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The Effect of Alfentanil on Cerebral Blood Flow Velocity and Intracranial Pressure during Isoflurane-Nitrous Oxide Anesthesia in Humans

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Background: **Intravenous opioids often are used as a component of anesthesia during neurosurgical procedures. However, the cerebrovascular effects of alfentanil administered to patients are controversial. In this study, the effect of alfentanil in patients with and without intracranial pathology was studied.**

Methods: **Sixteen neurosurgical patients and 16 patients scheduled for orthopedic procedures were studied. Anesthesia was maintained with isoflurane (0.4–0.6 vol% inspired) and nitrous oxide (50%) in oxygen. Within each group, the patients were assigned randomly to receive either 25 or 50 μg/kg intravenous alfentanil. During normocapnia and without surgical stimulation, the right middle cerebral artery flow velocity, and mean arterial pressure were measured every minute for 10 min after the administration of alfentanil. In the neurosurgical patients, intracranial pressure, cerebral perfusion pressure, and cerebral arteriovenous oxygen content difference were determined also. Neurosurgical patients received intravenous phenylephrine to maintain mean arterial pressure as needed.**

Results: **There was no significant change in middle cerebral artery flow velocity and arteriovenous oxygen content difference in the neurosurgical patients. In the high-dose group, intracranial pressure increased by 2 mmHg at 4 min but was otherwise unchanged. Despite phenylephrine administration, there was an immediate but transient decrease in mean arterial pressure in the high-dose group and a corresponding decrease in cerebral perfusion pressure. In the orthopedic patients, mean arterial pressure decreased significantly. Middle cerebral artery flow velocity decreased in the high-dose group but remained unchanged in the low-dose group.**

Conclusions: **Based on the flow velocity and metabolic data, alfentanil is neither a cerebral vasodilator nor a vasoconstrictor in these doses. Furthermore, there was no clinically significant increase in intracranial pressure when alfentanil was administered in either dose. (Key words: Anesthesia: neurosurgical. Anesthetics, intravenous: alfentanil; opioid. Brain: cerebral metabolism; cerebral blood flow velocity; intracranial pressure; perfusion pressure. Equipment: intracranial pressure; transcranial Doppler.)**

SYNTHETIC opioids often are used as part of the anesthetic management of neurosurgical patients. These agents purportedly have little or no effect on the cerebral vasculature and therefore are safe for patients at risk of intracranial hypertension. This supposition has been questioned by a number of investigations, although the data remain inconclusive.#,¶,**,†† Marx *et al.*# and Jung *et al.*[1] reported that both sufentanil and alfentanil increased cerebrospinal fluid pressure (CSFP) in humans, whereas fentanyl did not. The mechanism of the increase in CSFP was thought to be direct arterial cerebrovasodilation. Sufentanil has been shown to increase cerebral blood flow (CBF) in dogs[2] but not in normal healthy humans.[3] A similar canine study with alfentanil failed to show cerebrovasodilation,†† and no flow studies have been conducted in humans. More re-

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cently, Markovitz *et al.*[4] studied children with increased intracranial pressure (ICP) undergoing ventriculoperitoneal shunt revisions and reported there was no increase in ICP in response to alfentanil administration. Alfentanil caused a concentration-dependent contraction of canine basilar arteries *in vitro*¶ and minimal cerebral vasoconstriction with slightly decreased ICP in rats *in vivo*.** The purpose of the present investigation was to determine, in a dose-response study, what effect alfentanil has on CBF velocity and whether it causes ICP to increase in patients with abnormal intracranial elastance[5] and therefore at risk of intracranial hypertension.

Materials and Methods

The study was approved by the University of Washington Human Subject Review Committee and informed consent was obtained from each patient or guardian. Sixteen neurosurgical patients (ASA physical status 2 or 3) and 16 patients (ASA physical status 1 or 2) scheduled for elective orthopedic surgery were enrolled in the study. The ages and weights of each group (mean ± SD) were 48.9 ± 12.1 yr (neurosurgical patients) and 35.9 ± 12.1 yr (orthopedic patients) and 74.5 ± 12.6 kg *versus* 72.8 ± 12.6 kg, respectively. Seven of the neurosurgical patients had supratentorial tumors; the rest had intracranial aneurysms. No grade V patients (Hunt and Hess classification) were enrolled. In the low-dose group, three patients were grades I–III and two were grade IV, whereas four patients in the high-dose group were in grades I–III. Within each neurosurgical and orthopedic group, patients were assigned randomly to receive either the "low-dose" alfentanil, 25 μg/kg, or the "high-dose" alfentanil, 50 μg/kg.

No premedication was administered. Routine monitors including electrocardiogram, pulse oximetry, and end-tidal capnometry were used in all patients. Additionally, bilateral fronto-occipital electroencephalogram (EEG) was recorded and processed using aperiodic analysis (Lifescan, Diatek, San Diego, CA). The activity edge (the frequency that represents the upper limit of the frequency below which 80% of the EEG power is contained) was recorded continuously. The right middle cerebral artery was insonated transtemporally using a transcranial Doppler (Transpect, Medasonics, Fremont, CA). The mean cerebral artery flow velocity (Vmca) was calculated from the formula: Vmca = (systolic flow velocity − diastolic flow velocity)/3 + diastolic flow velocity. The technique of Vmca determination using the 2-MHz transcranial Doppler has been described previously.[6] Briefly, the Doppler probe was anchored securely to the right temporal area using a head harness or modified Greenberg flexible arm so that the angle of insonation remained constant throughout the study. Doppler signals from the right middle cerebral artery were identified and measured at a depth of 45–50 mm. The shift in frequency spectra of the Doppler signal converted into velocity was displayed on a video monitor, and peak systolic and diastolic middle cerebral artery flow velocities in centimeters per second were obtained manually using the cursor to read the average value from two to three cardiac cycles. Manual rather than automatic readings were used because of the often-present artifacts from electrocardiogram or other electrical sources. To eliminate respiratory fluctuations, readings were taken during the end-expiratory phase.

Additional monitors in the neurosurgical group included an indwelling radial arterial catheter, a retrograde jugular bulb catheter, and one of the following: a subarachnoid bolt (four patients), a Camino catheter (five patients), or a lumbar subarachnoid drain (seven patients). The subarachnoid bolt or Camino catheter (San Diego, CA) for ICP monitoring was either *in situ* or placed following induction of anesthesia. Patients undergoing tumor resections had lumbar subarachnoid drains placed following induction. No patient whose ICP was monitored *via* lumbar subarachnoid drain had obstructive hydrocephalus, and a pulsatile waveform on the monitor was ascertained before commencement of the study. A 5.5-inch 16-G catheter was inserted into the right internal jugular vein and advanced in a retrograde fashion into the jugular bulb.[7] Placement was verified in the first three patients using plain x-ray. Subsequently, catheters were placed according to the length of the catheter with the tip measured to be just behind the mastoid process.

Anesthesia was induced with 4–6 mg/kg thiopental, 0.1 mg/kg vecuronium, and 1.5 mg/kg lidocaine, and maintained with 50% nitrous oxide in oxygen and 0.4–0.6 vol% (inspired) isoflurane following tracheal intubation. Mechanical ventilation was begun. Following at least 15 min of stable anesthesia in all groups, and during normocapnia with stable hemodynamics, baseline measurements were obtained, and patients then received either low-dose or high-dose alfentanil intravenously as a bolus. Surgical stimulation only commenced after the completion of the study. In the neurosurgical patients, because of the additional monitors

that were placed, usually 30 min elapsed before alfentanil was given. Mean cerebral artery flow velocity, mean arterial pressure (MAP), HR, and processed EEG (activity edge) were measured and recorded every minute for 10 min. The neurosurgical patients also had ICP or CSFP measurements recorded every minute and simultaneous arterial and jugular venous blood samples obtained at times 0, 5, and 10 min. Arteriovenous oxygen content difference ($AVDO_2$) was calculated according to the following formula: $AVDO_2 = [Hgb \times (Sa_{O_2} - SjV_{O_2}) \times 1.39] + [(Pa_{O_2} - PjV_{O_2}) \times 0.003]$ vol%, where Hgb = hemoglobin concentration, Sa_{O_2} = arterial oxygen saturation, SjV_{O_2} = jugular bulb oxygen saturation, Pa_{O_2} = arterial oxygen partial pressure, and PjV_{O_2} = jugular bulb oxygen partial pressure. Blood gas partial pressures and hemoglobin oxygen saturations were determined using a Stat Profile 5 blood gas analyzer (Nova Biomedical, Waltham, MA).

Phenylephrine was administered to the neurosurgical patients if the MAP decreased from baseline values. The orthopedic patients received phenylephrine only if the MAP was 60 mmHg or below. Changes after alfentanil administration were analyzed within each group using two-way analysis of variance for repeated measures to assess the influence of dose and time. Dunnett's test was used for *post hoc* testing. A P value of less than .05 was considered significant.

Results

The ICP results for both neurosurgical groups are shown in figure 1. All values are reported as mean ± SE. In the high-dose group, ICP increased by 2 mmHg at 4 min, a difference that reached statistical significance. Otherwise, there were no changes in ICP in either group.

Results for MAP, ICP, cerebral perfusion pressure (CPP), Vmca, Pa_{CO_2}, HR, and EEG for both neurosurgical groups are presented in table 1. Mean arterial pressure was unchanged in the low-dose group but decreased significantly in the high-dose group in the first 3 min despite phenylephrine administration in three patients. Cerebral perfusion pressure correspondingly decreased during this period. There was no change in CPP in the low-dose neurosurgical group.

There was no significant change in Vmca after alfentanil administration, and Pa_{CO_2} was unchanged over the course of the study. There was a significant decrease in EEG activity edge at times 2 and 3 min in the low-dose group and at times 1 and 2 min in the high-dose group (table 1). There was no significant change in

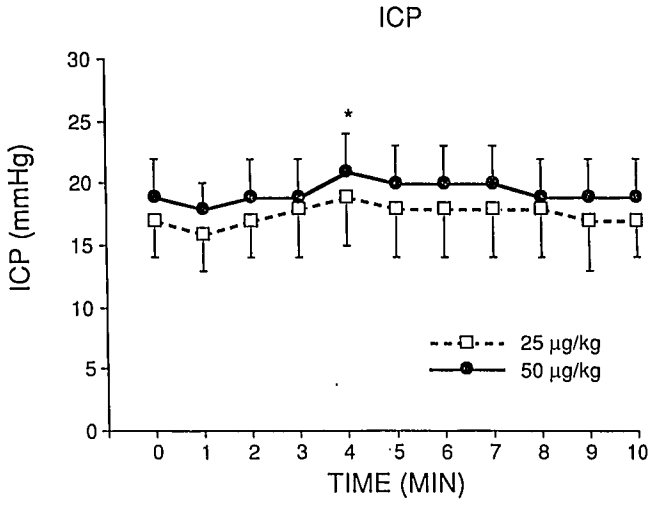

Fig. 1. Intracranial pressure (ICP) measurements following low-dose (25 µg/kg) and high-dose (50 µg/kg) alfentanil administration in neurosurgical patients. All values are mean ± SE (overlapping bars removed for clarity), and n = 8 for all measurements. The ICP at 4 min in the high-dose group was significantly higher than baseline value (P = .05). Otherwise, there was no change in ICP with either dose.

$AVDO_2$ in either the low-dose or the high-dose group (fig. 2).

Mean arterial pressure, Vmca, Pa_{CO_2}, HR, and EEG results for both orthopedic groups are shown in table 2. All values are presented as the mean ± SE. Following the administration of alfentanil, MAP in both groups decreased significantly to a mean value of 64 ± 3 mmHg and 62 ± 4 mmHg, respectively, by 4 min. Subsequently, the MAP increased but had not reached baseline values by 10 min. In both groups, decreases in MAP at all times after 3 min were significant. After administration of alfentanil, the flow velocity decreased significantly in the high-dose group but remained unchanged in the low-dose group.

The EEG activity edge in the low-dose group was unchanged by alfentanil initially but increased slightly near the end of the study. In the high-dose group, there was a transient decrease in EEG activity edge immediately following alfentanil administration.

Discussion

These data show that alfentanil administration was not associated with a clinically significant increase in ICP in patients who were at risk of intracranial hypertension. Furthermore, our data suggest that, in the doses administered, alfentanil has negligible effects on cerebral function (EEG), flow velocity (Vmca), metab-

Table 1. Results from the Neurosurgical Patients in Response to Low- and High-dose Alfentanil

	0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min
Low dose (25 μg/kg)											
MAP (mmHg)	79 ± 3	73 ± 5	76 ± 3	80 ± 2	78 ± 2	76 ± 2	74 ± 3	72 ± 3	76 ± 3	74 ± 3	77 ± 3
ICP (mmHg)	17 ± 3	16 ± 3	17 ± 3	18 ± 4	19 ± 4	18 ± 4	18 ± 4	18 ± 4	18 ± 4	17 ± 4	17 ± 3
CPP (mmHg)	62 ± 4	57 ± 6	58 ± 6	62 ± 5	60 ± 5	58 ± 4	56 ± 5	54 ± 5	59 ± 5	57 ± 5	60 ± 5
Vmca (cm/s)	52 ± 7	50 ± 7	50 ± 6	50 ± 7	52 ± 7	51 ± 6	50 ± 6	50 ± 6	51 ± 6	53 ± 6	50 ± 5
Pa_{CO_2} (mmHg)	37 ± 2	36 ± 2	36 ± 2	37 ± 2	35 ± 2	36 ± 1	36 ± 1	37 ± 1	36 ± 2	36 ± 2	36 ± 2
HR (beats/min)	74 ± 5	64 ± 5*	61 ± 5*	58 ± 5*	58 ± 4*	59 ± 5*	60 ± 4*	61 ± 4*	61 ± 4*	61 ± 4*	60 ± 4*
EEG (activity edge) Hz	8 ± 1	6 ± 1	5 ± 1*	6 ± 1*	6 ± 1	6 ± 1	8 ± 1	8 ± 1	8 ± 1	8 ± 1	8 ± 1
High-dose (50 μg/kg)											
MAP (mmHg)	80 ± 5	67 ± 4*	71 ± 5*	72 ± 2*	77 ± 4	77 ± 3	77 ± 3	74 ± 4	79 ± 3	80 ± 4	79 ± 4
ICP (mmHg)	19 ± 3	18 ± 2	19 ± 3	19 ± 3	21 ± 3*	20 ± 3	20 ± 3	20 ± 3	19 ± 3	19 ± 3	19 ± 3
CPP (mmHg)	61 ± 5	49 ± 3*	53 ± 4*	50 ± 5*	57 ± 3	58 ± 3	58 ± 3	56 ± 4	60 ± 3	62 ± 3	61 ± 3
Vmca (cm/s)	46 ± 5	41 ± 3	42 ± 3	44 ± 3	44 ± 4	41 ± 3	43 ± 5	43 ± 5	45 ± 4	45 ± 5	44 ± 4
Pa_{CO_2} (mmHg)	37 ± 2	37 ± 1	36 ± 1	36 ± 1	37 ± 1	37 ± 1	38 ± 1	37 ± 1	37 ± 1	37 ± 1	37 ± 1
HR (beats/min)	71 ± 3	58 ± 4*	54 ± 3*	53 ± 3*	53 ± 3*	54 ± 3*	54 ± 3*	54 ± 3*	54 ± 2*	55 ± 2*	55 ± 3*
EEG (activity edge) Hz	10 ± 1	8 ± 1*	8 ± 1*	9 ± 1	9 ± 1	9 ± 1	8 ± 1	9 ± 1	9 ± 1	9 ± 1	9 ± 0

Values are mean ± SE; n = 8 for all cells.

MAP = mean arterial pressure; ICP = intracranial pressure; CPP = cerebral perfusion pressure; Vmca = mean cerebral artery flow velocity; Pa_{CO_2} = arterial carbon dioxide tension; HR = heart rate; EEG = electroencephalogram.

*$P < .05$ *versus* time 0.

olism ($AVDO_2$), and ICP. With the exception of systemic blood pressure and its corresponding effect on CPP, no significant difference between the two dose groups was observed.

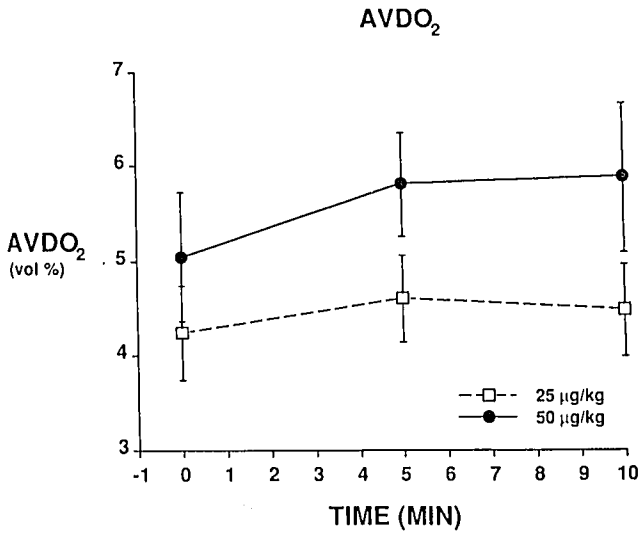

Fig. 2. Arteriovenous oxygen content difference ($AVDO_2$) following low-dose (25 μg/kg) and high-dose (50 μg/kg) alfentanil administration in neurosurgical patients. All values are mean ± SE, and n = 8 for all measurements. There was no significant change with low-dose alfentanil. The increase in $AVDO_2$ with high-dose alfentanil at times 5 and 10 min did not reach statistical significance.

Responses of the orthopedic patients to the two doses of alfentanil were similar to the neurosurgical patients in most respects. There was no change in Vmca in the low-dose group, but a significant decrease occurred in the high-dose group. There was no initial change in EEG activity in the low-dose group, and the subsequent increase in activity toward the end of the study can be attributed to a rebound or overshoot phenomenon as the effect of low-dose alfentanil waned. A significant transient decrease in EEG activity was observed in the high-dose group. Superficially, these observations suggest that alfentanil is a dose-related indirect arterial cerebrovasoconstrictor (decrease in flow coupled to decrease in metabolism), and that this response is attenuated in patients with increased ICP. However, careful examination of the systemic blood pressure data led us to believe that the observed decrease in Vmca in the high-dose group is more likely a result of the untreated systemic hypotension. In a number of these patients, the blood pressure had decreased to below the limit of autoregulation (MAP < 50–60 mmHg) and therefore resulted in a decrease in flow.

Thus, our findings are similar to data reported in animal studies.¶,**,†† How then do we reconcile our findings with other human studies in which alfentanil was reported to cause an increase in ICP in patients with altered intracranial elastance? Marx *et al.*# reported that alfentanil increased CSFP in patients with intra-

Table 2. Results from the Orthopedic Patients in Response to Low- and High-dose Alfentanil

	0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min
Low-dose (25 μg/kg)											
MAP (mmHg)	80 ± 4	77 ± 5	66 ± 3*	64 ± 3*	64 ± 3*	65 ± 3*	65 ± 4*	68 ± 3*	71 ± 4*	74 ± 3*	74 ± 4
Vmca (cm/s)	56 ± 8	52 ± 6	51 ± 7	53 ± 7	52 ± 7	55 ± 8	55 ± 8	55 ± 8	56 ± 8	54 ± 6	56 ± 7
Pa_{CO_2} (mmHg)	42 ± 2	41 ± 2	40 ± 2*	40 ± 2*	40 ± 2*	40 ± 2*	40 ± 2*	40 ± 2*	40 ± 2*	40 ± 2*	41 ± 2*
HR (beats/min)	67 ± 4	61 ± 3	55 ± 3*	52 ± 3*	52 ± 3*	51 ± 3*	52 ± 3*	52 ± 4*	52 ± 3*	52 ± 4*	52 ± 4*
EEG (activity edge) Hz	12 ± 1	12 ± .5	11 ± 0	12 ± 1	13 ± 1	13 ± 1	14 ± 1*	13 ± 1	14 ± 1*	14 ± 1*	14 ± 1*
High-dose (50 μg/kg)											
MAP (mmHg)	81 ± 6	72 ± 5*	60 ± 4*	60 ± 5*	62 ± 4*	65 ± 4*	66 ± 3*	67 ± 4*	68 ± 4*	67 ± 3*	69 ± 4*
Vmca (cm/s)	48 ± 5	43 ± 4*	42 ± 3*	42 ± 3*	44 ± 3*	43 ± 4*	43 ± 4*	44 ± 4*	44 ± 4*	45 ± 4*	45 ± 3*
Pa_{CO_2} (mmHg)	37 ± 1	37 ± 1	36 ± 1	36 ± 1	35 ± 1	36 ± 1	36 ± 1	36 ± 1	36 ± 1	36 ± 1	36 ± 1
HR (beats/min)	78 ± 4	64 ± 4*	57 ± 4*	55 ± 4*	54 ± 3*	55 ± 3*	55 ± 3*	55 ± 3*	55 ± 2*	56 ± 2*	56 ± 3*
EEG (activity edge) Hz	11 ± 1	9 ± 1*	10 ± 1*	11 ± 1	11 ± 1	12 ± 1	12 ± 1	12 ± 1	12 ± 1	12 ± 1	11 ± 1

Values are mean ± SE.

MAP = mean arterial pressure; Vmca = mean cerebral artery flow velocity; Pa_{CO_2} = arterial carbon dioxide tension; HR = heart rate; EEG = electroencephalogram.

* $P < .05$ *versus* time 0.

cranial tumors. The baseline CSFP was 12.6 ± 1.8 mmHg, and the peak increases was 2.0 ± 0.6 mmHg. As they observed similar findings in patients who received sufentanil, which has been reported to cause an increase in CBF in dogs,[2] they postulated that alfentanil also may be a direct cerebral arterial vasodilator. However, in this initial report by Marx *et al.*,# not only was the absolute magnitude of increase in ICP small, but MAP was not supported, and therefore indirect cerebrovasodilation caused by autoregulatory compensation may have explained their findings. More recently, Moss[8] reported on the response of five adult patients with hydrocephalus to the intravenous administration of 1 mg alfentanil and observed a mild to moderate increase in ICP in association with a significant decrease in MAP. He, too, postulated that, at least in some of these patients, vasodilation from compensatory autoregulation may have contributed to the increase in ICP. These observations are consistent with our findings, as we supported the MAP in the neurosurgical patients with phenylephrine; therefore, no autoregulatory vasodilation should occur, and we observed no clinically significant increase in ICP.

In a subsequent study by Jung *et al.*,[1] MAP was supported and they still observed a significant albeit small increase of 3.5 mmHg in CSFP from a baseline of 9.5 ± 1.3 mmHg. These authors hypothesized that alfentanil causes direct cerebral arterial vasodilation, but this has never been documented. With some minor exceptions, our protocol and experimental design were similar to the study of Jung *et al.* Our patients had higher baseline ICP, and we also measured Vmca and $AVDO_2$. Based on our observations, we conclude that alfentanil causes neither arterial cerebrovasodilation nor vasoconstriction. Other potential causes of increase in ICP, however, have not been ruled out. These include cerebral venodilation leading to increase in blood volume, increase in brain volume, or increase in cerebrospinal fluid volume. Considering the time course of the reported increases in ICP,[1,#] however, it is difficult to imagine how alfentanil may affect nonvascular compartments in such a rapid fashion. Moreover, with the exception at 4 min in the high-dose group, we did not observe any significant increase in ICP in our patients despite a relatively high baseline ICP.

Our ICP findings also are remarkably similar to the results recently reported by Markovitz *et al.*[4] They administered a cumulative dose of alfentanil (70 μg/kg) to children with increased ICP and observed no statistically significant increases in ICP. However, they reported one individual with a 16-mmHg increase in ICP. One patient in each of our neurosurgical groups also had an increase in ICP of 5 mmHg 2 to 3 min after alfentanil administration. There was no change in Vmca at the time of the increase in ICP. This increase in ICP could be due to a time lag in our blood pressure support, and consequently, we were unable to prevent the onset of the compensatory cerebral vasodilation. These observations suggest that we should remain cautious with the administration of alfentanil in these patients. Clinical studies examining intraoperative brain conditions, however, failed to discern any difference be-

tween alfentanil and sufentanil or fentanyl, either in retractor pressure[9] or in the observed brain "tightness."[10]

Potential criticisms in the design of our study include patient selection, use of the transcranial Doppler, and the background anesthetic. In selecting the neurosurgical patients, it would have been ideal to study patients with similar cerebral volume/pressure dynamics. However, because of a difference in compensatory mechanisms, even patients with tumors of similar size may not have similar ICPs. Therefore, it is difficult to select a population of comparable patients by either clinical or radiographic criteria. Consequently, we chose to study a heterogeneous group of patients and randomly assign them to two dosage groups. The average ICP was nearly identical in both groups, as was the range. Given the overall increased baseline ICPs of these patients, one might expect them to have increased intracranial elastance and therefore would be likely to have an exaggerated pressure response to factors that increase the volume of intracranial contents.

The transcranial Doppler was chosen because it can measure rapidly occurring changes in blood flow velocity. The previously reported increases in ICP appear to be transient.#,[1] If this increase is secondary to an alteration in CBF, the change cannot be measured easily by conventional CBF measurement techniques. The potential drawback of transcranial Doppler technology is that it measures blood flow velocity and not actual CBF. Correlation between Vmca and absolute CBF has been shown to be poor.[11] However, relative changes in Vmca within each individual correlate well with changes in CBF.[11] Variations in flow velocity with arterial carbon dioxide tension also have been shown to agree with reported variations in CBF.[12] Therefore, changes in Vmca can be used to detect either dilation or constriction of the cerebral vasculature in a given patient.

This premise also depends on the assumption that the diameter of middle cerebral artery is not influenced by alfentanil. Since the middle cerebral artery is a conductance vessel and change in cerebrovascular resistance is effected largely by change in resistance vessels, it is unlikely that alfentanil would have direct vasodilatory or vasoconstrictive effects on the middle cerebral artery. In addition, cerebral vasodilation without a corresponding increase in cerebral metabolic rate should decrease $AVDO_2$. As $AVDO_2$ did not decrease, there is no evidence to suspect that alfentanil in these doses increases cerebral metabolic rate, hence cerebrovasodilation could not have occurred. The transient decrease in EEG activity edge further substantiated that alfentanil did not have cerebral stimulatory effect. We therefore conclude that the lack of change in Vmca accurately reflects the lack of change in CBF.

Two doses of alfentanil (25 μg/kg and 50 μg/kg) were studied to help determine whether any potential cerebrovascular effect of alfentanil was dose-dependent. We chose to study the drug during a relatively steady anesthetic state and prior to surgical stimulation because changes in Pa_{CO_2} and stimulation such as tracheal intubation may have profound effects on cerebral hemodynamics. The anesthetic regimen was chosen to allow an adequate inspired oxygen concentration and to ensure loss of consciousness. It may be argued that both isoflurane and N_2O could cause cerebrovascular vasodilation. However, the dose of isoflurane was below that which is thought to cause cerebrovasodilation, and the lack of increase in flow velocity during isoflurane anesthesia at similar doses has been documented.[13] There was no change in ICP in patients who had monitors in place before induction of anesthesia. Furthermore, if the background anesthetic had produced vasodilation, it would have tended to increase intracranial elastance and exaggerate any vasodilatory effects of alfentanil.

In conclusion, we found no evidence of cerebrovasodilation in response to alfentanil administration as measured by Vmca and $AVDO_2$ data in a heterogeneous group of neurosurgical patients. Furthermore, there was no clinically significant change in ICP following these two doses of alfentanil administration. One should be aware, however, that some patients may experience a significant decrease in MAP and perhaps CPP following alfentanil administration.

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