Prediction of late ischemic complications after cerebral aneurysm surgery by the intraoperative measurement of cerebral blood flow

JOHN D. PICKARD, F.R.C.S.(Ed.), MARGARET MATHESON, B.Sc., JAMES PATTERSON, B.Sc., AND DAVID WYPER, PH.D.

Divisions of Neurosurgery and Clinical Physics, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland

The response of cerebral blood flow (CBF) to drug-induced hypotension was measured in 20 patients who underwent craniotomy for clipping of a cerebral aneurysm following subarachnoid hemorrhage. A modified intravenous xenon-133 injection technique was used to monitor CBF. In 15 patients, CBF increased significantly with hypotension, and only one developed a late neurological deficit. In five patients, CBF fell with halothane-induced hypotension, and four developed delayed neurological deficits. Measurement of the intraoperative CBF response to halothane-induced hypotension may reveal those patients at greatest risk of developing late neurological deficits and who require more intensive postoperative monitoring and early use of the induced hypertension technique.

KEY WORDS • subarachnoid hemorrhage • cerebral ischemia • controlled hypotension • cerebral blood flow • cerebral aneurysm

INTRACRANIAL surgery for ruptured cerebral aneurysms may be followed by the late development of cerebral ischemia, starting some days after an apparently uncomplicated operation. Delayed cerebral ischemia may also follow carotid ligation for internal carotid artery aneurysms. Measurement of cerebral blood flow (CBF) has revealed that the ability of the cerebral circulation to compensate for changes in arterial blood pressure (autoregulation of CBF) is impaired in both man and primate following a recent subarachnoid hemorrhage (SAH). The probability of an ischemic episode after carotid ligation is much higher if CBF falls more than minimally with carotid clamping. Hence, delayed ischemic episodes may reflect the inability of part of the cerebral circulation in some individuals to compensate for periods of hypotension or hypoxia. Two findings are compatible with this concept: the deficit sometimes develops in association with a fall in the patient's blood pressure, and it may be reversed by raising the patient's blood pressure and expanding his blood volume.

We have asked the question: what is the incidence of impaired autoregulatory capacity of CBF following SAH? Are patients with such impairment at greater risk of developing late cerebral ischemia after intracranial aneurysm surgery? For ethical reasons, the only occasion when the response of the cerebral circulation to hypotension can be assessed is intraoperatively, when hypotension is deliberately produced to assist dissection and clipping of the aneurysm.

Clinical Material and Methods

The full details of our modification of the intravenous xenon-133 (133Xe) injection technique for the intraoperative situation have been published recently. Global CBF is obtained from the clearance of 133Xe measured by a collimated scintillation counter mounted unobtrusively under the head by clamping the detector onto the headrest support. Analysis of the head clearance curve is restricted to the period between 1 and 3 minutes after the start of the curve, and initial-slope analysis is used for CBF computation for three reasons: 1) physiological

*Collimated scintillation counter manufactured by Nuclear Enterprises, Sighthill, Edinburgh, Scotland.
parameters cannot be considered constant over longer time periods; 2) a bicompartimental model is probably not valid for the anesthetized sick brain; and 3) this time period, combined with pulse-height analysis, minimized the problem of scattered radiation from the airways.

Twenty patients with proven SAH were studied. There were four males and 16 females, and their mean age was 46 years ± 11 SD. The mean period from the last SAH to craniotomy was 11 ± 5 days (range, 3 to 28 days). Ten patients had preexisting systemic hypertension (diastolic blood pressure greater than 80 mm Hg). None of the patients was diabetic. Seventeen of the patients were premedicated with dexamethasone (4 mg every 6 hours) and five patients received tranexamic acid (1.5 gm every 6 hours). On the Hunt and Hess scale, their preoperative grades were as follows: 12 were in Grade I, four in Grade II, and four in Grade III; there were no Grade IV or V patients. Four aneurysms were associated with the posterior communicating artery, five with the anterior communicating artery, six with the middle cerebral artery, two with the internal carotid bifurcation, and one each with the basilar, ophthalmic, and pericallosal arteries.

Anesthesia was induced with sodium thiopentone (250 to 400 mg intravenously), and endotracheal intubation was assisted using suxamethonium. Anesthesia was maintained by hyperventilation with nitrous oxide (65%) and oxygen (35%). Supplements of diazepam, fentanyl, pentazocine, or Althesin were given, and muscle relaxation achieved with pancuronium, alcuronium, or d-tubocurarine. The variety of supplementary agents reflects our intention not to require the neuroanesthetist to alter his normal practice in any way.

Halothane was used as the main hypotensive agent in 19 of the 20 patients, supplemented with Arfonad (trimethaphan camysylate) in one and sodium nitroprusside in two patients. Althesin (alphadolone acetate) was used in one patient. Spinal drains were used routinely, and mannitol (25 gm) was given prior to any brain retraction in 11 patients. In the following analysis, no CBF values were used that were obtained within 15 minutes of the administration of mannitol. An arterial cannula was used to monitor blood pressure and to take samples for arterial \( pCO_2 \), \( pO_2 \), and pH.

**Results**

**Cerebral Blood Flow**

There were two patterns of response of CBF to hypotension prior to the aneurysm being clipped. In 15 of the 20 patients (Group A), CBF increased by a mean of 58 ± 14% when arterial blood pressure was reduced from a mean of 84 ± 5 to 51 mm Hg ± 2 SEM (Fig. 1). In sharp contrast were the other five patients (Group B), in whom CBF fell by 48 ± 12% despite a similar hypotensive response. When the mean arterial blood pressure returned to baseline after the aneurysm was clipped, there was a small increase in CBF in Group A but none in Group B (Fig. 2). Although baseline flows appeared to be higher in Group B than in Group A patients, the difference was not statistically significant.

**Postoperative Course**

Groups A and B did not differ with respect to age (45 years ± 11 (SD) and 48 ± 9 years, respectively), delay between last bleed and operation (11 ± 6 and 10 ± 2 days), hypertensive status, steroid premedication, preoperative grade, site of aneurysm, or incidence of intraoperative complications (five of 15 and two of five, respectively).

Both groups included patients with immediate postoperative deficits appropriate to the particular aneurysm (Group A: six transient and one persistent deficit; Group B: one persistent deficit). However, Groups A and B did differ in their late postoperative behavior; the incidence of freshly developing late deficits was much greater in Group B (four of five
Intraoperative cerebral blood flow

![Graph showing CBF and Mean Arterial Pressure](image)

**Fig. 2.** Measurement of intraoperative global cerebral blood flow (CBF) before and after the period of drug-induced hypotension. The aneurysm was clipped between the two measurements.

patients) than in Group A (one of 15 patients); (p < 0.001, chi-square test).

The late deficit in the Group A patient (Case 3), who had a right middle cerebral aneurysm, was an exacerbation of a preoperative left hemiparesis that became more dense 48 hours postoperatively in association with poorly controlled seizures. A small low-density area of possible infarction in the right middle cerebral artery distribution was already present on a preoperative CT scan. In two Group B patients (Cases 7 and 11), the late deficit was associated with falls in blood pressure. One patient with a right ophthalmic aneurysm (Case 11) was well until the 4th day after operation, when she became confused and drowsy on sitting up. She developed progressive, permanent blindness in the right eye. The other patient, with a right middle cerebral aneurysm (Case 7) was well until the 7th day, when her blood pressure fell from 160/100 to 110/60 mm Hg, she developed a left facial palsy, and became confused for 48 hours. The deficit resolved when the blood pressure returned to normal. In two Group B patients (Cases 2 and 4), the late deficit was not apparently provoked by falls in arterial blood pressure. However, changes in intracranial pressure, which was not recorded, may have reduced cerebral perfusion pressure. One patient with a right middle cerebral aneurysm (Case 4) developed a progressive, permanent left hemiplegia 48 hours postoperatively. Case 2, with a basilar aneurysm, illustrates the multifactorial nature of the problem. During the operation, the right posterior cerebral artery had to be included in the clip, as the aneurysm ruptured. However, this patient was well until the 3rd day after surgery, when she developed a progressive left hemiparesis and confusion. She died on the 5th day when her hemoglobin had risen to 17.1 gm%. Hence, quite apart from her proven impaired autoregulation of CBF, her collateral circulation was compromised not only by occlusion of the proximal segment of the right posterior cerebral artery, but also by increased blood viscosity.

**Discussion**

These results suggest that, in the majority of patients, intraoperative global CBF does not fall with halothane-induced hypotension, but actually increases significantly by a mean of 58%. These patients have a low probability of developing late deficits. In the minority of patients, intraoperative global CBF falls with halothane-induced hypotension. This group appears to have a very high risk of developing new late neurological deficits, some of which are irreversible. It must be stressed that our global CBF technique will not predict immediate postoperative deficits, presumably caused by excessive brain retraction or inaccurate clip application; for this analysis a focal technique is required, such as the direct cortical response. However, there remains the difficult problem of reliable, unobtrusive, and representative sampling with such focal techniques in the operative setting.

In normal man and animals, CBF remains unchanged until the mean arterial blood pressure has decreased to 55% to 65% of baseline with hemorrhage and to 35% to 40% of baseline with halothane. This autoregulatory capacity is globally impaired following recent SAH, and is present in apparently Grade I or II patients and animals. Although Griffiths, et al., concluded that there was no overall impairment of autoregulation in patients after SAH, review of their data reveals that in nine of their 20 patients CBF fell with nitroprusside-induced hypotension. We were not able to make the distinction in Group B patients between true impairment of autoregulation (linear decrease of CBF with progressive hypotension) and merely upward shift of the lower limit of autoregulation. This distinction requires many more CBF estimations per patient than allowed for by the total dose of 133Xe administered and the build-up of background activity over short time periods.
The increase in CBF with halothane-induced hypotension in Group A suggests that halothane is acting as a direct cerebral vasodilator under these circumstances. The net effect on CBF reflects the competition between falling cerebral perfusion pressure and cerebral vasodilatation. In Group B patients, either halothane may not have such a marked cerebral vasodilator action or the impairment of autoregulatory vasodilation in response to falling perfusion pressure is much greater than in Group A. Whatever the mechanism, this finding confirms that Group B patients have a greatly reduced cerebrovascular capacity to dilate.

The small post-hypotensive hyperemia seen in Group A but not seen in Group B patients may reflect the same phenomenon. Merory, et al., have noted that patients with an increase in CBF on the day following craniotomy have a better prognosis than those in whom postoperative CBF is reduced relative to the preoperative value.

Considerable controversy surrounds the concept that new late neurological deficits follow progression of cerebral vasospasm as seen on angiography. Certain other factors are important, as, for instance, in Case 2. The capricious relationship between spasm and deficit may reflect the ability of the individual’s cerebral circulation to accommodate to such narrowed vessels: tissue ischemia may be exacerbated when a further stress is applied, such as hypotension, hypoxia, raised intracranial pressure, or further proximal arterial narrowing.

These preliminary results suggest that measurement of the intraoperative response to halothane-induced hypotension may reveal those patients at greatest risk of developing late cerebral ischemia and who require more intensive monitoring and early use of the induced hypertension technique. Whether other hypotensive agents and methods of anesthesia will differentiate Group A from Group B patients as clearly as does halothane should be studied. A preoperative test that gave the same clues as does the intraoperative measurement of autoregulatory capacity would be very helpful.

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References


Full details of this group of patients were presented to the Second International Workshop on Cerebral Vasospasm in Amsterdam, The Netherlands, in July, 1979. This study received the 1980 Cairnes Memorial Essay Award from the Society of British Neurological Surgeons. Address reprint requests to: John D. Pickard, F.R.C.S.(Ed.), Wessex Neurological Centre, Southampton General Hospital, Tremona Road, Southampton, S09 4XY, England.