Polymorphonuclear leucocyte transfusion in neonatal septicaemia

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SUMMARY In one neonatal intensive care unit during a 15 month period 6 infants developed septicaemia which was resistant to antibiotic treatment. The infants' mean gestational age and birthweight were 32.7 weeks and 1519 g respectively. Intravenous infusions of polymorphonuclear leucocytes were given. Three infants died and the remainder survived without complications. No side effects of the treatment were identified.

Newborn infants are particularly susceptible to infection and both humoral and cellular mechanisms may be affected.^{1,2} The preterm infant is less immunologically competent, and stress or illness in the newborn period may have an adverse effect on normal bacterial killing.³ In the past four years transfusion of polymorphonuclear leucocytes (PMN) has occasionally been used^{4,5} in both acute⁶ and prolonged⁷ sepsis in neonates. We describe the clinical course in 6 infants with septicaemia refractory to antibiotics for periods ranging between 3 and 10 days, who received slow infusions of fresh PMN concentrates.

Methods and results

PMN concentrates were prepared in the form of single donor buffycoats. Blood (420 ml) from random healthy donors plus 63 ml CPD anticoagulant were centrifuged at 1200 Hz for 10 minutes. The supernatant platelet-rich plasma with the top layer of red cells and buffy coat were re-centrifuged at 2400 Hz for 30 minutes. Most of the supernatant was then removed leaving a preparation with characteristics listed in Table 1.

All donations were screened for HBs Ag by radioimmunoassay and the red cells were cross matched against serum from the infant and, whenever possible, from the mother. PMN concentrates were kept at ambient temperature ($20 \pm 3^\circ\text{C}$) and were used as soon as possible after preparation. After 24 hours the mean plasma pH was 7.0, the mean potassium value was 2.0 mmol/l and no lysis of red cells was detected. PMN concentrates were not irradiated before transfusion.

Table 2 gives details of the timing of onset of septicaemia, use of antibiotics, PMN transfusions, and eventual outcome. All of the three infants who died had positive blood cultures until the time of death. Patient 1 developed acute renal failure on day 16 and underwent peritoneal dialysis on days 19 and 20. His course was also complicated by a coagulopathy, persistent ductus arteriosus, and cardiac failure. Patient 2 developed disseminated intravascular coagulation and ventilatory failure on day 17, with subsequent deterioration. Patient 3 had superimposed respiratory distress syndrome, persistent ductus arteriosus, and terminal pulmonary haemorrhage. Patients 4, 5, and 6 survived their septicaemic illness. They had failed to achieve negative blood cultures after intravenous antibiotic treatment for 3, 5, and 6 days respectively. Negative blood cultures were, however, obtained in patients 4 and 6 after one PMN infusion, and in patient 5 after two infusions. The septicaemia did not recur and all three were physically and developmentally normal at follow up after one year.

Table 3 shows the volume and rate of PMN infusion and the effects on the infants' peripheral

Table 1 *Characteristics of PMN concentrate*

	Mean	Range
Total volume (ml)	35	30-40
Total leucocytes ($\times 10^9/\text{l}$)	1.8	1.1-2.8
Total neutrophils ($\times 10^9/\text{l}$)	1.0	0.5-1.6
Total platelets ($\times 10^9/\text{l}$)	100	70-150
Packed red cell volume (%)	22	15-35

Table 2 Clinical details of the 6 infants who received polymorphonuclear leucocyte (PMN) infusions

Infant No	Sex	Gestational age (weeks)	Birthweight (kg)	Diagnosis and age at onset (days)	Antibiotics used and time sequence (days)	Age at PMN infusion(s) (days)	Outcome and age (days)
1	M	28	1.28	<i>Escherichia coli</i> septicaemia (14)	Gentamicin 3-23 Cefuroxime 14-23 Chloramphenicol 14-23	20 21	Died 23
2	F	32	1.33	<i>Escherichia coli</i> septicaemia (15)	Penicillin 6-18 Gentamicin 6-24 Cloxacillin 6-10 Chloramphenicol 17-22 Ticarcillin 24-25 Cefuroxime 24-25	21 22 23 24	Died 25
3	M	32	1.80	<i>Klebsiella septicaemia</i> and meningitis (3)	Penicillin 3-12 Cloxacillin 3-12 Gentamicin 4-14 Chloramphenicol 5-14 Mezlocillin 10-14	13	Died 14
4	M	32	1.75	<i>Klebsiella septicaemia</i> and encephalitis (25)	Tobramycin 23-47 Mezlocillin 24-47 Cefuroxime 28-47	28 29 30	Negative blood culture 29
5	F	34	1.12	<i>Escherichia coli</i> septicaemia (6)	Gentamicin 6-21 Mezlocillin 6-21 Ticarcillin 10-21	11 12 13	Negative blood culture 13
6	M	36	1.84	<i>Staphylococcus aureus</i> Group B β -haemolytic streptococcus septicaemia (8)	Penicillin 8-51 Cloxacillin 9-51 Gentamicin 9-51	14	Negative blood culture 14

Table 3 Polymorphonuclear leucocyte (PMN) transfusions and effects on haemoglobin, platelets, and white cell count

Infant No	PMN transfusion, total volume (ml)	PMN transfusion, volume/kg bodyweight (ml)	Duration of infusion (hours)	Rate of infusion (ml/kg bodyweight/hour)	Haemoglobin (gm/dl)		Platelets ($\times 10^9/l$)		White cell count ($\times 10^9/l$)	
					Before	After	Before	After	Before	After
1	36	28	16	1.8	9.1	9.9	*15	31	19.6	17.2
2	154	84	48	1.8	9.6	8.2	*13	14	16.3	5.4
3	144	63	36	1.8	11.4	13.9	<10	38	4.1	27.5
4	23	12	12	1.0	10.3	10.2	<10	<10	7.1	9.4
5	144	112	49	2.3	14.5	14.4	*5	105	1.9	6.1
6	20	10	10	1.0	9.4	10.9	23	175	21.4	20.9

*Simultaneous platelet transfusions.

blood values. The mean white counts before and after infusion were $11.7 \times 10^9/l$ and $14.4 \times 10^9/l$ respectively. Infants 1, 2, and 5 had simultaneous transfusions of platelet concentrate (15 ml, 15 ml, and 18 ml) containing only small amounts of white cells. No side effects attributable to the infusions were identified. The mean values of urea, electrolytes, creatinine, and alanine aminotransferase were unaltered, but the mean plasma values of protein and albumin rose by 10 and 4 gm/l respectively. Infant 1 was being treated with intermittent positive pressure ventilation and peritoneal dialysis before PMN transfusion: the latter played no identifiable part in the continued deterioration. The other 5 infants had unchanged respiration rate, oxygen requirement, pulse, temperature, dextrostix, and capillary gas measurements during the infusions.

Discussion

The susceptibility of the neonate to bacterial infection has long been recognised.^{8,9} Complement factors are deficient in the newborn and their serum concentration increases with gestational age.¹⁰ Moreover, bacterial infection may impair white cell activity in the newborn.¹¹ These considerations prompted Laurenti to treat infants with PMN transfusions as soon as sepsis was suspected,⁷ and although those with fulminant illness were excluded from the study, a lower mortality was shown in these infants. Christensen⁶ showed the technique to be valuable in 7 infants with early onset septicaemia and associated neutropenia. The infants in our study differed from the cohorts treated by Laurenti and Christensen in that they were selected on the basis

of persistent and severe septicaemia that had failed to respond to systemic antibiotic treatment.

Our methods of preparation and administration of PMN infusions again differed notably from those of other workers. Although the preparations were not irradiated and contained considerable numbers of lymphocytes, there was no clinical evidence of any graft versus host reaction. Neither were the PMN concentrates screened for cytomegalovirus (CMV). Where facilities exist, however, CMV screening should be carried out. Laurenti⁷ transfused PMN concentrate (20 ml/kg body weight) within 6 hours of collection, while Christensen⁶ gave 10 to 15 ml/kg body weight over 45 minutes. Since rapid PMN transfusions may cause potentially harmful osmotic changes, rates less than 2.5 ml/kg body weight/hour were chosen in our study; using up to 14 hours of transfusion time. PMN have been shown to remain active after 48 hours' storage.¹³

Christensen recommends using PMN concentrates in septic infants who have associated neutropenia, and especially in those with depletion of mature marrow neutrophils. We elected to omit bone marrow examinations on the 6 infants in view of their critical clinical state. Moreover, three of our patients were not neutropenic before transfusion. In preterm infants with proved septicaemia there is an important defect in neutrophil chemotaxis,¹² and Laurenti has suggested this may represent a rational basis for PMN transfusion even in the absence of neutropenia.

Chiswick¹⁴ has highlighted the need for more controlled studies of this technique. Our experience suggests that PMN transfusions may contribute to the resolution of septicaemia refractory to antibiotic treatment in some low birthweight infants.

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