tomy, we have become convinced that these usually have nothing to do primarily with the brain circulation.

It is perhaps too rigid to assert that repairing the brain circulation never improves its function. But as a practical matter, the flow range in the acute situation between impaired function and infarction is so narrow that it is exceedingly rare that the brain would stay in it very long. Either adequate collateral circulation would develop within a few days at the most, or infarction will almost always occur.

References

The Effect of Haematocrit on Cerebral Perfusion and Clinical Status Following Carotid Occlusion in the Gerbil


SUMMARY The effect of haematocrit on the sequelae of carotid occlusion has been studied in the gerbil stroke model. In 72 animals one carotid artery was clipped. After 30 minutes, the area of cerebral hemisphere filling with a carbon suspension administered intravenously was measured on coronal brain slices and related to the haematocrit. Exchange transfusion of autologous packed red blood cells or plasma produced a haematocrit range of 26% to 59%. At high haematocrit a larger area of non perfusion was more commonly encountered, and the anterior cerebral artery territory was more frequently affected along with that of the middle cerebral. Fifty-seven animals had temporary occlusion of both carotid arteries. Survival was adversely affected at high haematocrit. The role of haematocrit in affecting the pathophysiology of cerebral ischaemia is discussed. Stroke, Vol 13, No 2, 1982

THE INCREASED PREVALENCE of cerebrovascular accidents in polycythaemia has long been recognised, and several studies have demonstrated the importance of haematocrit as a risk factor in cerebral infarction.\footnote{In a study of experimental middle cerebral artery occlusion in cats, Sundt et al showed that injections of autologous packed red blood cells increased both the mortality and the volume of the resultant infarct.\footnote{Haemodilution with albumin resulted in a smaller mean infarct size though the effect was not statistically significant. The numbers of animals in the study was small however and haematocrit levels not given. We have therefore used the gerbil stroke model to study in more detail the effect of varying the haematocrit level on the results of carotid occlusion.}}

Reprints: Dr. Steven S. Pollock, The Reta Lila Weston Institute of Neurological Studies, The Middlesex Medical School, London, WIN-8AA.

Methods

Mongolian gerbils of either sex weighing between 50 and 95 grams were anaesthetised by an intra-peritoneal injection of pentobarbitone (60 mgm/100 grams 'Sagatal' May and Baker Ltd). The right femoral artery was cannulated for withdrawal of blood samples, exchange transfusion, and for blood pressure monitoring. Haematocrit levels were determined (Hawkesly microhaematocrit centrifuge) prior to exchange transfusion of 0.3 ml aliquots of autologous plasma or red blood cells and after 30 minutes of carotid occlusion.

Through a midline cervical incision either the right or both common carotid arteries were dissected free of the vagus nerve and jugular vein and occluded with aneurysm clips.

Two protocols were followed:

A. Unilateral Carotid Occlusion. An aneurysm clip was placed on the right common carotid artery for 30 minutes. Blood pressure was monitored throughout. In some animals only haematocrit samples were removed. In others, plasma or packed red cells were injected after removal of arterial blood before the clip was applied. At the end of the 30 minutes, with the clip still in place 0.5 mls of a carbon black suspension (Pelikan Werke C11/1431A) was injected into the femoral vein. The brain was removed into formal saline after decapitation. Three coronal sections of 50μ were cut at the level of the optic chiasm on a freezing microtome, dehydrated in alcohol, and cleared in Oil of Wintergreen. Carbon perfusion of the cerebral capillary bed was observed microscopically and measured by computerized planimetry (Reichert Jung. M.O.P. 'Digiplan'). The results were expressed as the percentage area lacking full filling of the capillary bed.

B. Bilateral Carotid Occlusion. Bilateral carotid clips were placed for 30 minutes after haematocrit estimation and exchange transfusion as in A. Blood pressure was recorded throughout. After removal of the clips the cervical incision was sutured and the animals returned to their cages. The number of deaths and the clinical state of survivors was assessed at 24 hours.

Results

One hundred and fifty-nine animals were operated upon. There were 30 protocol failures. Twenty-one died under anaesthesia, 3 became severely hypertensive, and 3 showed evidence of post-transfusion haemolysis. Two bled from the femoral artery and in one the carbon suspension injection failed. There are thus 129 results to be considered.

A. Unilateral Carotid Occlusion (72 animals). The mean haematocrit before transfusion was 44 ± 5% and the mean blood pressure 79.9 ± 16.5 mms Hg. The maximum change of blood pressure during the period of transfusion and clipping was calculated with a mean of 14 (± 11.7) mms Hg. Forty-eight animals were transfused, 25 with plasma and 23 with red cells. Resultant haematocrit levels ranged from 26% to 59%.

Areas of incomplete carbon perfusion were seen in 28 cases. There was no difference in the initial haematocrit and blood pressure levels in these affected animals, though there was a slight (non significant) excess of females and of heavier animals (over 70 gr) in those affected. Perfusion was incomplete in 25 of 48 transfused animals but in only 3 of 24 not transfused (p < 0.05 Chi square), the higher proportion in the transfused group being found whether red cells or plasma was given.

The territory of the middle cerebral artery was affected in all 28 cases. The anterior cerebral artery territory was involved bilaterally in 8 cases and ipsilaterally in 3. Although the numbers are small, there is a suggestion that the anterior cerebral territory is more frequently involved in the animals with a higher haematocrit (table 1).

The area of brain showing no ingress of carbon suspension, as expressed as the mean percentage of the area of the coronal slices, ranged from 7 to 58%. The anterior cerebral territory accounted for 5.2 ± 1.0% of the area. Inspection of the data relating the unperfused area and the animals haematocrit (fig. 1) suggested that there were two populations with a larger (> 30%) and a smaller (< 30%) area of involvement. The anterior territory was involved in 10 of the 17 with a large area affected, but in only 1 of the 11 with a smaller area (p < 0.05). This one example of anterior cerebral artery territory involvement in the small group was an animal with a very high haematocrit (59%), and very patchy poor perfusion. In both the large and small groups the area was significantly correlated with the level of the haematocrit (r = 0.77 p < .05 small group; r = 0.67 p < .01 large group). The regression lines are parallel and outside each others 95% confidence bounds (t = 0.13 on 24 degrees of Freedom).

B. Bilateral Carotid Occlusion (57 animals). The mean haematocrit before transfusion was 48 ± 3% and the blood pressure 87.6 ± 18.3 mms Hg. Thirty animals were transfused, 9 receiving red cells and 21 plasma. The final haematocrit ranged from 32 to 62%. After 24 hours, 20 animals appeared normal. Twelve showed neurological deficit consisting of one or more of the following signs: unresponsiveness, ptosis, splaying of the contra-lateral limbs, or circling. Twenty-five were dead. There was no difference in the initial haematocrit, body weight, or blood pressure between the 3 groups defined by outcome, but females were again more susceptible with an increased mortality (Chi square 7.1 p < .01).

Overall there was a higher morbidity and mortality

| Table 1. Arterial Territory Involved, Related to HCT |
|-----------------|----------------|-------------|
| HCT (%)         | n   | Middle cerebral | Anterior cerebral |
| ≤ 38            | 10  | 10            | 3            |
| 39-49           | 7   | 7             | 2            |
| ≥ 50            | 11  | 11            | 6            |
FIGURE 1. Effect of HCT on size of territory not perfused after unilateral carotid ligation. Ordinate HCT in %, Abscissa size as % of area of coronal slice (see methods).

FIGURE 2. Effect of HCT on clinical outcome after bilateral carotid ligation. A. All animals; B. Non-transfused animals; C. All transfused animals; D. Animals transfused with packed red cells; E. Animals transfused with plasma.
in the transfused group compared with the group of animals in whom only haematocrit samples had been removed (fig. 2). However, if the comparison is restricted to the animals who after transfusion had haematocrit levels within the range shown by non transfused animals, there was no significant increase in sequelae or mortality (Chi square 2.14 for morbidity 2.39 for mortality N.S.).

An effect of haematocrit on mortality and morbidity was detectable. The mortality was higher (Chi square 5.7 p < 0.05), as was the morbidity (Chi square 5.4 p < 0.05), in the animals with haematocrit over 51. In those with a haematocrit below the normal range (45-51), there was no change in mortality but there was an increase in morbidity (not significant). In the group of animals not transfused, there is also a trend toward higher morbidity and mortality with higher haematocrit, but the numbers are small and the results not significant.

Discussion

The circle of Willis in the gerbil appears to be unique among small mammals. The posterior cerebral artery is fed from the internal carotid artery and the only communication between the carotid and vertebrobasilar territories consists of small (30 to 60 μ) branches of the superior cerebellar artery. It has been assumed that variations in the number and calibre of these connecting vessels determines the vulnerability of the species to carotid occlusion.

Bilateral clipping of the carotid arteries effectively tests the ability of the posterior communicating channels to supply the cerebral hemispheres. In our material, 30 minutes of bilateral carotid occlusion produced a mortality at 24 hours of 44% and a morbidity of 21%. In contrast with previous reports, females appeared more susceptible.

The outcome of unilateral carotid occlusion is influenced both by the adequacy of posterior collaterals, and also cross connections between the two anterior cerebral arteries. The area of the carotid territory that failed to fill after carotid occlusion showed evidence of falling into two groups. In one, less than 30% of the cross sectional areas of coronal slices at the level of the optic chiasm failed to fill. In this group, the anterior cerebral territory was only involved in one animal which had a very high haematocrit and an atypical patchy distribution of non perfused areas. In the other group, a large area (> 30%) remained unperfused and the anterior cerebral artery territory was much more commonly involved (60% of 9% p < 0.05). The area affected is likely to reflect the adequacy of the combined collateral potential of the anterior and posterior connections.

The attempt to manipulate the haematocrit by acute isovolaemic transfusion of red cells or autologous plasma produced two effects. First, it appeared to increase the susceptibility of the animals to the effects of bilateral carotid occlusion per se, though the excess morbidity and mortality over the normal haematocrit range was not striking. The finding of areas of non filling with carbon black in the presence of unilateral carotid occlusion was also more common after transfusion without regard to the material infused. In this case, there was evidence that the excess vulnerability related to transfusion was detectable in the normal haematocrit range. Presumably the stress of exchange transfusion has undetected cardiac or other sequelae which explain this effect.

Over and above this response to transfusion there was evidence of an effect of an altered haematocrit. Thus the proportion of animals with unilateral occlusion developing perfusion failure in the anterior cerebral artery territory was greater with an elevated haematocrit. Further, there was a relationship between the haematocrit and the size of the area not filling in both a large and a smaller sub-group. In animals subjected to temporary bilateral carotid occlusion, there was also evidence of an increased mortality and morbidity with an elevated haematocrit.

These data suggest that the area of a cerebral infarct might be greater in the aftermath of vessel occlusion in the presence of a high haematocrit, as is also indicated by the results of a study on CAT scans in patients with carotid occlusion. This would support the proposal by Gottstein that patients found to have a high haematocrit at the time of an occlusive cerebral ischaemic episode may benefit from haemodilution.

Acknowledgments

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