

Desflurane and Isoflurane Have Similar Effects on Cerebral Blood Flow in Patients with Intracranial Mass Lesions

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Background: Before desflurane is advocated for patients undergoing neurosurgical procedures, it is necessary to determine the effect of desflurane on cerebral blood flow (CBF). In this study, CBF values are compared between desflurane and isoflurane at two doses. In addition, CBF reactivity to CO₂ and the effect of prolonged exposure were compared between the two agents.

Methods: Cerebral blood flow measurements with intravenous ¹³³Xe were performed in 24 patients undergoing craniotomy for mass lesions, randomized to receive either isoflurane or desflurane in oxygen and air. Cerebral blood flow was determined at 1 and 1.5 MAC concentrations at Pa_{CO₂} of 25 mmHg in the absence of surgical stimulation. Intraoperatively, with 1.25 MAC anesthesia, CBF was determined at target Pa_{CO₂} of 25 and 35 mmHg. In 15 patients, an additional measurement at 1.25 MAC was made before closure.

Results: At 1.0 MAC, mean ± SD CBF values for the desflurane and isoflurane groups were 18 ± 2 and 20 ± 3 ml · 100 g⁻¹ · min⁻¹, respectively. At 1.5 MAC, CBF values were the same for the two anesthetics; 17 ± 3 ml · 100 g⁻¹ · min⁻¹ for isoflurane and 19 ± 4 ml · 100 g⁻¹ · min⁻¹ for desflurane. During 1.25 MAC anesthesia, there were no differences between groups, with CO₂ reactivity 1.3 ± 1.2 ml · 100 g⁻¹ · min⁻¹ · mmHg⁻¹ for desflurane and 1.6 ± 0.6 ml · 100 g⁻¹ · min⁻¹ · mmHg⁻¹ for isoflurane. There was no demonstrable decrease in CBF with prolonged exposure to either agent.

Conclusions: Desflurane and isoflurane are similar in terms of absolute CBF, the response to increasing doses, and the preservation of CO₂ reactivity. (Key words: Anesthetics, volatile; desflurane; isoflurane. Brain; cerebral blood flow. Measurement techniques: ¹³³Xe washout.)

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DESFLURANE, a new volatile anesthetic agent, has several favorable characteristics, including stability in soda lime, minimal biodegradability, and a blood:gas partition coefficient of 0.42. Human studies have confirmed that emergence from anesthesia is more rapid with desflurane than with isoflurane.¹ Although this property has been cited to be most beneficial during short "outpatient procedures," the difference between isoflurane and desflurane wakeup times may become more significant as the duration of anesthetic exposure increases.² Thus, desflurane may be preferred in patients undergoing prolonged neurosurgical procedures, because postoperative awakening facilitates the performance of an early neurologic examination.

With minimal effects on cerebral blood flow and intracranial pressure, in the concentrations routinely used, isoflurane is currently the most commonly used volatile anesthetic during neurosurgical procedures. The purpose of this randomized controlled study in patients with intracranial mass lesions was to compare the effects of desflurane and isoflurane on cerebral blood flow (CBF) at two concentrations (1.0 and 1.5 MAC), and to assess their effects on cerebrovascular reactivity to changes in Pa_{CO₂} during 1.25 MAC anesthesia. In addition, the effect on CBF of prolonged exposure to these agents was compared.

Materials and Methods

This study was approved by the Institutional Review Board and informed consent was obtained from all participants. A total of 24 ASA physical status 2 and 3 patients, between the ages of 18 and 75 yr, were randomized to receive either isoflurane or desflurane during craniotomy for intracranial mass lesions (18 supra- and 6 infratentorial). Patients received diazepam 5-10 mg p.o. approximately 1 h before arrival in the operating room. Four patients not receiving an oral premedication were given midazolam 3-5 mg intravenously. Moni-

CEREBRAL BLOOD FLOW: DESFLURANE VERSUS ISOFLURANE

toring consisted of five-lead electrocardiogram and direct arterial blood pressure from a radial artery catheter. Administration of the selected volatile anesthetic was initiated in an air-oxygen mixture adjusted to an FI_{O_2} of 0.40. Isoflurane was administered with a TEC-4 Forane (Ohmeda, Madison, WI) vaporizer, while desflurane was administered through a heated and pressurized vaporizer installed on a DM5000 anesthesia machine modified by Ohmeda. Volatile agent concentration, end-tidal carbon dioxide, and oxygen were measured with a Puritan Bennett Datex (Wilmington, MA) model 254 infrared gas analyzer modified for desflurane. Anesthesia was induced with thiopental 4–8 mg/kg and vecuronium 0.2–0.4 mg/kg. On the attainment of suitable muscle relaxation, the trachea was intubated and the end-tidal volatile anesthetic concentration was adjusted to an age-appropriate level of 1 MAC (Desflurane MAC: 7.25% for 18–30-yr-old patients, 6% for patients 31 yr of age or older). No supplementary opioids were administered. Ventilation was adjusted to maintain $PE_{T}CO_2$ at 21 ± 1 mmHg.

After a stabilization period of at least 15 min, regional cerebral blood flow (rCBF) was determined by the intravenous ^{133}Xe method (Run 1), which has previously been described and validated.³ Briefly, approximately 20 mCi of ^{133}Xe dissolved in saline was rapidly injected intravenously. Tracer washout was recorded with a Cerebrograph 10a (Novo Diagnostic Systems, Bagsvaerd, Denmark) CBF device utilizing multiple scintillation detectors, while expired respiratory gas was sampled at the proximal portion of the endotracheal tube to generate the input function. Data were acquired for 11 min after xenon injection, from which a two-compartment model was generated,⁴ with CBF calculated using the Initial Slope Index.⁵ After the initial CBF measurement, the inhalational agent concentration was increased and maintained at 1.5 MAC for at least 10 min, at which point the rCBF measurement was repeated (Run 2). For these first two CBF determinations, five scintillation detectors positioned over the middle cerebral artery territory of each hemisphere were used. Throughout these two CBF determinations, patients received no surgical or tactile stimulation.

After the completion of Run 2, the anesthetic level was maintained at 1.25 MAC for the duration of the surgical procedure. To determine CBF reactivity, an additional pair of CBF determinations at this concentration were obtained after dural reflection at target Pa_{CO_2} of 25 (Run 3) and 35 (Run 4) mmHg, using a single scintillation detector ipsilateral to, but outside,

the craniotomy site, and a second detector placed homologously over the contralateral hemisphere. The Pa_{CO_2} was increased by the addition of exogenous carbon dioxide into the breathing circuit.

In 15 of the patients studied, an additional CBF measurement at 1.25 MAC was made after the removal of the mass lesion, just before dural closure (Run 5). The purpose of this final CBF measurement was to determine whether or not CBF in humans decreases spontaneously over time, as has been reported for animals during halothane⁶ and isoflurane⁷ anesthesia.

Data are expressed as mean \pm SD, and CBF is reported as the average value obtained for all detectors. Within-group comparisons were made by paired *t* test, and between-group comparisons were made by repeated-measures ANOVA. Cerebral blood flow values after prolonged anesthetic exposure were analyzed for differential effects on CBF between agents and for any evidence of a time effect on CBF. Gender distribution between groups was compared by Chi-square analysis. The threshold for statistical significance was set at $P < 0.05$.

Results

A total of 111 CBF determinations were performed. Of these, one measurement at 1.5 MAC desflurane and one at 1.0 MAC isoflurane run could not be processed because of technical difficulties. For these patients, both the 1.0 and 1.5 MAC runs were eliminated from the analysis. A summary of demographic data and baseline hemodynamic data is shown in table 1. There were no significant differences between groups with regard to age, weight, or sex distribution, as well as thiopental dose administered during induction. Seven patients

|| McPherson RW, Traystman RJ: Effect of time on cerebrovascular responsivity to Pa_{CO_2} during isoflurane anesthesia (abstract). ANESTHESIOLOGY 71:A105, 1989

Table 1. Demographic Data

	Desflurane (n = 12)	Isoflurane (n = 12)
Age (yr)	41 \pm 12	48 \pm 12
Weight (kg)	76 \pm 14	68 \pm 11
Male/female	8/4	4/8
Supratentorial/infratentorial mass	8/4	10/2
Thiopental dose (mg/kg)	7.8 \pm 1.8	6.8 \pm 2.3

Values are mean \pm SD. There were no significant differences between groups.

Table 2. Cerebral Blood Flow (CBF) at 1.0 and 1.5 MAC without Surgical or Tactile Stimulation and Intraoperative CBF at 1.25 MAC with Mild and Moderate Hypercarbia

	Agent	Run 1, 1.0 MAC (n = 11)	Run 2,† 1.5 MAC (n = 11)	Run 3, 1.25 MAC (n = 12)	Run 4, 1.25 MAC (n = 12)
Pa _{CO₂} (mmHg)	Desflurane	25 ± 3	26 ± 3	25 ± 3	35 ± 3
	Isoflurane	26 ± 3	25 ± 2	27 ± 2	37 ± 2
MAP (mmHg)	Desflurane	75 ± 8	81 ± 16	81 ± 11	82 ± 11
	Isoflurane	78 ± 9	69 ± 6‡§	79 ± 9	79 ± 8
Temperature (° C)	Desflurane	35.2 ± 0.4	34.9 ± 0.5	35.0 ± 0.6	35.1 ± 0.7
	Isoflurane	35.5 ± 0.5	35.3 ± 0.4	35.2 ± 0.5	35.2 ± 0.5
Time (min)*	Desflurane	37 ± 17	54 ± 17	216 ± 40	225 ± 40
	Isoflurane	29 ± 7	48 ± 8	185 ± 40	196 ± 45
CBF (ml · 100 g ⁻¹ · min ⁻¹)	Desflurane	18 ± 2	19 ± 4	20 ± 9	33 ± 18#
	Isoflurane	20 ± 3‡	17 ± 3§	20 ± 5	35 ± 11#

* Minutes after induction.

† Mean arterial pressures during Run 2 were significantly different between groups.

‡ Significantly different compared with desflurane.

§ Significantly different compared with 1.0 MAC.

Significantly different compared with Run 3.

from each group had preoperative CT-scan evidence of elevated intracranial pressure, as evidenced by mid-line shift or significant flattening of the sulci and gyri. Cerebral blood flow values in the patients with these CT findings was consistently lower by an average of 20% across all runs. The CBF response to changes in agent concentration or Pa_{CO₂}, however, were not significantly effected by the presence or absence of these CT findings.

At 1.0 MAC, CBF in the isoflurane group was slightly higher than in the desflurane group (table 2). There was a small decrease in CBF when the isoflurane dose was increased to 1.5 MAC. At the higher MAC value,

CBF was the same for the two anesthetics. At 1.5 MAC, blood pressure was lower with isoflurane, although mean arterial pressure was maintained above the expected normal autoregulatory threshold of 50 mmHg. The Pa_{CO₂}, temperature, and elapsed time between the various runs and anesthetic induction did not differ between groups.

Individual CBF results for all patients at 1.25 MAC during mild and moderate hypocarbia are depicted in figure 1, with mean values tabulated in table 2. There were no differences detected between groups. The CO₂ reactivity was preserved with both agents and was calculated to average 1.3 ± 1.2 ml · 100

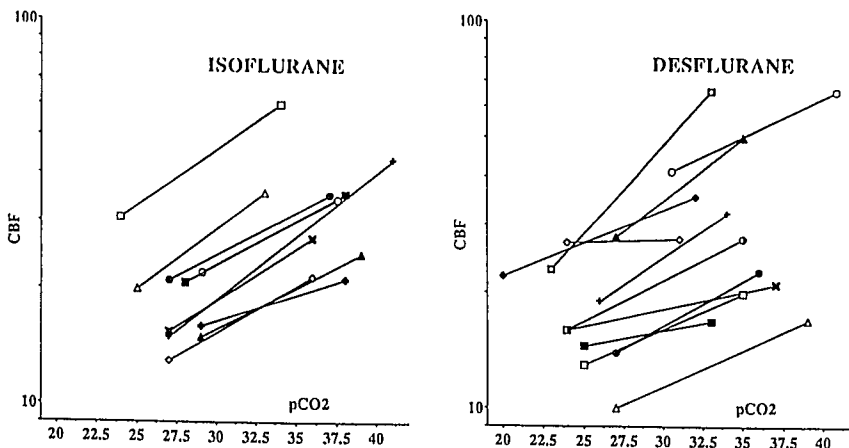


Fig. 1. Individual CBF results for all patients at 1.25 MAC desflurane or isoflurane during mild and moderate hypocarbia. Cerebral blood flow in ml · 100 g⁻¹ · min⁻¹; Pa_{CO₂} in mmHg.

CEREBRAL BLOOD FLOW: DESFLURANE VERSUS ISOFLURANE

$\text{g}^{-1} \cdot \text{min}^{-1} \cdot \text{mmHg}^{-1}$ for desflurane and $1.6 \pm 0.6 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1} \cdot \text{mmHg}^{-1}$ for isoflurane.

There was no demonstrable decrease in CBF with prolonged exposure of either agent (table 3). For the 15 patients included in this arm of the study, initial intraoperative CBF data were collected a mean of 3.8 h postinduction in the desflurane patients *versus* 3.0 h for the isoflurane patients ($P < 0.03$). Final CBF determinations were made approximately 2.5–3 h later. For both runs, anesthetic dose was maintained at 1.25 MAC, with no differences in mean arterial pressure, heart rate, hematocrit or Pa_{CO_2} , or MAC between the early and late CBF determinations. For both groups, however, there was a mean decrease in temperature of 0.5°C , although only approaching statistical significance for the desflurane group ($P = 0.053$). No difference in CBF was noted between those patients receiving desflurane or isoflurane at the time of the initial measurement. The effect of time on CBF for the two agents was not significantly different.

Discussion

Studies with desflurane in neurosurgical patients, to date, have been limited to the measurement of intracranial pressure. Muzzi *et al.*,⁸ comparing lumbar cerebrospinal fluid pressure (LCSFP) during 1 MAC desflurane anesthesia in hypocapnic patients with supratentorial mass lesions with midline shift, described a gradual increase in LCSFP from a baseline level of 11 mmHg to a level of 18 mmHg, just before dural incision. No measurements of CBF were made in this study. In an earlier study by the same group, the administration of 0.5 MAC desflurane in 50% N_2O was associated

with no change in LCSFP as compared with baseline.⁹ Ebrahim *et al.* also assessed the effect of desflurane 1 MAC on intracranial pressure (ICP), and found no increase in a series of patients with no preoperative CT evidence of midline shift.[#]

In our study, CBF data for isoflurane and desflurane are compared at two different doses during a period in which the patients were receiving no surgical or tactile stimulation. Neither ICP nor LCSFP were measured in our study. Seven of 12 patients in each group had CT evidence of increased intracranial pressure. Even so, we found no differences in CBF response to either agent attributable to the presence or absence of these CT findings. Thus, despite the possibility of an increase in ICP indicated by the isolated study of Muzzi *et al.*,⁸ there appears to be no adverse cerebrovascular effect attributable to desflurane.

Other CBF studies with desflurane, to date, have been limited to two canine studies by Lutz *et al.*^{10,11} With increasing doses of desflurane during normocarbica, a progressive increase in CBF was detected in the one study.¹⁰ In the subsequent study, which was designed to delineate the effect of hypocarbica during desflurane, this desflurane dose-related effect was not apparent.¹¹ Thus, during hypocarbica (Pa_{CO_2} 22–24), MAC levels of 0.5, 1, and 1.5 yielded similar CBF values. The ICP was not found to increase in either of studies of dogs with normal intracranial anatomy.

In our study, hyperventilation preceded the measurement of CBF. The differences between agents during initial CBF determinations during hypocarbica, although statistically significant, were of small enough

NDA data on file, Anaquest, Liberty Corner, New Jersey.

Table 3. Cerebral Blood Flow ($\text{ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$) at 1.25 MAC: Effect of Prolonged Exposure

	Isoflurane (n = 7)		Desflurane (n = 8)	
	Run 3	Run 5	Run 3	Run 5
Time postinduction (h)	3.0 ± 0.5	5.6 ± 1.6*	3.8 ± 0.5†	6.7 ± 0.9*
Pa_{CO_2} (mmHg)	27 ± 2	26 ± 3	25 ± 2	25 ± 2
Mean arterial pressure (mmHg)	80 ± 13	86 ± 13	80 ± 12	82 ± 13
Temperature ($^\circ \text{C}$)	35.2 ± 0.3	35.7 ± 0.4*	35.0 ± 0.6	35.4 ± 0.8
Hematocrit (%)	31.4 ± 2.7	31.6 ± 3.5	34.6 ± 3.4	34.1 ± 1.6
Cerebral blood flow ($\text{ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$)	20 ± 6	23 ± 6	19 ± 6	23 ± 8

Values are mean ± SD.

* Significantly different from Run 3.

magnitude to be deemed clinically irrelevant. For both isoflurane and desflurane, cerebral vascular reactivity in this study was well maintained, with the responses herein described within the range reported both in awake human studies^{12,13} and in our earlier studies of anesthetized patients.¹⁴ It is, therefore, unlikely that the administration of desflurane in the hypocarbic patients would have an adverse effect on CBF or CO₂ reactivity.

Studies in animals have shown a decrease in CBF over time with prolonged exposure to halothane.⁶ Whether or not there is a similar effect in animals with isoflurane is controversial.^{7,15} A recent transcranial Doppler study in children showed that pulsatility and blood flow velocity remain stable with prolonged isoflurane exposure.¹⁶ Our results confirm that, with hypocapnia, CBF remains stable during isoflurane anesthesia, and indicate that CBF remains constant for prolonged desflurane exposure, as well. It is noted, however, that the dissipation of the effect of hyperventilation, with time, may tend to mask a decrease in CBF attributable to prolonged anesthetic exposure. In either case, the effects seen with isoflurane and desflurane are similar.

Isoflurane, for some time, has been the most commonly used volatile anesthetic during neurosurgery. This agent has a long record of safety.¹⁷ Our study demonstrates that, with mild to moderate hypocapnia, the effects of desflurane are similar to those of isoflurane in terms of absolute CBF, in the response to increasing doses of anesthetic, and in the preservation of CO₂ reactivity. The aforementioned gradual increase in ICP seen by one group of investigators has yet to be confirmed by other studies, and is unlikely to be due to an increase in CBF.

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