Top up transfusions in neonates

There are four reasons for giving top up transfusions to preterm infants: to replace acute blood loss; to replace chronic blood loss; to treat hypotension; and to reverse the chronic anaemia that is characteristically seen at 7 to 8 weeks of age in preterm infants and earlier in survivors of haemolytic disease caused by blood group incompatibility.

Replacement of acute blood loss

A neonate who has suffered an acute intrapartum haemorrhage or postnatal haemorrhage must have an immediate blood transfusion. Ideally, ABO and Rh compatible blood that is less than two days old (checked by an emergency cross match) should be given, but in an emergency fresh, uncrossmatched, O negative blood can be used. Transfusion should be continued until the systolic blood pressure is greater than 40 mmHg and the packed cell volume is 35–40%. This aspect of neonatal transfusion is not contentious.

Replacement of chronic blood loss

A baby weighing 1000 g has a blood volume of 80 ml of which about 35 ml are red cells. His red cells have a shortened survival time and his erythropoietin production is suppressed.¹ Severe illness may cause red cell haemolysis and depress the marrow. This is well recognised in sepsis,² and probably also occurs in ill, hypoxic neonates on ventilators whose transfusion requirements considerably exceed their blood losses, either haemorrhagic or iatrogenic. It is iatrogenic blood losses, however, that pose a major problem for the critically ill preterm neonate. Despite the use of transcutaneous or continuous PO₂ and PCO₂ monitors he may require a minimum of eight to 10 blood gas analyses per day; in ill hypotensive infants transcutaneous monitors are unreliable, umbilical artery catheters with a transducer in their tip do not measure PaCO₂ or pH, and all continuous recording devices require calibration. As well as blood gas measurements, sick babies have multiple blood samples withdrawn for haematological, biochemical, and serological analyses.

Blood gases may be measured on a 100 µl sample, and it is 20 years since Wilfrid Payne at the Hammersmith Hospital reported that he could do 10 biochemical investigations on 1 ml.³ Many neonatal

paediatricians, however, have to work with laboratory services that are at best covertly uncooperative, and at worse overtly hostile to requests for ultramicroscopic analyses with the quick turn round essential for neonatal intensive care. This can result in unnecessarily large volumes of blood being sampled from neonates.

Three approaches have been used to maintain adequate haemoglobin concentrations in the baby. Transfusion may be carried out when he has had the equivalent of 1% of his birth weight removed as blood—that is, 10 ml in the baby weighing 1000 g, or when he has had 10% of his blood volume removed—that is, 8 ml in the baby weighing 1000 g. Both approaches are equivalent to permitting the loss of about one pint of blood from an adult. Alternatively, the blood may be transfused when the baby's packed cell volume (PCV) drops below some preset point. Whichever approach is used, it usually results in the baby having blood transfused with the same frequency, and at about the same PCV—that is, 35–40% when he is given about 15 ml/kg of packed red cells. These practices, and in particular the cut off point for PCV of 35–40%, have never been evaluated in prospective randomised controlled trials and are based on two pieces of evidence, both of which I find convincing.

Firstly, many clinicians feel that when the PCV in an ill baby weighing less than 2000 g falls below 35–40% the baby deteriorates (my own belief is that the danger point is nearer 40% than 35%). The baby may have increased apnoea, he may show signs of heart failure, develop a metabolic acidaemia, or his requirements for ventilatory support may increase. In addition, if the PCV is allowed to fall as low as 25–30%, the volume of blood required to increase the PCV to 40% introduces problems of vascular overload.

Secondly, the physiological justification for this approach comes from evaluation of the data on systemic oxygen transport and tissue oxygen extraction in the neonate.⁴ There are three factors to be considered in systemic oxygen transport: cardiac output, PCV, and the position of the oxyhaemoglobin dissociation curve. The neonatal cardiovascular system is working at the limits of the Frank-Starling curve⁵ and has little if any capacity for maintaining tissue oxygen delivery by increasing cardiac output in the presence of anaemia. In the neonate the ability of the tissues to extract oxygen

from the blood is seriously compromised by the left shifted oxyhaemoglobin dissociation curve, and this is made worse if the baby is already hypoxic because of severe lung disease. Thus it is logical to keep the PCV in the optimal range. I know of no data about the optimal PCV in neonates, but in animals the cardiac output begins to increase once the PCV falls below 35–40%.⁶ I have no doubt, therefore, that in the ill baby of very low birth weight the PCV must be kept above 35–40%.

Hypotension

There is now a wealth of evidence that hypotension is bad for small babies. It is of clear aetiological importance in periventricular haemorrhage and periventricular leucomalacia,⁷ necrotising enterocolitis, and renal failure. Hypotensive babies with respiratory distress syndrome are more likely to die.⁸ The normal blood pressure in the babies most likely to require transfusion—that is those less than 32 weeks old and weighing less than 1500 g—averages 50–55/30–35 mmHg. Clinical experience suggests that the systolic pressure must be kept above 35–40 mmHg and the mean above 25–30 mmHg.

When hypotension is seen after birth it is commonly due to a low blood volume.⁹ Later in the first week, hypotension may be due to volume depletion (blood sampling, dehydration), haemorrhage (from catheters, disseminated intravascular coagulation, or within the brain), drugs (tolazoline, pancuronium), or severe illness (sepsis). Furthermore, positive pressure ventilation can compromise venous return and cardiac function, and so it is particularly important to maintain a ventilated infant's blood volume.¹⁰

Although infusion of an inotropic drug such as dopamine can be valuable in severely ill babies, under most circumstances volume expansion is the appropriate treatment. For the reasons outlined above, if the PCV is less than 40% the transfusion should be given as blood (10–15 ml/kg), but if the PCV is over 40% a similar volume of plasma or albumin can be used.

Late anaemia

By 7 to 8 weeks of age, the haemoglobin concentration in many babies of less than 1500 g in weight has fallen to 7–8 g/dl, and similar haemoglobin concentrations may occur even earlier in infants who have had Coombs' positive haemolytic disease of the newborn. By this age, in the absence of lung disease and in the presence of a rise in haemoglobin A concentrations, a shift to the

right of the oxygen dissociation curve, and improved cardiovascular function, tissue oxygen delivery remains good even at haemoglobin concentrations of 7–8 g/dl.⁴ If anaemia is accompanied by a good reticulocytosis ($>150 \times 10^9/l$) no treatment is indicated, in the expectation that the haemoglobin will rise spontaneously. If the haemoglobin falls below 7 g/dl, however, or if the infant feeds poorly, or is dyspnoeic at rest, 25–35 ml/kg of packed red cells should be transfused.¹¹

Risks of transfusion

Neonatologists must of course minimise the need for transfusion by asking laboratory colleagues to cooperate by providing adequate ultramicroscopic analytical systems. We should minimise iatrogenic blood loss by complementing arterial blood gas analysis with some form of continuous blood gas monitoring system, either intravascular or transcutaneous, although we must acknowledge the limitations of transcutaneous monitoring for preventing retinopathy of prematurity. In particular, the occasional wildly inaccurate transcutaneous PO_2 measurement means that several arterial blood samples for blood gas analyses will be needed every 24 hours in babies at risk from retinopathy of prematurity.

Although cases of neonatal acquired immune deficiency syndrome (AIDS) related to transfusion have been reported,¹² they occurred before testing of donors for human immunodeficiency virus (HIV) antibody had become routine and before groups at risk voluntarily stopped donating blood. In the current furore about AIDS neonatologists must try and maintain a sense of proportion. The likelihood of a neonate acquiring AIDS from donor blood in the United Kingdom is remote: it has been estimated at less than one case in 1 000 000 transfusions.¹³ This is less than the risk of developing or dying from hepatitis,¹⁴ or contracting cytomegalovirus infection from the donor blood,¹⁵ and much less than the risk of a baby weighing 1000 g dying if the systolic blood pressure and packed cell volume are allowed to remain below 40 mmHg and 40%, respectively. Indeed, for the past five years a much greater priority for neonatologists should have been to obtain donor blood that was free of cytomegalovirus infection rather than free of HIV.¹⁶

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