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## *Isoflurane and Cerebrospinal Fluid Pressure in Neurosurgical Patients*

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The effect of isoflurane on cerebrospinal fluid pressure (CSFP) was determined in 20 patients undergoing craniotomy for intracranial supratentorial neoplasm or hematoma. In 15 of these patients, following endotracheal intubation, hyperventilation sufficient to result in  $P_{aCO_2}$  25–30 torr was begun simultaneously with the introduction of 1 per cent isoflurane. In the remaining five patients ventilation was equivalent, but normocapnia was maintained by adding  $CO_2$  to the inspired gases. In the hypocapnic patients CSFPs did not increase above awake values (range 5–45 torr) following isoflurane administration. In the normocapnic patients CSFPs consistently increased. In three of these five patients the increases were precipitous, but were corrected rapidly by establishment of hypocapnia. The authors conclude that the known cerebral vasodilator properties of isoflurane can be countered effectively by hypocapnia. Furthermore, unlike the situation with halothane, it is not necessary to establish hypocapnia prior to introducing isoflurane in order to avoid CSFP increases. (Key words: Anesthesia, neurosurgical. Anesthetics, volatile: isoflurane. Brain: blood flow. Cerebrospinal fluid: pressure.)

ISOFLURANE, an inhalational anesthetic, is similar to halothane in its physical, chemical, and anesthetic properties, although its structure (halogenated ether) more closely resembles that of methoxyflurane.<sup>1</sup> Like halothane, isoflurane is a cerebral vasodilator.<sup>2</sup> With halothane, this effect may result in increases in intracranial pressure (ICP), particularly in patients who have decreased intracranial compliance. In a previous study<sup>3</sup> we demonstrated that this undesirable

effect of halothane on ICP is minimized or abolished by establishing hypocapnia ( $P_{aCO_2}$  26–28 torr) for several minutes prior to initiating halothane administration. In contrast, simultaneous initiation of hyperventilation and halothane did not always prevent significant increases in cerebrospinal fluid pressure (CSFP). The purpose of the present study was to examine the effects of isoflurane on CSFP in patients with intracranial space-occupying lesions, and the possible modifying effects of hypocapnia.

### Materials and Methods

Twenty adults undergoing craniotomy for supratentorial neoplasm or hematoma were studied. The protocol was approved by the institutional committee on human studies. Informed consent was obtained from either the patient or the responsible relative. Premedication was limited to atropine, 0.4 mg. Prior to induction of anesthesia, we placed a radial-artery cannula to monitor blood pressure and blood gases and a lumbar subarachnoid malleable needle to monitor CSFP. Pressures were transduced with the zero reference at midcranial level. Loss of CSF during placement of the malleable needle was limited to one or two drops of fluid. All patients were supine with a 10–15-degree head-up tilt. Prior to inducing anesthesia we confirmed the patency of the CSF pathway between the head and the lumbar subarachnoid space by observing the appropriate increase in CSFP when we lifted the patient's head. We reconfirmed patency at the end of the recording period by observing an immediate increase in CSFP with digital pressure on the exposed cranial dura.

With the patient breathing 100 per cent oxygen,

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TABLE 1. Cerebrospinal Fluid Pressure (CSFP), Mean Arterial Blood Pressure (MAP), Cerebral Perfusion Pressure (CPP), and  $P_{aCO_2}$  before and after Isoflurane Administration (Mean  $\pm$  SEM)

	Hypocapnia (n = 15)	Normocapnia (n = 5)
Before induction		
CSFP (torr)	17 $\pm$ 3	15 $\pm$ 3
MAP (torr)	102 $\pm$ 4	98 $\pm$ 5
CPP (torr)	85 $\pm$ 3	83 $\pm$ 4
$P_{aCO_2}$ (torr)	41 $\pm$ 1	38 $\pm$ 3
After isoflurane (at time of maximum change in CSFP; 5–10 min)		
CSFP (torr)	11 $\pm$ 2	23 $\pm$ 2*
MAP (torr)	83 $\pm$ 6	93 $\pm$ 13
CPP (torr)	72 $\pm$ 4	70 $\pm$ 9
$P_{aCO_2}$ (torr)	27 $\pm$ 1	38 $\pm$ 3*

\* Significantly different from hypocapnia group,  $P < 0.05$ .

anesthesia was induced by intravenous injection of thiopental (250–500 mg), followed by succinylcholine (120 mg) and endotracheal intubation. We then administered either gallamine (200 mg) or pancuronium (6–10 mg) intravenously (neither relaxant is known to have any direct effect on ICP) and initiated mechanical ventilation with an inspired gas mixture of 1 per cent isoflurane (calibrated vaporizer), 60 per cent  $N_2O$  and oxygen, at a total gas flow rate of 5 l/min. Minute ventilation was set to produce hypocapnia. In 15 of the 20 patients,  $P_{aCO_2}$  levels of 25–30 torr were achieved, while in five, normocapnia was maintained by the simultaneous addition of  $CO_2$  to the inspired gases. The CSFP and arterial blood

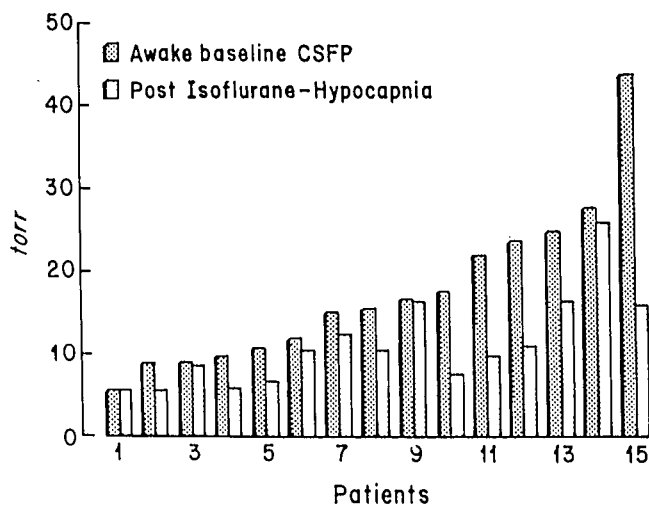


FIG. 1. Changes in cerebrospinal fluid pressure (CSFP) with isoflurane and simultaneous hypocapnia. For each patient the awake CSFP and the CSFP at the time of peak change following simultaneous introduction of isoflurane and hyperventilation are shown. The CSFP did not increase in any patient, and in several patients with elevated awake CSFPs, striking reductions were observed.

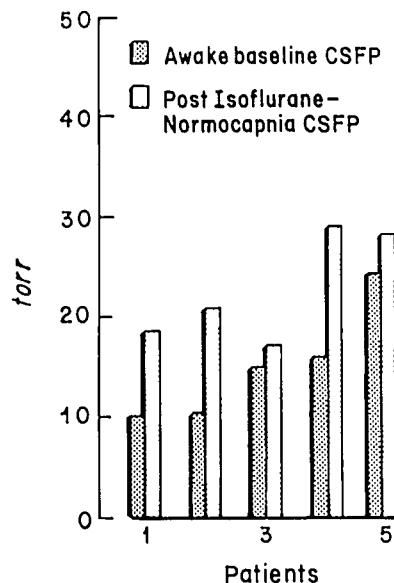


FIG. 2. Changes in cerebrospinal fluid pressure (CSFP) with isoflurane and normocapnia. In all five patients isoflurane at normocapnia increased CSFP. The increases in Patients 1, 2, and 4 were judged to be precipitous and were aborted by decreasing  $P_{aCO_2}$ .

pressure were recorded continuously from just prior to induction of anesthesia until incision of the cranial dura. In those patients initially maintained at normocapnia, inspired  $CO_2$  was discontinued if the CSFP response to isoflurane was arbitrarily judged by the responsible anesthesiologist to be excessive. Blood loss was replaced as needed. Intravenous fluids were limited to a maximum of 500 ml of 5 per cent dextrose in lactated Ringer's solution during the period of recording. Diuretics and hyperosmotic agents were not administered. Mean values in the hypocapnic and normocapnic groups were compared using Student's  $t$  test for unpaired data;  $P < 0.05$  was considered significant.

## Results

The awake preoperative CSFPs in the 20 patients ranged from 5 to 45 torr. The 15 hypocapnic and the five normocapnic subjects had similar mean awake values for CSFP, arterial blood pressure, and  $P_{aCO_2}$  (table 1). The CSFP changes observed in both groups during induction and intubation were similar in type and magnitude to those previously reported.<sup>3</sup> These consisted of an immediate decrease in CSFP after thiopental administration, followed by variable and brief (1–2 min) increases in pressure with laryngoscopy and intubation. Thereafter, the responses of CSFP to isoflurane differed between the two groups. In the hypocapnic patients CSFP never increased above the awake control value following introduction of isoflurane (fig. 1). In four of five patients with elevated preoperative CSFPs (>20 torr) striking

reductions of CSFP occurred with simultaneous initiation of hyperventilation and isoflurane. In the normocapnic group CSFP increased in each patient within 1–3 min following introduction of isoflurane (fig. 2). In three of these patients the rates of increase were judged to be excessive and the increases were aborted by discontinuing inspired  $\text{CO}_2$ ; this resulted in  $\text{Pa}_{\text{CO}_2}$ s near 30 torr within 5 min. In the remaining two patients the increases were slight and transient, peaking at 6–10 min and returning to baseline in 10–20 min. Cerebral perfusion pressures (CPP) at the time of peak changes of CSFP decreased to similar extents in the two groups because of a greater reduction in mean arterial blood pressure in the hypocapnic patients (table 1). During the period of observation  $\text{Pa}_{\text{O}_2}$  remained above 100 torr and  $\text{pH}$  varied appropriately with changes in  $\text{Pa}_{\text{CO}_2}$  in both groups.

### Discussion

Isoflurane has been demonstrated to produce cerebral vasodilation.<sup>2</sup> This effect is dose-related and qualitatively similar to that of halothane. The increase in CSFP that we observed in our normocapnic patients following introduction of isoflurane was anticipated, and can be fully explained by this cerebral vascular effect. We also anticipated that, like halothane, isoflurane introduced simultaneously with initiation of hyperventilation would not predictably block this response, and that prior establishment of hypocapnia would be necessary to do so. This was not the case. Without exception, in 15 patients with intracranial mass lesions CSFP did not increase following simultaneous initiation of hyperventilation and isoflurane administration.

Why isoflurane differs from halothane in this regard is not known. A study in man suggests that isoflurane may be a less potent cerebral vasodilator<sup>§</sup>,

§ Murphy FL, Kennell EM, Johnstone RE, et al: The effects of enflurane, isoflurane, and halothane on cerebral blood flow and metabolism in man. Abstracts; annual meeting of the American Society of Anesthesiologists, October 1974, pp. 61–62.

this was not confirmed by a canine study.<sup>2</sup> In addition, equivalent concentrations of halothane and isoflurane were not used in the two studies. In the halothane study (MAC = 0.74 per cent) inspired concentrations ranged from 0.5 to 1.0 per cent (with 60 per cent  $\text{N}_2\text{O}$ ). In the present study, inspired isoflurane concentration (MAC = 1.28 per cent) was maintained at 1 per cent (with 60 per cent  $\text{N}_2\text{O}$ ). Thus, it is probable that the isoflurane concentrations used (relative to MAC) were, in most instances, somewhat less than those of halothane. This, together with a possibly lesser effect of isoflurane on cerebrovascular resistance, may explain the differences observed.

Regardless, it is clear that hypocapnia is necessary to prevent CSFP increases in patients at risk when using isoflurane for maintenance of anesthesia. It would also seem prudent to induce hypocapnia prior to introducing isoflurane even though the results of the present study suggest that this is not necessary, at least in the majority of patients. In this regard, one must remember that hypocapnia is a relative state referenced to the patient's awake ventilatory status. This was illustrated dramatically by one patient in the normocapnic group of this study who, because of his CNS disease, had been spontaneously hyperventilating for three days preoperatively. While  $\text{Pa}_{\text{CO}_2}$  was maintained at the awake "normocapnia" level of 27 torr during isoflurane administration, his CSFP increased markedly and this trend was reversed only after  $\text{Pa}_{\text{CO}_2}$  was decreased to 23 torr. An opposite but equally distorted response might be expected in patients with chronically elevated blood  $\text{CO}_2$  tensions in whom normalization of CSF  $\text{pH}$  has occurred.

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