Hemodilution in Acute Stroke

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IT SEEMS APPROPRIATE to attempt to improve cerebral blood flow (CBF) in stroke. By so doing, oxygen delivery to the brain will increase and removal of the waste products of metabolism will be more efficient. Better flow should also increase the fragmentation and dispersal of existing thrombi and inhibit extension and spread of intravascular thrombosis. One approach to increase CBF is to improve the flow properties of blood by lowering viscosity. The two main determinants of blood viscosity in cerebral vessels are flow and hematocrit. As flow falls, viscosity rises. So any manoeuvre which raises CBF will lower viscosity. Lowering hematocrit by hemodilution reduces viscosity dramatically. This improvement in flow may be due either to the reduction in viscosity or to the reduction in the oxygen carrying capacity of the blood, which would necessitate an increase in flow to maintain oxygen delivery. Initially, it was suggested that viscosity was likely to be more important, but subsequent work to clarify the problem from the same laboratory and from elsewhere indicates that oxygen delivery is the dominant factor. Therefore, since the improvement in flow after hemodilution is largely due to a reduction in oxygen carrying capacity, should it be used in acute stroke?

There is little debate about the need to reduce elevated hematocrit in polycythemic patients in the immediate aftermath of stroke. Their blood flow is often extremely low and reducing hematocrit increases CBF and often improves conscious level and alertness. Furthermore, hemodilution actually achieves a small increase in oxygen delivery. But should patients without polycythemia who have a hematocrit in the accepted "normal range" have the hematocrit reduced in order to improve cerebral blood flow? Wood and Kee, in this issue, argue that they should. Several studies have shown that reducing hematocrit in this group produces an increase in flow and Wood et al, 1984, have shown that it also produces an improvement in EEG in acute stroke. Harrison et al, 1981, have shown that infarct size after carotid occlusion increases with rising hematocrit. It was proposed that efficiency of flow through collateral vessels was reduced by high hematocrit and viscosity and that infarct size increased accordingly. Asplund et al, 1984, have published some very encouraging results of a pilot study of hemodilution in acute stroke which has indicated that the size of handicap following stroke is reduced by hemodilution. In this issue they describe the protocol for a large multicentre trial of hemodilution in acute stroke in Scandinavia and a similar study is in progress in Italy.

As yet there is insufficient evidence to indicate an optimal hematocrit. In the experimental animal, Sunder-Plassmann et al, 1972, have suggested that a hematocrit of 30 is optimal for improvement in blood flow and maximal oxygen delivery. Wood and Kee, in this issue, make a case for attempting to reduce the hematocrit to 33%. However this increase in flow is to a large extent achieved by an increase in the cardiac output. Elderly men may not have the same capacity for increasing cardiac output safely as young animals and Kusunoki et al, 1981, have suggested that the optimal level is nearer 40%. However, each case needs to be considered on its merits and patients with pulmonary disease or possibly poor cardiac reserve may need to be kept at higher hematocrit levels.

In the prevention of stroke, the possibility of reducing hematocrit and viscosity and of improving flow should be considered. The patient with severe atheroma is particularly at risk. Peri-operatively, patients undergoing carotid endarterectomy, coronary artery by-pass grafting or an operation where there may be significant hypotension are vulnerable. Occlusive vascular events are also more likely to occur in patients with infection or who have suffered trauma or who have an underlying neoplasm. It is possible that post-operative strokes in such patients might have been prevented by pre-operative hemodilution. The blood removed to achieve this pre-operatively, could be stored and used during surgery to replace any blood loss.

There are three modes of hemodilution — isovolemic, hypervolemic and hypervolemic. In the majority of cases, with normal blood volume, isovolemic hemodilution is the most appropriate, where the exact volume of blood removal is replaced by fluid. Hypervolemic hemodilution, where the volume of blood removed is only in part replaced, may prove to be appropriate therapy in patients who also have cardiac failure or high blood pressure. Hypervolemic hemodilution has the disadvantage of increasing intracranial pressure and cerebral blood volume and until more evidence is available, should probably be avoided imme-
diately after stroke. Fluid replacement to restore a normal blood volume is clearly indicated in patients with low blood volume who are dehydrated or who have bled.

The choice of diluent is not straightforward. Crystalloid solutions may fail to remain within the circulation for long enough and dextrose should probably be avoided in acute stroke for metabolic reasons. Plasma in many ways is ideal but it is expensive, may be in short supply and with current concern about AIDS may prove unpopular. Ideally, one should re-infuse the patient’s own plasma and this is possible if an appropriate cell-separator is available. Low molecular weight dextran has been a commonly used plasma substitute and the main problem of allergic reactions can now be overcome (Asplund et al., this issue). However, the need remains for a more suitable plasma expander, ideally with oxygen carrying properties. Oxygen delivery to the tissues may be improved by using drugs, like bezafibrate, which shift the oxygen dissociation curve favorably. 12

There are several theoretical problems with hemodilution. 13 Firstly if there are sudden changes in blood volume, blood pressure may fall and this would not be without danger in patients with critical myocardial or cerebral perfusion. Patients with impaired cardiac reserve need to be hemodiluted with care and Wood and Kee, in this issue, recommend that the pulmonary wedge pressure be measured during treatment. Removal of blood is likely to stimulate platelet numbers and activity. This effect is less if the patient is treated with erythropoiesis, where the patient’s plasma and platelets are re-infused, but if this method is unavailable using an anti-platelet agent at the same time as venesection may be advisable. Increasing cerebral blood flow may produce a rise in intracranial pressure 14 and an increase in cerebral edema, possibly even if the circulating blood volume is not substantially increased. Furthermore, it is theoretically possible that increasing flow might lead to an extension of a hemorrhage.

The time is ripe for some detailed blood flow/metabolism studies to be performed before and after hemodilution, using e.g. positron emission techniques. In this issue, Asplund et al describe the background and protocol of a multicentre trial of hemodilution in ischémic stroke in Scandinavia. A similar large scale study is in progress in Italy and the results of both of these are awaited with interest. Hemodilution is unlikely to be of value in all cases of stroke and it is hoped that these studies will be able to indicate which subgroups are most likely to benefit.

References
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