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Platelet consumption during neonatal extracorporeal life support (ECLS)

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This paper reports the results of a retrospective study of blood use and blood loss in 40 neonates during extracorporeal life support (ECLS). Immediately after onset of bypass 39±2.5ml platelets, 59.4±6.5ml packed red blood cells (PRBC) and 15.0±5.4ml fresh frozen plasma (FFP) per patient were needed. The average daily amount given per patient was 49.0±3.0ml of platelets and 48.0±3.4ml and 9.6±3.9ml of PRBC and FFP respectively. The 10 patients who had bleeding complications received 50.0±6.3ml/day of platelets compared to 49.0±3.4ml in the other patients. The majority of blood loss during the entire period of ECLS was from samples, averaging 43.0±1.5ml/day. Neck wound drainage, 6.7±2.5ml/day per patient, lasted for the entire period.

Introduction

Bleeding is the most common complication seen during neonatal extracorporeal life support (ECLS) and has been related to systemic heparinization and thrombocytopenia.[1–4] The incidence of major bleeding complications is approximately 15%, the most severe being intracranial haemorrhage.[5] Bleeding disturbance, such as oozing from the cannulation site, occurs in almost all patients on ECLS. Conservative techniques are currently used to manage bleeding complications, including lowering the activated clotting time (ACT) levels and maintaining the platelet count above 100 000/mm^3.[4] The decision to transfuse platelets if the concentration drops below 100 000/mm^3 is arbitrary, but is based on the observation that bleeding is less when the amount is kept at this level.[6] If severe bleeding persists there may be a need to disconnect ECLS either temporarily or permanently.

To reduce the bleeding complications of ECLS a system utilizing heparin-coated materials or postcircuit heparin neutralization, eliminating the need for systemic heparinization, has been suggested.[7–9] We also emphasize the importance of reducing platelet consumption and improving platelet haemostatic function during ECLS. However, before any measurement is applied it is necessary to analyse the pattern and possible sources of platelet consumption during ECLS. We therefore retrospectively studied blood use and blood loss in 40 neonates who were placed on

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ECLS. This information may indicate not only how to reduce platelet consumption but also how to improve haemostasis during ECLS. Improved haemostasis during ECLS may extend the indications for ECLS, particularly for premature infants with respiratory failure who are at high risk of intracranial haemorrhage.

Materials and methods

The records of 40 neonates requiring ECLS for respiratory failure at the University of Michigan Medical Center during the period from September 1985 to December 1989 were studied retrospectively. In this period a total of 152 neonates required ECLS. Forty patients were selected because they represented a 'normal' ECLS population. Patients' diagnoses, outcome and bleeding complications are given in Table 1. Case selection for ECLS treatment and the technique of ECLS was as described previously.[1] Factors examined included the amount of blood transfused and the amount of blood loss during ECLS.

Blood requirements were determined by recording the volume of platelets, the volume of packed red blood cells (PRBC) and the volume of plasma, given as fresh frozen plasma (FFP) transfused after the onset of ECLS. Immediately after onset of bypass, one unit of platelets was transfused, regardless of platelet numbers. After that platelets were administered when the platelet count fell below 100 000/mm^3. Platelet consumption was examined by recording the volume of platelets transfused to maintain platelet count above 100 000/mm^3. The haematocrit was kept above 45% by the transfusion of PRBC to maximize the oxygen-carrying capacity of blood during ECLS. Plasma was administered as indicated to increase blood volume when the haematocrit was over 45%. The preparation of blood products from whole blood was performed following the guidelines of the American Association of Blood Banks.[10] Further processing was performed at the Blood Bank and Transfusion Service at the University of Michigan.[11] The amount of PRBC and plasma needed to prime the circuit was not included in our study. The priming volume of the extracorporeal circuit was approximately 300–500ml and was composed of one unit of packed red blood cells (200ml), 50ml tris(hydroxymethyl)aminomethane (THAM) solution, 40–50ml of albumin or fresh frozen plasma, 100 units of heparin and 300mg calcium gluconate. The haematocrit of the prime was between 35% and 40%.

The amount of blood loss from the surgical site was determined by the neck wound drainage by weighing the surgical dressing hourly. The amount of blood drawn for sampling was also examined. All data are reported as mean ± SEM.

Table 1 Bleeding complications related to diagnosis in 40 neonates

Primary disease	Number of patients	Number of bleeding complications	Survivors
MAS	18	5	17
RDS	10	2	**10**
PFC	5	2	**5**
GBSP	2	0	**2**
CDH	2	0	**2**
Pneumonia	1	0	**1**
Sepsis	1	0	**0**
PPHN	1	0	**1**
Total	40	9	**38**

MAS = meconium aspiration syndrome; RDS = respiratory distress syndrome; PFC = persistent fetal circulation, GBSP = group B *Streptococcus* pneumonia; CDH = congenital hernia diaphragmatic hernia; PPHN = persistent pulmonary hypertension in newborns.

Results

Bleeding complications

Ten (25%) patients were considered to have bleeding complications (Table 1). Two patients had intracranial haemorrhage diagnosed by ultrasound, one of whom died. Two had haematuria, one had significant gastro-intestinal bleeding and one had cardiac tamponade. Cardiac tamponade was noticed during ECLS on day 2 by echocardiogram and the condition of the infant improved after pericardiocentesis was performed. Four had significant bleeding at the surgical site. One needed a neck re-exploration on ECLS day 5.

Blood loss

The average wound neck drainage per

patient was 6.7±2.5ml/day. In patients with surgical bleeding complications (n=4) it was 44.0±14.0ml/day. In all other patients (n=36) neck bleeding was constant at 4.4±1.0ml/day. Blood loss from blood samples drawn for haematological and chemical survey was 43.0±1.5ml/day, 88% of total loss (Figure 1).

Blood requirements

The total daily average blood products required per patient were 49.0±3.0ml platelets, 48.0±3.4ml PRBC and 9.6±3.9ml plasma Immediately after onset of bypass 39±2.5ml of platelets were transfused, regardless of platelet numbers (Figure 2). The average daily amount given per patient was 49.0±3.0ml of platelets to maintain the desired count of greater than 100 000/mm^3. Platelet transfusion in the 10 patients with bleeding complication was 50.0±6.3ml compared to 49.0±3.4ml in the other patients. In the first four hours after the onset of bypass an average of 59.4±6.5ml PRBC per patient was given (Figure 3). The need for PRBC transfusion was constant at a rate of 48±3.4ml/day. In the initial four-hour period 15.0±5.4ml of plasma was given (Figure 4). The average per patient was 9.6±3.9ml/day.

Discussion

Approximately 49ml of platelets are required daily during ECLS to maintain the platelet count above 100 000/mm^3. There was no significantly greater amount of platelets transfused to patients with bleeding complications compared to patients without bleeding complications. Serious bleeding complications occurred in 25% of the patients, causing death in one patient. They had probably decreased platelet haemostatic function. It is clear, however, that ECLS caused considerable platelet consumption in all patients, requiring daily supplementation. ECLS therefore seems to affect platelets, and all patients are apparently at risk of bleeding complications. For this reason premature infants with respiratory insufficiency are not considered for ECLS, particularly because

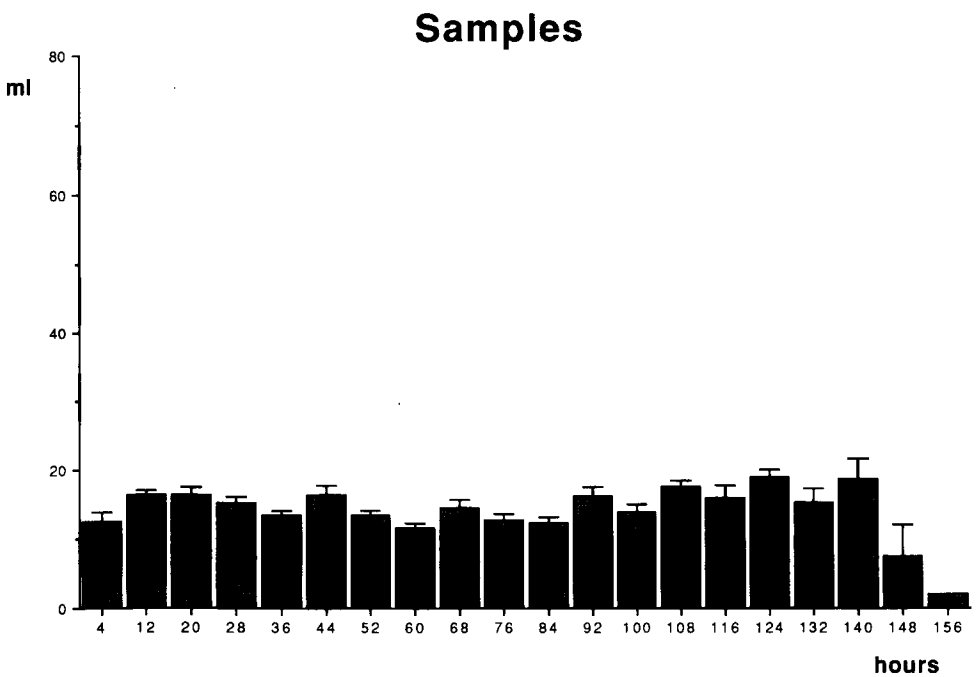

Figure 1 The average volume of blood samples drawn per patient during different time intervals after start of ECLS

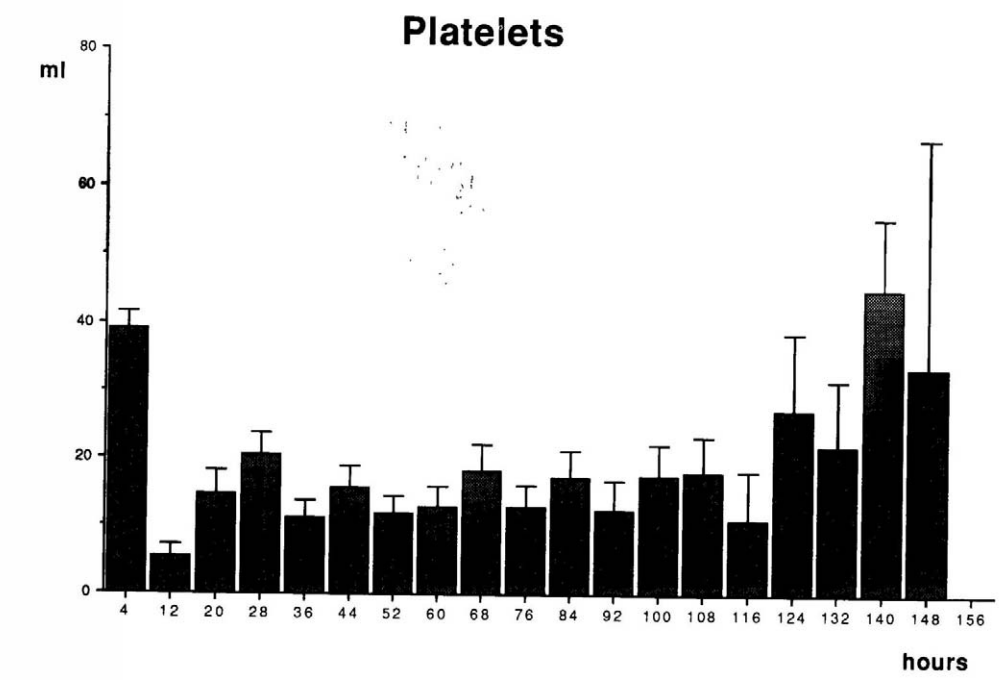

Figure 2 The average amount of platelets per patient transfused during different time intervals after start of ECLS

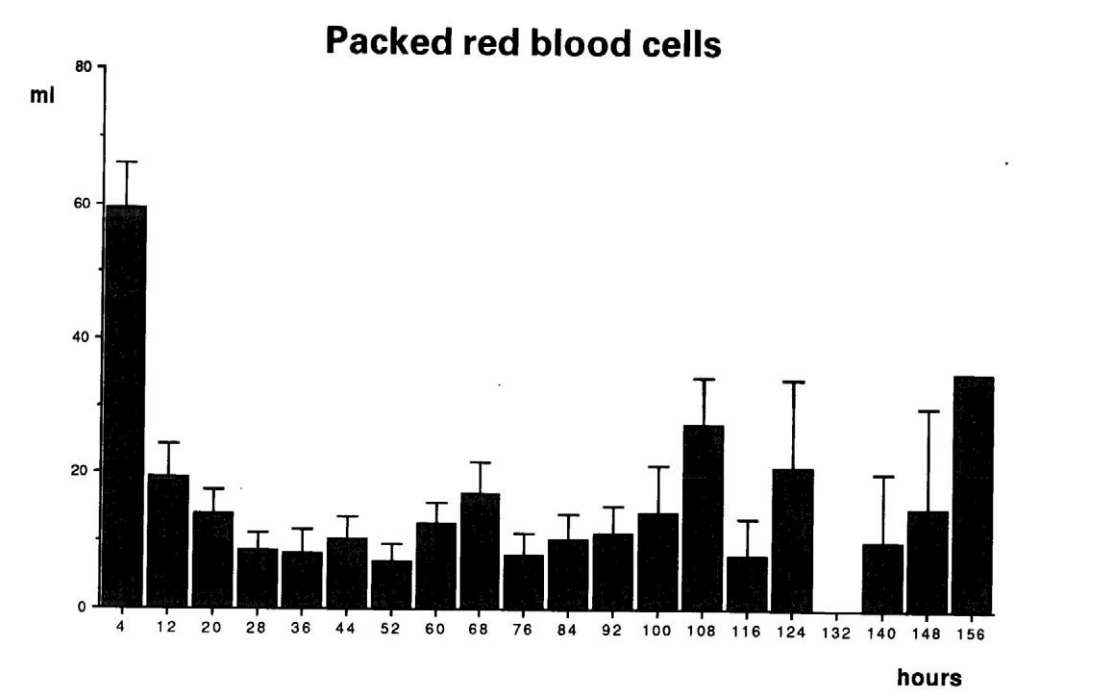

Figure 3 The average amount of PRBC per patient transfused during different time intervals after start of ECLS

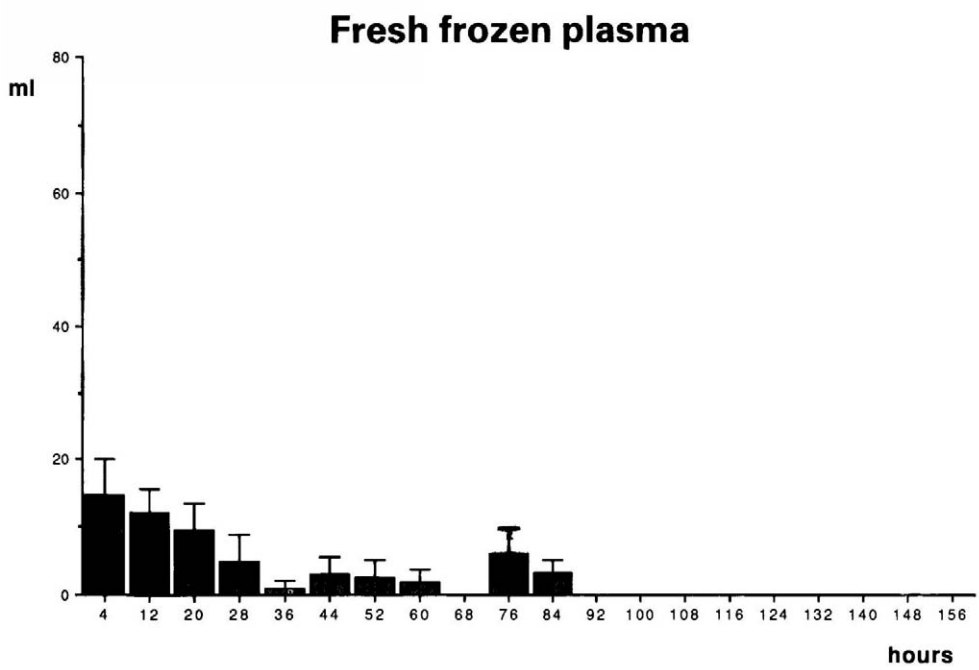

Figure 4 The average amount of FFP per patient transfused during different time intervals after start of ECLS

of the high risk of intracranial haemorrhage. We therefore emphasize the importance of decreasing platelet consumption and of optimizing the preservation of platelet function. This may safely extend ECLS treatment to premature infants with respiratory failure.

The considerable platelet consumption and decreased platelet function during ECLS may be caused by two main factors. First, exposing blood to the artificial surface of the extracorporeal circuit causes platelet interaction with the biomaterials and a 'whole body inflammatory reaction'.[12–15] Platelet interaction with biomaterials results in severe reduction of platelet numbers by platelet deposition on the materials and by systemic aggregation and sequestration of platelets, particularly in the liver.[12,13] Coating the surface of the extracorporeal circuit (with heparin, for example) could improve biocompatibility and modify platelet deposition.[14] It is also likely that the 'whole body inflammatory reaction' seen in cardiopulmonary bypass (CPB) for open-heart surgery will occur during ECLS.[15,16] This whole body inflammatory reaction is known to affect platelet haemostatic function. It has been demonstrated that the administration of proteinase inhibitors during CPB caused a significant improvement of haemostasis during and after bypass.[17–20] It would be tempting to introduce this treatment for ECLS as well, although as the patient is exposed to the circuit for an average of 4–5 days in ECLS, in contrast to a few hours during CPB, studies are needed first to examine the pattern of activation of the plasmatic systems during ECLS.

The second factor, platelet consumption and dysfunction, may be caused by the relatively large prime of the circuit. Because the pump prime does not contain platelets, platelet numbers drop immediately after the start of ECLS. To counter this effect an average of 39ml of platelets were routinely transfused to compensate for the dilution. This results in a large contribution of less functional donor platelets affecting haemostasis during ECLS. A rapid platelet consumption can be anticipated due to the short lifespan of donor platelets. This situation is maintained during ECLS by the need for continuous platelet trans-

fusions. To decrease or to eliminate the use of donor platelets because of these negative effects it is necessary to reduce the prime, which can be achieved by miniaturization of the circuit.[21–23]

Next to the frequent platelet transfusions, a significant amount of PRBC and FFP were also required during ECLS, particularly in the initial four-hour period. The need for these substitutions during the initial period cannot be explained by blood loss but by the need to treat hypotension after the onset of ECLS.[24] At the initiation of bypass, patients will often have a transient fall in mean arterial pressure and during this phase PRBCs and FFPs are given to keep the mean arterial pressure above 50mmHg. This temporary hypotension is due to haemodilution and hypovolaemia as the circulating volume equilibrates in the patient. Haemodilution is a result of the prime composition and the large priming volume as compared to the circulating volume of a neonate. The prime haematocrit is between 35% and 40% and additional PRBC transfusions are needed to increase the haematocrit to 45–50%. A further result of haemodilution is a decrease in plasma oncotic pressure which leads to an increase of extracellular fluid. Furthermore, the release of vaso-active inflammatory mediators from blood-surface interaction may also contribute to acute hypotension by causing vasodilation and increased vasopermeability.[15,16] After the initial period to stabilize the patient, PRBCs are given primarily to compensate for blood loss due to samples, averaging 43ml/day per patient, drawn for haematological and chemical studies. PRBC transfusion could be reduced by decreasing sample size and frequency. On-line control of vital blood chemistry might be another important tool to decrease blood sampling.

In summary, neonatal extracorporeal life support is intrinsically associated with a considerable platelet consumption, requiring frequent platelet transfusions to maintain a platelet count greater than 100 000/mm^3. Platelet consumption is caused mainly by two factors: blood-surface interaction and dilution. The latter factor results in a large contribution of less vital donor platelets. These two factors also probably decrease platelet haemostatic function, resulting in 25% bleeding complications and exclusion of premature infants from ECLS treatment. We stress the importance of decreasing platelet consumption and of preserving platelet haemostatic function to reduce bleeding complications during ECLS. This may result in safe ECLS treatment of premature infants with respiratory failure.

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