

The Effect of Desflurane and Isoflurane on Cerebrospinal Fluid Pressure in Humans with Supratentorial Mass Lesions

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Desflurane, a new volatile anesthetic, produces cerebral vasodilation. The purpose of this study was to compare the effects of 1 MAC desflurane with those of isoflurane on cerebrospinal fluid pressure (CSFP) in patients with supratentorial mass lesions and a mass effect on computerized tomography (CT scan). Twenty adult patients undergoing craniotomy for removal of supratentorial mass lesions were studied. Ten patients received desflurane and 10 patients received isoflurane. Prior to induction of anesthesia, a radial artery catheter was inserted and a 19-G needle was inserted into the lumbar subarachnoid space to measure CSFP. Baseline arterial blood gases and CSFP were measured with the patient awake and unmedicated. Anesthesia was induced with thiopental (6–9 mg/kg) and muscle relaxation achieved with vecuronium (0.2 mg/kg). The lungs of all patients were hyperventilated to achieve an arterial CO₂ tension of 24–28 mmHg. Anesthesia was maintained with 1 MAC volatile anesthetic, either 7.0% desflurane or 1.2% isoflurane in an air:O₂ mixture to maintain an inspired O₂ fraction (FI_{O₂}) of 0.50. Patients were not administered any other anesthetic until the dura was incised. Mean arterial pressure was kept within 20% of the patient's mean ward values with the use of esmolol or phenylephrine. CSFP, mean arterial pressure, end-tidal CO₂ concentration (PET_{CO₂}), hemoglobin O₂ saturation, and cerebral perfusion pressure were recorded with the patient awake, immediately postinduction with thiopental, post-intubation, after institution of the volatile anesthetic, and every 5 min until the dura was incised. There was no difference in the mean (± SD) awake CSFP between the desflurane (11 ± 4 mmHg) and the isoflurane (10 ± 2 mmHg) groups. CSFP significantly decreased in all patients after administration of thiopental, followed by a variable increase with laryngoscopy and intubation. During administration of desflurane, the CSFP gradually increased (to 18 ± 6 mmHg) in all patients until the dura was incised. The CSFP was significantly greater than baseline measurement beginning 20 min after the institution of desflurane. There was no statistically significant change in the mean CSFP in the isoflurane group at any time during the study period after the volatile anesthetic was instituted. CSFP was 8 ± 2 mmHg at the time of dural incision in the isoflurane group. CSFP in the desflurane group became significantly greater than the CSFP in the isoflurane group beginning 10 min after institution of the volatile anesthetic. The results of this study indicate that, in hypocapnic neurosurgical patients with supratentorial mass lesions, the administration of 1 MAC desflurane resulted in an increase in CSFP. This is in contrast to 1 MAC isoflurane, which did not produce an increase in CSFP. (Key words: Anesthetics, volatile: desflurane; isoflurane. Brain: intracranial pressure. Carbon dioxide: hypocapnia. Cerebrospinal fluid: pressure.)

DESFLURANE is a new volatile anesthetic with a blood:gas solubility (blood:gas partition coefficient = 0.42) similar to that of N₂O (0.47), resulting in rapid induction and emergence from anesthesia.¹ This property suggests that desflurane may be a useful volatile anesthetic for neurosurgical procedures because it is often desirable to have patients awake immediately after surgery in order to evaluate their neurologic status. Canine studies indicate that desflurane is a potent cerebral vasodilator.² If applicable to humans, this effect may result in increased intracranial pressure (ICP) in patients with abnormal intracranial elastance. In a previous study, isoflurane N₂O:O₂ anesthesia was shown to have no significant effect on cerebrospinal fluid pressure (CSFP) in hypocapnic patients (Pa_{CO₂} 25–30 mmHg) with supratentorial mass lesions.³ The purpose of this study was to compare the effects of 1 MAC desflurane with those of 1 MAC isoflurane on CSFP in patients with supratentorial mass lesions.

Materials and Methods

With Institutional Review Board approval, and informed consent, 20 adult patients (ages 20–75 yr) undergoing craniotomy for removal of supratentorial mass lesions were studied over a 3-month period. All patients had an intracranial mass with surrounding edema and a midline shift on computerized tomography (CT scan). Patients were excluded from the study if their medical history included the presence of coronary artery disease, moderate or severe chronic obstructive pulmonary disease, or exposure to general anesthesia within 7 days prior to the study. Patients being treated with calcium entry blockers, systemic vasodilators, or drugs that affect anesthetic requirements (*e.g.*, opioids, benzodiazepines, or α_2 agonists) were also excluded from the study. None of the patients in the study received preanesthetic medications.

Prior to induction of anesthesia, a radial artery catheter was inserted and a 19-G lumbar subarachnoid needle (Becton Dickinson & Co., Rutherford, NJ) was placed to measure CSFP. All patients were supine and placed in a 10–15° head-up position. Pressures were transduced with the zero reference at midcranial level throughout the study period. Prior to induction of anesthesia, patency of the cerebrospinal fluid (CSF) pathway between the head and lumbar subarachnoid space was confirmed by passive elevation of the patient's head and observation of an ap-

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appropriate increase in CSFP. Respiratory and cardiac variations in the CSFP waveform were observed in all patients. Patency was reconfirmed at the end of the recording period by observing an immediate response in CSFP with digital pressure on the exposed dura. Baseline arterial blood pressure, arterial blood gases, and CSFP were measured with the patients awake and unmedicated. End-tidal CO₂ tension (PET_{CO₂}) was measured while the patient breathed 100% O₂ via a close fitting face mask.

Anesthesia was induced with incremental doses of intravenous thiopental (6–9 mg/kg total dose), and muscle relaxation achieved with vecuronium (0.2 mg/kg). The lungs of all patients were then hyperventilated to achieve a PET_{CO₂} of 18–22 mmHg, estimated to achieve an arterial CO₂ tension (Pa_{CO₂}) of 24–28 mmHg. Tracheal intubation was achieved without further drug administration. The adequacy of hyperventilation was confirmed by continuous monitoring of PET_{CO₂} and measurement of arterial blood gases after tracheal intubation and 45 min after the institution of the volatile anesthetic. Anesthesia was instituted and maintained with 1 MAC volatile anesthetic, either 7.0% end-tidal desflurane or 1.2% end-tidal isoflurane in an air:O₂ mixture to maintain an FI_{O₂} of 0.50. Desflurane was administered from a DM-5000 vaporizer modified by Ohmeda to deliver desflurane. In the group receiving desflurane, end-tidal desflurane concentrations and PET_{CO₂} were monitored continuously by an infrared analyzer (model 254, Datex Puritan Bennett). Isoflurane was administered with a Ohio Medical Forane[®] vaporizer using a Modulus 2 Ohio anesthetic machine. In the group receiving isoflurane, end-tidal isoflurane concentrations and PET_{CO₂} were monitored by mass spectroscopy (Perkin-Elmer). Patients were not administered any other anesthetic agents until the dura was incised. Intravenous fluids were limited to less than or equal to 500 ml lactated Ringer's solution prior to dural incision. Arterial blood pressure was kept within 20% of the patients mean ward values with the use of esmolol (10 mg · ml⁻¹) given as bolus doses or phenylephrine (10 mg · 250 ml⁻¹) given as a continuous infusion regulated by a minidrip infusion set, as needed throughout the recording period.

CSFP, arterial blood pressure, PET_{CO₂}, O₂ saturation, body temperature, and cerebral perfusion pressure were recorded at baseline (patient awake), immediately post-induction with thiopental, postintubation, before institution of the inhalational agent, and every 5 min during administration of the volatile anesthetic until the dura was incised.

Values for CSFP, mean arterial pressure, cerebral perfusion pressure, Pa_{CO₂}, and PET_{CO₂} obtained postinduction, postintubation, and at 5-min intervals during the administration of the volatile anesthetic were compared to the awake baseline values in each group and between the groups by two-way analysis of variance with repeated-

measures testing. Differences were considered significant when $P < 0.05$. In addition, the rate of change of CSFP during the administration of the volatile anesthetic from time 0 until the dura was incised was calculated for each group, and the mean slope of the change in CSFP with time for each group was compared by Student's *t* test for unpaired data.

Results

There was no significant difference in the tumor size (largest measurable dimension on the CT scan) between the two groups. The mean tumor size in the group receiving desflurane was 4.6 ± 1.2 cm (SD). The mean tumor size in the group receiving isoflurane was 4.8 ± 1.4 cm. There was no significant difference in the thiopental dose between the two groups (7.7 ± 1.3 mg/kg [desflurane] vs. 7.7 ± 0.9 mg/kg [isoflurane]). There was no difference in the mean arterial pressure or cerebral perfusion pressure between the two groups at any time during the study period (table 1). With the institution of the volatile anesthetic it took 6 ± 4 min to achieve 1 MAC in each group. Desflurane 1 MAC ($7.1 \pm 0.6\%$) or isoflurane 1 MAC ($1.18 \pm 0.03\%$) was maintained throughout the remainder of the study. The group receiving desflurane received 0.61 ± 0.65 mg · kg⁻¹ esmolol and an infusion of phenylephrine administered over 35 ± 29 min. The group receiving isoflurane received 0.60 ± 0.84 mg · kg⁻¹ esmolol and an infusion of phenylephrine administered over 31 ± 43 min.

There was no difference in the mean baseline CSFP between the group receiving desflurane (11 ± 4 mmHg) and the group receiving isoflurane (10 ± 2 mmHg) (fig. 1, table 1). As expected, the CSFP decreased significantly in all patients after the administration of thiopental, to 7 ± 4 mmHg in the group receiving desflurane and 6 ± 2 mmHg in the group receiving isoflurane. This was followed by an increase in CSFP with laryngoscopy and intubation to 12 ± 5 mmHg in the group receiving desflurane and 10 ± 2 mmHg in the group receiving isoflurane. In both groups, hyperventilation produced a Pa_{CO₂} of 27 ± 3 at intubation. This Pa_{CO₂} was maintained throughout the administration of the volatile anesthetic. At the institution of the inhalation agent, the CSFP was 11 ± 5 mmHg in the group receiving desflurane and 8 ± 2 mmHg in the group receiving isoflurane. In the group receiving isoflurane, there was no significant change in the CSFP when compared to baseline at any time during the study period after the institution of the volatile anesthetic. In contrast, in the group receiving desflurane, the CSFP gradually increased to 18 ± 6 mmHg during approximately 45 min until the time the dura was opened. The CSFP was significantly greater than the baseline value beginning 20 min after institution of desflurane and was

TABLE 1. Mean CSFP, MAP, CPP, and PaCO₂ Recorded Before and After Administration of Inhalational Agent

	CSFP (mmHg)		MAP (mmHg)		CPP (mmHg)		PaCO ₂ (mmHg)	
	ISO	DES	ISO	DES	ISO	DES	ISO	DES
Baseline	10 ± 2	11 ± 4	107 ± 28	94 ± 21	99 ± 25	81 ± 15	37 ± 3	36 ± 2
Induction	6 ± 2*	7 ± 4*	99 ± 22	89 ± 20	93 ± 21	81 ± 19	28 ± 3†	26 ± 3†
Intubation	10 ± 2	12 ± 5	119 ± 19	114 ± 16	109 ± 18	101 ± 15	27 ± 2	27 ± 3
10 min	8 ± 4	13 ± 5‡	90 ± 13	83 ± 19	79 ± 8	71 ± 20	27 ± 3†	26 ± 2†
45 min	8 ± 2	18 ± 6*‡	97 ± 15	93 ± 16	89 ± 14	75 ± 15	27 ± 2	25 ± 1‡

CSFP = cerebrospinal fluid pressure; MAP = mean arterial pressure; CPP = cerebral perfusion pressure; ISO = isoflurane; DES = desflurane.

* Significantly different from baseline value ($P < 0.05$).

† PaCO₂ calculated from PETCO₂.

‡ Significantly different from isoflurane value ($P < 0.05$).

significantly greater than the isoflurane value beginning 10 min after the institution of the volatile anesthetic. The rate of increase in CSFP (slope of the change = 0.14 ± 0.08 mmHg · min⁻¹) in the group receiving desflurane was significantly greater than the rate of change in the group receiving isoflurane (slope of the change = -0.02 ± 0.07 mmHg · min⁻¹) throughout the recording period.

Discussion

The results of this study indicate that in patients with supratentorial mass lesions, mean CSFP increased following the administration of 1 MAC desflurane despite prior establishment of hypocapnia. In the group of patients receiving isoflurane, the mean CSFP did not increase. All patients awakened promptly at the end of the surgical procedure. None had a new neurologic deficit. One patient receiving desflurane developed status epilepticus within 30 min of the end of the procedure requiring treatment. This was believed to be a result of the patient's underlying pathology and not of the volatile anesthetic.

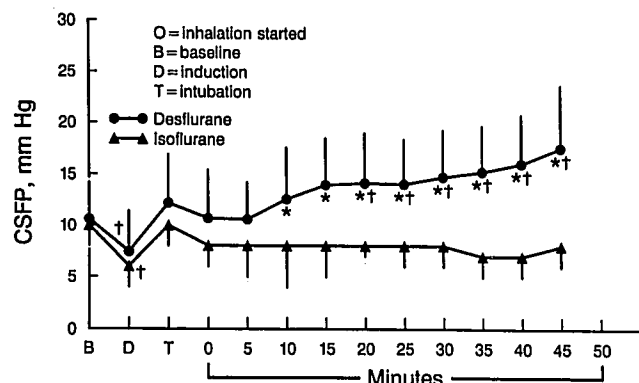


FIG. 1. Mean cerebrospinal fluid pressure (CSFP) (\pm SD) versus time for desflurane and isoflurane groups. Point B = awake baseline CSFP measurement; point D = CSFP measurement immediately after induction; point T = CSFP measurement immediately after intubation; and point O = CSFP when inhalational agent started. *Significantly different from isoflurane values ($P < 0.05$). †Significantly different from awake baseline values.

An important assumption in this study is that lumbar CSFP reflects ICP in patients with supratentorial masses. The patients in this study were clinically free of pathology judged likely to obstruct the CSF pathways between the intracranial and lumbar CSF pathways. We were able to demonstrate patency of these CSF pathways by observing appropriate increases in CSFP with head elevation and digital pressure on the exposed cranial dura at the beginning and end of the study, respectively. In dogs, analysis of volume–pressure relationships at various locations in the neuroaxis during inflation of an epidural balloon revealed that an intracranial-cisterna magna pressure gradient develops when the lateral ventricular pressure is approximately 20 mmHg.⁴ If these canine data can be extrapolated to human subjects, the lumbar CSFP measured in the present study should correlate with the ICP in most patients with supratentorial tumors. None of the patients in the present study had a baseline CSFP equal to or greater than 20 mmHg. Only one patient had a CSFP substantially greater than 20 mmHg during the study period, and this was an observed increase that occurred after institution of the volatile anesthetic.

Previous studies have reported increased ICP in canines undergoing desflurane anesthesia.^{2,5} These studies on the cerebrovascular effects of desflurane have reported that desflurane is a potent cerebral vasodilator producing a dose-related decrease in cerebrovascular resistance that resulted in an increase in cerebral blood flow (CBF).² This vasodilation was associated with an ICP (15 ± 5 mmHg) significantly greater than that in normal unanesthetized canine values (3 ± 1 mmHg).⁶ This increase in ICP was unrelated to depth of anesthesia, remaining unchanged from 0.5 to 2.0 MAC desflurane, and was similar to that observed in dogs receiving isoflurane anesthesia (13 ± 4 mmHg).⁷ A subsequent canine study demonstrated that the cerebral vasculature remained responsive to changes in PaCO₂ during desflurane anesthesia.⁵ Although hyperventilation produced significant increases in cerebrovascular resistance and decreases in CBF, there was no significant effect on ICP (which was 14 ± 3 mmHg at nor-

hypocapnia). These results are qualitatively similar to those obtained in dogs under isoflurane anesthesia,⁸ in which hyperventilation produced a 60% decrease in CBF and a 2-fold increase in cerebrovascular resistance, but ICP (measured as CSFP) did not significantly change. The lack of effect of hyperventilation on ICP in these two canine studies may have been due to the fact that both studies were performed on dogs with normal intracranial compliance.

In the present study, CSFP at the beginning of the administration of desflurane (11 ± 5 mmHg) was not significantly different from the awake baseline value (11 ± 4 mmHg). After 20 min of desflurane administration, the CSFP was 14 ± 4 mmHg, significantly greater than baseline. Based on the canine data, this initial increase might be explained as an increase in CBF and/or cerebral blood volume (CBV) secondary to dilation of the cerebral resistance and capacitance vessels. Such an effect on the cerebral vasculature would be expected to be maximal shortly after beginning the administration of desflurane. Instead, administration of desflurane resulted in a gradual progressive increase in CSFP until the dura was incised. This progressive increase in CSFP in the group receiving desflurane may be due to increases in CSF production and/or decreases in CSF reabsorption. The gradual increase in ICP during time of exposure to desflurane is similar to that reported for enflurane.⁹ It was reported that the increase in ICP during enflurane anesthesia was accompanied by a gradual increase in CSF volume that was not compensated for by a reciprocal decrease in CBV. These findings are consistent with the known effects of enflurane, which increases the rate of formation of CSF¹⁰ and increases the resistance to reabsorption of CSF.¹¹

The effects of desflurane on cerebral hemodynamics differ from those reported for isoflurane. While isoflurane also may produce a dose-related increase in CBF¹² that is accompanied by an increase in ICP,¹³ similar in magnitude to that produced by desflurane, the increase in CBF and ICP can be attenuated with hyperventilation.^{9,14} During isoflurane anesthesia, hyperventilation produces a decrease in CBV, which results in a decrease in ICP. Although CBV gradually increases with time of exposure to isoflurane, this increase in CBV is offset by a reciprocal decrease in CSF volume so that there is no net increase in ICP.⁹ The changes in CBV and ICP that occur with time of exposure to isoflurane are consistent with the effects of isoflurane, which have no effect on the rate of CSF production¹⁵ and decrease the resistance to reabsorption of CSF.¹¹ This results in a decrease in CSF volume with prolonged isoflurane anesthesia.¹⁶ These effects may then explain the clinical finding that, in patients with intracranial tumors undergoing neurosurgery, isoflurane anesthesia together with hyperventilation actually decreases ICP.³

It has also been hypothesized that the continuous increase in CSFP observed in the patients receiving desflurane may be secondary to an increase in cerebral metabolic activity with a resultant increase in CBF and CBV. It has been reported in animals that there is apparent functional tolerance to deep desflurane anesthesia in that the dose-related suppression of neuronal function as measured by EEG is limited with time.^{2,5} This is similar to tolerance reported for N₂O.^{17,18} However, the EEG changes were not accompanied by a measurable change in cerebral metabolic rate or CBF, and these EEG changes have not been observed in humans.¹⁹ Therefore, it is unlikely that tolerance to desflurane is the cause of the observed changes in CSFP with time. Other possible causes of the observed increase in CSFP include increased brain tissue volume from increased brain water content, although the intravenous fluids were restricted and were equal between the two groups, and an increase in intracranial elastance.

The results of the present study also demonstrated that 1 MAC isoflurane did not affect CSFP. This is consistent with data from a previous study in which patients with supratentorial masses given isoflurane had no significant change in CSFP.³ However, some important differences between the present and the previous study deserve attention. First, the patients in the previous study received 50% N₂O in conjunction with the isoflurane. Second, the authors did not measure end-tidal concentrations of isoflurane, and given their methodology it is likely that those patients were receiving less than 1 MAC isoflurane. Therefore, although the results from both studies were similar, there was a difference in the anesthetic technique.

It can be concluded that, in neurosurgical patients with supratentorial mass lesions, administration of 1 MAC desflurane resulted in a gradual but significant increase in mean CSFP. This is in contrast to 1 MAC isoflurane, which did not result in an increase in mean CSFP.

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References

1. Eger EI: Partition coefficients of I-653 in human blood, saline, and olive oil. *Anesth Analg* 66:971-973, 1987
2. Lutz LJ, Milde JH, Milde LN: The cerebral functional, metabolic, and hemodynamic effects of desflurane in dogs. *ANESTHESIOLOGY* 73:125-131, 1990
3. Adams RW, Cucchiara RF, Gronert GA, Messick JM, Michenfelder JD: Isoflurane and cerebrospinal fluid pressure in neurosurgical patients. *ANESTHESIOLOGY* 54:97-99, 1981
4. Takizawa H, Gabra-Sanders T, Miller JD: Analysis of changes in intracranial pressure and pressure-volume index at different locations in the craniospinal axis during supratentorial epidural balloon inflation. *Neurosurgery* 19:1-8, 1986

5. Lutz LJ, Milde JH, Milde LN: The response of the canine cerebral circulation to hyperventilation during anesthesia with desflurane. *ANESTHESIOLOGY* 74:504-507, 1991
6. Milde LN, Milde JH, Gallagher WG: Effects of sufentanil on cerebral circulation and metabolism in dogs. *Anesth Analg* 70:138-146, 1990
7. Newberg LA, Milde JH, Michenfelder JD: Systemic and cerebral effects of isoflurane-induced hypotension in dogs. *ANESTHESIOLOGY* 60:541-546, 1984
8. McPherson RW, Bran JE, Traystman RJ: Cerebrovascular responsiveness to carbon dioxide in dogs with 1.4% and 2.8% isoflurane. *ANESTHESIOLOGY* 70:843-850, 1989
9. Artru AA: Reduction of cerebrospinal fluid pressure by hypocapnia: Changes in cerebral blood volume, cerebrospinal fluid volume and brain tissue water and electrolytes. II. Effects of anesthetics. *J Cereb Blood Flow Metab* 8:750-756, 1988
10. Artru AA, Nugent M, Michenfelder JD: Enflurane causes a prolonged and reversible increase in the rate of CSF production in the dog. *ANESTHESIOLOGY* 57:255-260, 1982
11. Artru AA: Effects of enflurane and isoflurane on resistance to reabsorption of cerebrospinal fluid in dogs. *ANESTHESIOLOGY* 61:529-533, 1984
12. Newberg LA, Milde JH, Michenfelder JD: The cerebral metabolic effects of isoflurane at and above concentrations that suppress cortical electrical activity. *ANESTHESIOLOGY* 59:23-28, 1983
13. Newberg LA, Milde JH, Michenfelder JD: Systemic and cerebral effects of hypotension induced with isoflurane in dogs. *ANESTHESIOLOGY* 60:541-546, 1984
14. Drummond JC, Todd MM: The response of the feline cerebral circulation to P_{aCO_2} during anesthesia with isoflurane and halothane and during sedation with nitrous oxide. *ANESTHESIOLOGY* 62:268-273, 1985
15. Artru AA: Isoflurane does not increase the rate of CSF production in the dog. *ANESTHESIOLOGY* 60:193-197, 1984
16. Artru AA: Relationship between cerebral blood volume and CSF pressure during anesthesia with isoflurane or fentanyl in dogs. *ANESTHESIOLOGY* 60:575-579, 1984
17. Berkowitz BA, Finck AD, Hynes MD, Ngai SH: Tolerance to nitrous oxide analgesia in rats and mice. *ANESTHESIOLOGY* 51:309-312, 1971
18. Ruprecht J, Dworacek B, Bonke B, Dzoljic MR, van Eijnhoven JH, de Vlieger M: Tolerance to nitrous oxide in volunteers. *Acta Anaesthesiol Scand* 29:635-638, 1985
19. Rampil IJ, Lockhart SH, Eger EI, Yasyda N, Weiskopf RB, Cahalan MK: The electroencephalographic effects of desflurane in humans. *ANESTHESIOLOGY* 74:434-439, 1991