean end-tidal concentration of $15.5 \pm 0.3\%$ (2.2 MAC) desflurane.

TABLE 1. Systemic Hemodynamic and Metabolic Values before and during 60 Min of Desflurane-induced Hypotension

	Baseline	Hypotension to 50 mmHg	Baseline	Hypotension to 40 mmHg
MAP (mmHg)	86 ± 5	50 ± 0*	92 ± 6	40 ± 0*†
PAP (mmHg)	14 ± 1	14 ± 1	14 ± 3	12 ± 1
PAOP (mmHg)	6 ± 1	8 ± 1*	5 ± 1	8 ± 1*
Heart rate (beats per min)	122 ± 3	108 ± 6	124 ± 13	100 ± 4
CI (l · min ⁻¹ · m ⁻²)	3.3 ± 0.2	2.0 ± 0.1*	3.9 ± 0.6	1.9 ± 0.1*
\dot{V}_{O_2} (ml · min ⁻¹ · m ⁻²)	132 ± 8	126 ± 5	123 ± 5	118 ± 6
SVR (mmHg · l ⁻¹ · min · m ²)	24 ± 2	22 ± 1	24 ± 4	18 ± 0†
PaO ₂ (mmHg)	146 ± 4	150 ± 4	140 ± 9	143 ± 4
PaCO ₂ (mmHg)	38 ± 1	38 ± 0	38 ± 0	37 ± 0
pH	7.40 ± 0.01	7.38 ± 0.01	7.40 ± 0.01	7.39 ± 0.01
Hb (mg · dl ⁻¹)	13.4 ± 0.8	12.4 ± 0.6*	13.7 ± 0.5	13.3 ± 0.6*
Glucose (mg · dl ⁻¹)	90 ± 2	86 ± 3	104 ± 12	96 ± 7
Lactate (μmol · ml ⁻¹)	2.2 ± 0.2	2.1 ± 0.2	3.2 ± 0.8	3.1 ± 0.7

Values are mean ± SE.

* Significantly different from baseline values measured under 1 MAC desflurane ($P < 0.05$).

† Significantly different from values obtained at MAP = 50 mmHg ($P < 0.05$).

There were no significant differences in the baseline values obtained in the two groups of dogs. The systemic hemodynamic and metabolic values obtained at baseline and during hypotension induced to 50 mmHg are presented in table 1. As expected, the baseline MAP under 1 MAC (7.2%) desflurane (86 ± 5 mmHg) was significantly different from the MAP measured during induced hypotension (50 ± 0 mmHg). Hypotension produced with this concentration of desflurane was associated with a significant decrease in CI, from 3.3 ± 0.2 to 2.0 ± 0.1 l · min⁻¹ · m⁻². There was no change in SVR, and heart rate decreased. Because of the decrease in CI, PAOP increased significantly, from 6 ± 1 to 8 ± 1 mmHg, although these POAP values are still within the normal physiologic range. There was no change in \dot{V}_{O_2} with the increased concentration of desflurane. Despite the decreased CI and the absence of change in \dot{V}_{O_2} , there was no evidence of decreased peripheral perfusion and no indication of an-

aerobic metabolism, since the blood lactate concentrations did not change.

The systemic hemodynamic and metabolic values for hypotension at 40 mmHg (table 1) were similar to those measured at a MAP of 50 mmHg; the lower level of hypotension did not have much additional effect on these values. However, CI decreased significantly, from 3.9 ± 0.6 to 1.9 ± 0.1 l · min⁻¹ · m⁻², and SVR decreased significantly, from 24 ± 4 to 18 ± 0 mmHg · l⁻¹ · min · m². Heart rate decreased from 124 ± 13 to 100 ± 4 beats per min. The \dot{V}_{O_2} remained unchanged. Even at this low MAP, there was no lactate accumulation, which would have indicated anaerobic metabolism.

The cerebral hemodynamic and metabolic values obtained at the two levels of hypotension were likewise similar (table 2). The hypotension induced to 50 mmHg resulted in a CPP of 34 ± 1 mmHg, a significant, 50% decrease from the baseline CPP of 68 ± 4 mmHg. This was

TABLE 2. Cerebral Hemodynamic and Metabolic Values before and during 60 Min of Desflurane-induced Hypotension

	Baseline	Hypotension to 50 mmHg	Baseline	Hypotension to 40 mmHg
MAP (mmHg)	86 ± 5	50 ± 0	92 ± 6	40 ± 0*†
CPP (mmHg)	68 ± 4	34 ± 1*	75 ± 6	27 ± 1*†
CBF (ml · min ⁻¹ · 100 g ⁻¹)	78 ± 6	50 ± 3*	104 ± 15	42 ± 5*
CMRO ₂ (ml · min ⁻¹ · 100 g ⁻¹)	3.4 ± 0.3	2.7 ± 0.1*	3.1 ± 0.3	2.5 ± 0.3*
CVR (mmHg · ml ⁻¹ · min · 100 g)	0.9 ± 0.1	0.7 ± 0.1	0.9 ± 0.2	0.7 ± 0.1
ICP (mmHg)	8 ± 1	6 ± 1*	10 ± 2	3 ± 1*
PSSO ₂ (mmHg)	49 ± 1	44 ± 1	54 ± 3	40 ± 2*
ATP (μmol · g)	2.05 ± 0.03‡	2.12 ± 0.07		2.23 ± 0.06
EC	0.88 ± 0.003‡	0.90 ± 0.003		0.91 ± 0.006
PCr (μmol · g ⁻¹)	3.04 ± 0.09‡	3.46 ± 0.12		3.21 ± 0.09
Lactate (μmol · g ⁻¹)	1.35 ± 0.07‡	1.91 ± 0.11		2.27 ± 0.23

Values are mean ± SE.

* Significantly different from baseline values under 1 MAC desflurane ($P < 0.05$).

† Significantly different from values obtained at MAP = 50 mmHg

($P < 0.05$).

‡ Normal canine values for our laboratory from dogs anesthetized with halothane, isoflurane, or spinal anesthesia.

accompanied by a significant, 36% decrease in CBF from 78 ± 6 to 50 ± 3 $\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$ but no significant change in CVR. Concomitant with the decrease in CPP was a significant decrease in ICP, from 8 ± 1 to 6 ± 1 mmHg. There was a significant decrease in CMR_{O_2} , from 3.4 ± 0.3 to 2.7 ± 0.1 $\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$ with the increased concentration of desflurane required to induce hypotension.

The changes in the cerebral hemodynamic values obtained at hypotension induced to 40 mmHg (table 2) were similar in magnitude to those obtained at hypotension induced to 50 mmHg. When MAP was 40 mmHg, there was a significant, 64% decrease in CPP, from 75 ± 6 to 27 ± 1 mmHg. This was significantly lower than the CPP of 34 mmHg that occurred when the MAP was decreased only to 50 mmHg. This decrease in CPP at a MAP of 40 mmHg resulted in a significant, 60% decrease in CBF, from 104 ± 15 to 42 ± 5 $\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$ and a significant, 70% decrease in ICP, from 10 ± 2 to 3 ± 1 mmHg. There was no significant change in CVR. The increased concentration of desflurane also produced a significant decrease in CMR_{O_2} , from 3.1 ± 0.3 to 2.5 ± 0.3 $\text{ml} \cdot \text{min}^{-1} \cdot 100 \text{ g}^{-1}$.

Although there was a significant decrease in CBF at both levels of hypotension, O_2 extraction increased (O_2 tension in the sagittal sinus [PSS_{O_2}] was significantly decreased with hypotension at 40 mmHg), and there appeared to be adequate O_2 delivery for the CMR_{O_2} . The cerebral concentrations of the high-energy phosphates (ATP and phosphocreatine [PCr]) obtained at the end of each hypotensive period were within the limits of normal canine values for our laboratory obtained under halothane, isoflurane, or spinal anesthesia, although cerebral lactate concentrations were moderately increased.

The EEG during the baseline period under 1 MAC desflurane consisted of frequencies of 2–4 Hz with higher amplitudes than recordings in awake animals and with some delta components. At the concentration of desflurane (15.5%) required to produce hypotension to 50 mmHg, the EEG demonstrated higher-amplitude slow waves with some regular periodic polyspiking and with occasional episodes of burst suppression at the beginning of the hypotensive period. By the end of the 60 min at the same concentration of desflurane, the EEG demonstrated high-amplitude slow waves with an occasional periodic polyspiking and no longer included any burst suppression. With the concentration of desflurane (17.1%) required to produce hypotension of 40 mmHg, the EEG initially demonstrated an isoelectric pattern with occasional spikes and waves. By the end of the 60-min hypotensive period, the EEG showed the same pattern in one dog, but showed a pattern of burst suppression in three other dogs and continuous activity consisting of high-amplitude slow waves in a fifth dog (fig. 1). In this animal,

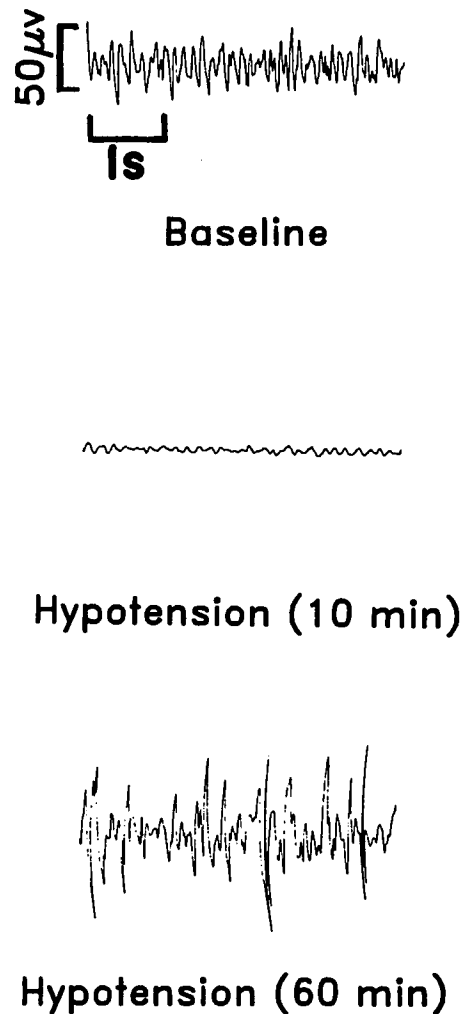


FIG. 1. Representative EEG tracings from one dog under 1 MAC desflurane (baseline) and at 10 and 60 min of induced hypotension to 40 mmHg (16.0% end-expired desflurane).

the end-tidal concentration of desflurane remained 16.0% throughout the hypotensive period. Despite these changes in EEG activity, there were no significant changes in the CMR_{O_2} measurements throughout the hypotensive period.

Discussion

The decrease in MAP in the dogs was produced primarily by a decrease in cardiac output; there was little change in SVR at a MAP of 50 mmHg, although SVR did decrease significantly with the higher concentration of desflurane needed to induce hypotension to 40 mmHg. This hemodynamic profile during desflurane-induced hypotension is similar to that reported for halothane-induced hypotension,¹⁹ for which there were similar decreases in cardiac output for similar changes in MAC concentrations of desflurane or halothane. The observed de-

crease in cardiac output is assumed to be due to a decrease in venous return, presumably from venous vasodilation produced by the desflurane, since there was no change in PAP. However, a decrease in myocardial contractility may be inferred from the small but significant increase in PAOP. The decrease in cardiac output was accentuated because there was no reflex increase in heart rate in response to the decrease in MAP. This indicates that desflurane may block the baroreflex, like halothane but unlike isoflurane. Despite the significant decrease in cardiac output and MAP, there was adequate peripheral perfusion and hence no anaerobic metabolism, as indicated by an absence of increase in blood lactate.

These cardiovascular hemodynamic changes differ from those recently reported for dogs,²⁰ in which 2 MAC (14%) desflurane caused a 50% decrease in MAP produced primarily by a significant decrease in SVR and a lesser but significant decrease in CI. Perhaps the higher concentrations of 15–17% desflurane used in the current study (2.2–2.4 MAC) significantly depressed the heart to a greater extent. These findings are in agreement with the reports of the cardiovascular effects of desflurane in swine¹ in which 1.6 MAC desflurane (12.6%) produced a 50% decrease in MAP, caused by a significant, 38% decrease in cardiac output and a significant, 31% decrease in SVR. The cardiovascular depression observed in this study was more profound than has been observed previously, but none of the previous studies has used such high concentrations of desflurane. Although the study in swine⁴ was not designed to assess myocardial contractility directly, the results strongly suggested that desflurane was a myocardial depressant because of the decreased stroke volume even with the increases in preload volume. These cardiovascular changes with desflurane-induced hypotension differ from those reported for isoflurane-induced hypotension in the same dog model²¹ and in baboons,²² in which hypotension was produced primarily by a decrease in SVR with little or no change in cardiac output.

The current study did not detect any detrimental systemic effects of hypotension induced with desflurane despite the decreased blood pressure and decreased cardiac output. Blood lactate concentrations obtained during the hypotensive period were unchanged from those obtained during the 1 MAC baseline period, and the base deficit (data not shown) also was unchanged. This maintenance of adequate peripheral perfusion is similar to the findings during isoflurane-induced hypotension, in which there was change neither in blood lactate concentration nor in the base deficit when the MAP was reduced to 40 mmHg with isoflurane.²¹ These findings are unlike those observed with trimethaphan, nitroprusside, or halothane, for which anaerobic metabolism did occur in the same dog model of induced hypotension.²³ This maintenance of peripheral perfusion during desflurane-induced hy-

potension occurred even though CI decreased and \dot{V}_{O_2} remained unchanged. This agrees with our previous report that increasing desflurane from 0.5 to 2.0 MAC did not decrease \dot{V}_{O_2} in dogs,²⁰ but is unlike the findings of Weiskopf *et al.*⁴ in swine, for which there was a significant decrease in \dot{V}_{O_2} .

During the hypotensive period, in which the MAP was at (50 mmHg) or below (40 mmHg) the normal lower limit of autoregulation of the cerebral vasculature in dogs, the CPP was significantly reduced (34 and 27 mmHg, respectively). At these levels of hypotension, CBF appeared to parallel MAP (or CPP) and was significantly decreased, indicating the loss of cerebral autoregulation. Whether this was because the MAP was outside the normal range of autoregulation or whether desflurane changed the limits of autoregulation cannot be determined by this study. The CBF measured during desflurane-induced hypotension was similar to that obtained when isoflurane²² was used to induce the same degree of hypotension (50 *vs.* 49 ml · min⁻¹ · 100 g⁻¹ at MAP = 50 mmHg; 42 *vs.* 44 ml · min⁻¹ · 100 g⁻¹ at MAP = 40 mmHg). These decreases in CBF are similar to those produced by other hypotensive agents, including trimethaphan, nitroprusside, and halothane, in the same animal model.²³

Also like isoflurane²¹ but unlike the other mentioned hypotensive agents,²³ the concentration of desflurane required to induce hypotension to these levels produced a significant decrease in CMR_{O_2} . These parallel decreases in both CBF and CMR_{O_2} resulted in concentrations of cerebral stores of high-energy phosphates similar to the normal canine values for our laboratory (although we did not measure cerebral metabolites from contemporaneously studied control animals specifically for this study) and similar to the cerebral energy stores measured during isoflurane-induced hypotension.²¹ In contrast, other hypotensive agents, including trimethaphan, nitroprusside, and halothane, produced a decrease in CBF similar to that of desflurane but a lesser reduction in CMR_{O_2} .²³ The decrease in CBF produced by these agents was associated with a significant decrease in cerebral stores of high-energy phosphates and a significant increase in cerebral lactate accumulation, indicating that incomplete cerebral ischemia had occurred during the hypotensive period. The similar concentrations of cerebral energy stores measured during desflurane-induced hypotension in this study and isoflurane-induced hypotension in other studies suggests that desflurane may maintain a favorable ratio of O_2 delivery to O_2 demand during profound hypotension similar to the ratio provided by isoflurane and may prevent the incomplete global ischemia that occurs with the profound hypotension produced in control animals in this model.^{23,‡} The mechanism for this maintenance

‡ Milde LN: Unpublished data, 1990.

of aerobic metabolism is presumed to be a decrease in CMR_{O_2} secondary to reduction in neuronal function²⁴ as measured by changes on the EEG.

The EEG changes observed in this study are similar to those reported previously.²⁰ The EEG at the beginning of the hypotensive period appeared to represent a deeper level of anesthesia than at the end of the hypotensive period, although the end-tidal concentration of desflurane remained constant throughout the hypotensive period. This is evidence that supports the phenomenon of tolerance. Tolerance may be demonstrated by the set of EEGs presented in figure 1, but comparison of EEGs among the dogs in this study cannot be made because the end-tidal concentration of desflurane was not the same for each dog, since the end point for the concentration of desflurane was blood pressure.

When hypotension was induced to either level of hypotension, the ICP decreased significantly, presumably because CBF was decreased significantly. Because these were normal dogs with normal intracranial elastance and with normoventilation, the observed cerebral hemodynamic changes cannot be extrapolated to patients with decreased intracranial elastance undergoing induced hypotension during neurosurgery.

In summary, hypotension can easily be induced and maintained with minor adjustments in the inspired desflurane concentration. Desflurane appears to be similar to isoflurane in its systemic and cerebral effects during induced hypotension. It acts to decrease MAP by means of a decrease in cardiac output and SVR complemented by inhibition of the baroreflex and maintenance of adequate peripheral perfusion. It produces a parallel decrease in CBF and CMR_{O_2} , resulting in the maintenance of aerobic metabolism and the absence of ischemia even at very low CPP. Clinical studies should be done to determine whether desflurane will be a useful hypotensive agent during surgery.

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