Cerebral arterial blood flow and aneurysm surgery

Part 2: Induced hypotension and autoregulatory capacity

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A study of 21 patients was conducted to clarify the autoregulatory capacity in patients subjected to induced hypotension during intracranial surgery for saccular aneurysms. Trimethaphan camsylate (Arfonad) was used for induced hypotension and arterial blood flow was measured with an electromagnetic flow probe on the internal carotid artery or one of its main intracranial branches. In Grade I and II patients the control arterial blood pressure (ABP) ranged from a mean of 90 to 135 mm Hg (average 110 mm Hg), with a lower level of autoregulation (LLAR) from 35 to 85 mm Hg (average 62 mm Hg). Grade III patients had a control ABP of between 105 and 145 mm Hg (average 124 mm Hg) and the LLAR was found to be between 60 and 95 mm Hg (average 76 mm Hg). There was a significant difference between the two groups with regard to both the control ABP and the LLAR. A surprising result obtained from these data was that the average lower autoregulatory range (the difference between control ABP and LLAR) is practically the same in the two groups. A systematic investigation of the upper limit of autoregulation was not possible for ethical reasons. In those few patients in whom spontaneous increase in the ABP made such observations possible, upper limits up to 150 mm Hg with a total autoregulatory capacity of about 75 mm Hg were observed. In some patients, however, lower limits and corresponding "breakthroughs" of cerebral blood flow were seen, demonstrating that the upper limit of autoregulation is markedly influenced by several factors.

KEY WORDS • cerebral aneurysm • subarachnoid hemorrhage • cerebral blood flow hypotension, controlled • cerebral blood flow autoregulation

In intracranial aneurysm surgery the surgeon should avoid as much as possible further trauma to an already damaged brain. Induced hypotension is intended to diminish the risk of an intraoperative rebleed, and to facilitate surgery. The primary objection to prolonged hypotension in such patients is due to the uncertainty regarding adequacy of cerebral tissue perfusion at low arterial blood pressure (ABP) levels. Cerebral blood vessels exhibit autoregulation, defined as the capacity to maintain constant blood flow in the face of changes in cerebral perfusion pressure (CPP). The lower limit of autoregulation (LLAR) is defined as...
the CPP below which falling pressure causes a concomitant reduction in blood flow. \cite{18,28,32}

Much work has been done to determine the extent of autoregulatory range. Unfortunately most of this information either applies to cerebral circulation under normal conditions or is the result of animal studies. \cite{2,25,26,31,39-42}

As stated by Fitch, et al., \cite{11} it is difficult to extrapolate from results of experimental studies to patients undergoing intracranial surgery. This is particularly true when hypotension is induced in patients in whom autoregulation is impaired or abolished, either globally or regionally. Despite the widespread use of the method, it seems as if the indications and particularly the procedures for induced hypotension are still not clearly defined. \cite{1,12} A comprehensive review of the current clinical status is given by Yashon, et al. \cite{55}

The present study was conducted to clarify the autoregulatory capacity in patients subjected to induced hypotension during intracranial surgery for saccular aneurysm.

**Clinical Material and Methods**

This study included 21 patients who were undergoing intracranial operation for a saccular aneurysm. The average interval since last subarachnoid hemorrhage was 10.1 days. Twelve patients were in clinical Grade I or II, and nine were in Grade III, according to the Hunt-Hess classification. \cite{23} A comprehensive survey of the technique employed is given in Part 1 of this study. \cite{8}

Anesthesia was induced with thiopentone and diallyl-nor-toxiferon and maintained with nitrous oxide and fentanyl citrate. In most cases hypotension was induced with two steps, beginning with a reduction to between 70 to 100 mm Hg depending on the preoperative ABP. Trimethaphan camsylate (Arfonad) was used for inducing hypotension in all patients. After the dura was opened and decompression secured, mean ABP (MABP) was reduced by the second step to as low as 40 mm Hg in some patients, although in Grade III patients and those with hypertension, a level of about 80 mm Hg was maintained. Lower pressures were accepted for short periods.

Electromagnetic flow probes of special design \cite{820} were used for the flow determination. The probes were implanted after induction of anesthesia.

In five cases flow was recorded from probes placed on the internal carotid artery (ICA) on the side of the neck ipsilateral to the aneurysm, and removed after the intracranial procedure. Two of these patients had their probes removed several hours after the intracranial procedure and only local anesthesia was used for this minor operation. The remaining 16 patients were monitored with the electromagnetic probe either on the intracranial portion of the ICA or on the main branches of this artery. All flow recordings were from the aneurysm side.

The ABP was measured by means of a catheter in the iliac artery. The determination of LLAR was made in all patients after opening of the dura. The \( \text{PaCO}_2 \) was kept between 32 and 40 mm Hg during these measurements. The figures presented are all mean values. Student's t-test was used for the statistical calculations.

**Results**

**Upper Autoregulatory Range**

Changes in MABP, or more correctly the CPP, are used to study the autoregulatory response. Figure 1 left shows the marked increase in MABP due to painful stimulus at skin incision. The instant rise in MABP from about 100 to 135 mm Hg shows a corresponding peaked flow increase while autoregulation acts within seconds. This sequence should be compared with the flow response during MABP recovery following induced hypotension (Fig. 2). A “breakthrough” in the flow tracing is observed. At the end of this recording there is a pressure-passive state with the autoregulation abolished at MABP levels at which the patient had a perfect autoregulation before hypotension was induced. It should, moreover, be noted that the \( \text{PaCO}_2 \) at this final stage of the surgical procedure is definitely higher than previously. The autoregulatory capacity was tested some 1 1/2 hours later when the patient was awake. The effect of intravenous angiotensin is shown in Fig. 3 and demonstrates reestablishment integrity of autoregulation at these MABP levels.

A systematic investigation of the upper limit of autoregulation was not possible in this study for obvious ethical and practical reasons. In the few patients in whom spon-
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Fig. 1. Tracing from the patient in Case 1, aged 62 years with an internal carotid artery (ICA) aneurysm. Painful stimulus due to skin incision caused marked and rapid rise in arterial blood pressure. The ICA flow shows nearly instant autoregulation. Autoregulatory range is from 135 to 60 mm Hg. Note slight dip in ICA flow at this lower level of blood pressure. Also note open dura. Gap in lower tracing x - x, is due to failure of recorder pen.

Fig. 2. Case 1. Arterial blood pressure (ABP) recovery after induced hypotension (compare with Fig. 1). At ABP levels above 125 mm Hg mean there is a pressure-passive condition in the internal carotid artery (ICA) system. Note reestablished flow after first short “breakthrough.” PaCO₂ increased from 28 to 36 and 34 mm Hg.
Fig. 3. Case 1. Testing integrity of autoregulation about 2 hours after operation with the patient awake. Mean ABP from 90 to 115 mm Hg due to intravenous vasopressor substance (angiotensin). PaCO₂ is 35 mm Hg. The flow probe was removed some hours later under local anesthesia.

Instantaneous increase in ABP made such observations possible, levels were seen up to between 135 and 150 mm Hg. The highest individual range of total autoregulation observed in this study was 75 mm Hg.

The reaction to rapid changes in the ABP was an initial increase or decrease in flow for a couple of seconds before autoregulatory mechanisms were able to reestablish the previous flow level (Fig. 1). However, during

Fig. 4. Tracing from the patient in Case 2, aged 55 years with an internal carotid artery aneurysm. Middle cerebral artery (MCA) flow (mean and instantaneous) during induced hypotension. Lower level of autoregulation (LLAR) is at 65 mm Hg, MCA flow is 75 ml/min. Preoperative (control) arterial blood pressure = 120 mm Hg mean. Fast ink jet recorder.
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Fig. 5. Patient in Case 3, aged 30 years with an internal carotid artery (ICA) aneurysm. Mean ICA flow and mean arterial blood pressure (MABP) during induced hypotension and intracranial surgical procedure. Typical pressure-passive vascular system at MABP levels below the lower level of autoregulation (LLAR). Note effect on flow of dura opening, and retractor mounting and removal.

sequences of slowly changing ABP as in Fig. 4, the regulatory response acted as an almost simultaneous adjusting mechanism.

Other patients showed impaired autoregulation as demonstrated in Fig. 5. In that tracing MABP is 115 to 120 mm Hg when the Arfonad infusion is started. The LLAR is about 95 mm Hg and the tracing goes on to a pressure-passive state. Dura splitting has a definite influence on flow, presumably by reducing the intracranial pressure (ICP) and thereby causing a higher CPP. Retractor mounting has a minor effect in the opposite direction, whereas retractor removal induces a flow increase in the order of 15 to 20 ml/min. This increase is suggestive of a local vasoparalysis.

Lower Level of Autoregulation

Figure 6 depicts the LLAR in the whole series plotted against the individual preoperative (control) ABP. In Grade I and II patients the control ABP ranged from 90 to 135 mm Hg (average 110 mm Hg) with an LLAR from 35 to 85 mm Hg (average 62 mm Hg). Grade III patients had an ABP of between 105 and 145 mm Hg (average 124 mm Hg) and the LLAR was found to be between 60 and 95 mm Hg (average 76 mm Hg). There was a significant difference (p < 0.05) between the two groups with regard to the control ABP and the LLAR. However, a surprising result obtained from these data showed that the average lower autoregulatory range (the difference between control ABP and LLAR) is practically the same in both groups: 47 to 48 mm Hg. In other words, the average autoregulatory capacity to hypotensive states is the same in the two groups but acting at higher ABP levels in Grade III patients. In Grade I and II patients there is a significant correlation between the control ABP and the LLAR (r = 0.741, p < 0.005). The regression line
The LLAR in humans with normocapnia has been found to be at an MABP of between 60 and 70 mm Hg. Harper suggests that the MABP can be reduced to about two-thirds of the individual ABP control level before reaching this lower autoregulatory limit under normocapnia and an intracranial normotensive state. This concurs with the findings in this study. Harper also claims that further fall in CPP, with progressive reduction in CBF, is tolerated within certain limits. Evidence for this is available in several clinical reports on deep hypotension below 40 mm Hg without untoward effects on cerebral function. However, from the data presented it seems justified to stress that the duration as well as the degree of systemic pressure reduction should be most carefully considered, particularly in patients clinically graded as II, III, or worse. It would seem that the clinical grading can give an indication as to the LLAR. A very important clinical point is that the LLAR is shifted to higher blood pressure levels in hypertensive patients. This is in accordance with recent observations by Jones, et al., in a study on renovascular hypertension in baboons.

Fitch, et al., have shown in baboons subjected to hemorrhagic hypotension that CBF decreases when ABP decreases to less than 60 to 65 mm Hg, while in animals subjected to

Fig. 6. Plots depicting the lower level of autoregulation (LLAR) in relation to preoperative (control) arterial blood pressure (ABP). Pressures are mm Hg mean. Left: Grade I and II patients. Right: Grade III patients. Dotted lines with figures indicate mean values which are significantly higher in Grade III patients.

shown to the left in the plot is expressed by $y = 53.7 + 0.895x$. No such correlation was found within the Grade III series ($r = 0.019$).

Discussion

As pointed out by several workers, the induction of anesthesia and painful stimuli such as skin incision represent critical stages in an operation by causing an increase in ABP. It is important to reduce such stimuli or lessen the response to them.

Cerebral perfusion pressure is defined as the difference between the input systemic ABP and the ICP. Theoretically, this pressure is the same as that to which the aneurysm wall is subjected (transmural pressure) and is thus the driving force behind aneurysm rupture. It is clear that a knowledge of ICP and ABP does not give an indication of the cerebral perfusion at a given moment. This is because the cerebral blood flow (CBF) also depends on vascular resistance and the individual capacity to adjust this to maintain a steady and optimal perfusion. The operative range of this control mechanism is usefully termed autoregulatory capacity. However, the ICP and the ABP are important guidelines to the understanding of the basic circulatory condition of a patient when deep hypotension is induced before surgical decompression at craniotomy.
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drug-induced hypotension (with halothane) autoregulation was operative at ABP levels as low as 35 to 40 mm Hg. They suggest that this discrepancy is due to a difference in resistance in the larger extraparenchymal arteries. Harper, et al.,19 in their “dual control” theory have suggested that the cerebral circulation can be described as two resistance series. The extraparenchymal arteries are influenced by the autonomic nervous system but the intraparenchymal arteries are regulated by intrinsic metabolic and myogenic mechanisms. Fitch, et al.,31 conclude that under conditions of hemorrhagic hypotension alone, sympathetic constriction of the extraparenchymal cerebral arteries reduces the possible range of autoregulation. From this it is tempting to extrapolate that cerebral arterial vasospasm seen in some patients with aneurysm rupture23 might have a similar untoward effect on the autoregulatory capacity.51,52 It is well known that such patients have a low tolerance to surgery particularly under deep, protracted hypotension.

Rate of Autoregulatory Response

It has been shown that the autoregulatory response is extremely rapid.55,56,61 Our findings demonstrate that vasomotor reaction to steep and marked pressure changes can adjust vascular resistance and reestablish flow at the previous level within less than 5 seconds. If the pressure changes are slow, an almost instant peak-to-peak regulation occurs.

Upper Limit of Autoregulation

Clinically, the main interest has been focused on the LLAR and the risk of causing ischemic damage from critical reduction in CBF at perfusion pressures below this limit of autoregulatory range. Logically, such a “range” should also have an upper limit and this has been shown to be so.4 Strandgaard, et al.49,50 found an upper limit of autoregulation in hypertensive patients at about 160 mm Hg, while in a normal individual this was found at 120 mm Hg. Thus it seems appropriate to speak of a shift in autoregulatory range or capacity to higher levels in hypertensive patients. This makes the often used term “loss of autoregulation” at lower ABP levels in such patients rather doubtful. A loss of autoregulation should more appropriately refer to a reduction or narrowing of the autoregulatory range or an otherwise impaired or sluggish vasomotor control. The most unequivocal loss of autoregulation is of course a complete vasoparalysis.27,43 However, there is nothing against the concept that the LLAR in hypertensive patients represents a simple saturation phenomenon (maximum individual dilatation) just as in normotensive patients.13,46

The term “breakthrough” seems appropriate when CPP exceeds the upper limit of autoregulation. This causes an increase in cerebral perfusion and the microvasculature is subjected to a higher intraluminal pressure. This can seriously damage the blood-brain barrier and lead to the formation or extension of vasogenic edema.51,43,44,46 From the scanty reports on the subject it appears that the autoregulatory range in humans could be somewhere from 60 to 70 mm Hg up to 150 to 160 mm Hg.29,56 However, considerably reduced ranges were seen in our study and this concurs with previous reports demonstrating that the upper limit is markedly influenced by several factors.20,31 Experimentally, Freeman and Ingvar14 have shown that if hypotension is extreme and prolonged the autoregulation may be abolished in the recovery period. Harper18 has pointed out that during hypercapnia, reduction and even abolition of autoregulation occurs. Keany, et al.,25,26 have shown that, following a period of halothane or nitroprusside-induced hypotension, autoregulation is disturbed for some time. Furthermore, Okuda, et al.,56 found that in such states of drug-induced disturbance of autoregulation, there is a persistence of normal responsiveness to changes in PaCO2. All these observations have clinical implications, and McDowall20,31 is obviously on strong ground when he advises against marked and rapid ABP recovery after deep prolonged hypotension. This is particularly so if hypotension has been induced by halothane or nitroprusside. It is clear that insufficient ventilation and hypercapnia aggravate these untoward effects on the vasoregulatory system. Our observations concur with the view that the upper limit and the individual capacity of the autoregulatory mechanism should have at least the same attention as its lower limit.

Much more remains to be learned about the autoregulation of CBF and the multiple factors that can affect this vasomotor control.

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system. The neurosurgeon still remains on uncertain ground with regard to the complexity of effects of anesthesia and hypotensive drugs, ventilation, arterial blood pressure, and intracranial pressure, as well as the surgical handling of the diseased brain.

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