CORRELATION BETWEENREPEATED RED BLOOD CELLSTRANSFUSIONS AND SEVERE INTRAVENTRICULARHEMORRHAGE IN PRETERM INFANTS WITH LOW BIRTH WEIGHT

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Abstract

Introduction: Red blood cell transfusions are extremely important in neonatal intensive care units, in many cases are lifesaving although that involves numerous risks. The literature cites increased incidence of disease forms after repeated transfusions of packed red blood cells. Some transfusion risks have been well defined; others less so and perhaps yet other risks are not even usually recognized as transfusion-related events. One of the most important life-threatening complications of RBC transfusions in premature infants is intraventricular hemorrhage, causing morbidity and mortality. *Objectives:* The aim of this study was to evaluate the severe intraventricular hemorrhage incidence after repeated transfusions of packed red blood cells in premature infants with low birth weight. *Material and Methods:* A retrospective study over a period of two years which included infants with birth weight<1500g and gestational age<32 weeks. The infants with coagulopathies and central nervous system malformations were excluded. The study group included 104 newborns divided into two groups: the study group -64 patients and control group-40 patients who had indications for red blood cell transfusions. All patients were performed transfontanelar ultrasound in dynamics. *Results:* Among infants who required RBC transfusions 24 patients (37.5%) developed severe complications – worsening of intraventricular hemorrhage, ventriculomegaly, hydrocephalus, 8 of them (12.5%) being extremely low birth weight (790-900g). These results arise a few controversial questions: are red blood cell transfusions fully responsible for the worsening of intraventricular hemorrhage? How can we differentiate IVH occurred after RBC transfusions and the IVH appeared as a complication of the associated pathology?

Key words: red blood cell transfusions, intraventricular hemorrhage, premature infants

Introduction

It is well known that each transfusion administered conveys risks and benefits. Some transfusion risks have been well defined; others less so and perhaps yet other risks are not even usually recognized as transfusion – related events (1). Although the known infectious risks of RBC transfusions from each donor exposure are traditionally focused on, the infections risk are extremely small and are decreasing over time with improvements in donor screening and laboratory infection surveillance (2). Other complications of RBC transfusion can be intraventricular hemorrhage, necrotizing enterocolitis, lung injury, organ dysfunction, hemolytic transfusion reactions and transfusion related – sepsis (3). Some studies reported a higher mortality rate in children who received a transfusion compared with children and adolescents who did not received a transfusion. Many reports suggest that IVH is also associated with prematurity (4,5). After RBC transfusions, because of wide fluctuations in blood pressure and blood flow though the immature capillary beds associated withlow deformability of the erythrocytesare more likely to induce rupture and hemorrhage leading to long-term disabilities or even death.Banked RBC (even after a few days) develop "Storage Lesion" that involves lessdeformability and depletion of nitric oxidesynthase (6).

The incidence of the intraventricular hemorrhage is currently 15 - 20% in infants born at<32 weeks gestational age (5). In the preterm infants IVH originates from the fragile involuting vessels of the subependymal germinal matrix, located in the caudothalamic groove. The pathogenesis of the IVH in preterm infants has been shown to be largely related to intravascular, vascular and extravascular factors (Table 1) (7).

a) The intravascular risk factors predisposing to IVH include ischemia/reperfusion, increase in cerebral blood flow, fluctuating CBF and increase in the cerebral venous pressure. Ischemia/reperfusion occurs commonly when hypotension is corrected quickly, whether due to desease or iatrogenic intervention.

Sustained increases in CBF may contribute to IVH and can be caused by seizures, hypercarbia, anemia and hypoglycemia, which result is a compensatory increase in CBF. Fluctuating CBS has also been demonstrated to be associated with IVH in preterm infants (8). Studies have showed that large fluctuations typically occurred in infants breathing out of synchrony with the ventilator.

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Table 1. The pathogenesis of the IVH in preterm infants.

Intravascular factors	Ischemia/reperfusion Fluctuating cerebral blood flow Increase in cerebral venous pressure (high intrathoracic pressure – ventilator) Platelet dysfunction and coagulation disturbances
Vascular factors	Tenuous, involuting capillaries with large luminal diameter
Extravascular factors	Deficient vascular support Excessive fibrinolytic activity

b) Vascular factors that contribute to IVH include the fragile nature of the involuting vessels of the germinal matrix. There is no muscularis mucosa and little adventitia in this area of relatively large diameter, thin-walled vessels. Capillaries in the germinal matrix of the VLBW brain are particulary susceptible to rupture because they lack supporting cells (pericytes). RBC pass through capillary spaces smaller than themselves. This can only occur because RBC deform and because they release nitric oxide thereby dilating the capillaries. Banked RBC have a time – associated reduction in deformability as part of the "Storage Lesion".Transfused RBC with poor deformability and lacking nitric oxide synthase can clog capillaries.All of these factors make the vessels susceptible to rupture.

c) Extravascular risk factors for IVH include deficient extravascular support and likely excesivefibrinolytic activity in pretern infants.

Objectives

The evaluation of the severe intraventricular hemorrhage incidence after repeated transfusions of packed red blood cells in premature infants with low birth weight and the differentiation prevalence of severe intraventricular hemorrhage in premature infants transfused with or without severe pathology associated.

Material and Methods

A retrospective study conducted over a period of two years, from January 2011 to December 2013 which included infants admitted to Neonatal Ward of "Louis Turcanu" Children's Emergency Hospital of Timisoara.The study group included 104 newborns divided into two groups: the study group -64 patients with gestational age <32 weeks and weight <1500g and control group- 40 patients who had indications for red blood cell transfusions. The infants with coagulopathies and central nervous system malformations were excluded. They also had ssociated pathology: respiratory distress syndrome, sepsis, necrotizing enterocolitis, pneumonia. All patients were performed transfontanelar ultrasound in dynamics. Were extracted demographic data (gestational age, sex, birth weight), clinical and laboratory results for each newborn (hemoglobin level, number of transfusions received, transfontanelar ultrasound, histopathological examination).

Results

Both groups showed similar gestational age, birth weight, sex, hemoglobin levels. Among infants who required blood transfusions 24 patients (37.5%) developed severe complications – worsening ofintraventricular hemorrhage,ventriculomegaly, hydrocephalus, 8 of them (12.5%) being extremely low birth weight (790-900g) . The control group did not experience worsening of existing intraventricular hemorrhage. Patients with most transfusions received (3,4) are those who have developed an increase in the severity of IV hemorrhage: to 9 of themthe form of the IVH increased from II to III degree, to 11 of them IVH increased from I to III degree and 4 of the infants developed IV degree IVH.In severe forms of the disease, those who required red blood cells transfusion had an increase in both the form of IV hemorrhage and the corresponding neurological syndrome.Althought we could not make a clear distinction between worsening of the IV hemorrhage after red blood cell transfusion or due to the complications of the associated pathology, we did make some observations: from the study group, those 24 patients (37.5%) who developed severe complications, 10 of them did because of the associated pathology and in others 14 patients we did noticed worsening of the intraventricularhemorrhage and the corresponding neurological syndrome, ventriculomegaly and hydrocephalus.

Discussions

Although the numbers of transfusions administered to preterm infants remains significant, they have decreased over the last 20 years, primarily due to the institution of restrictive transfusion guidelines in conjunction with the study of erythropoietin administration to preterm infants (4). Efforts have been made to limit transfusions and consequent donor exposures to the fewest number possible. If RBC transfusions is causally-liked with IVH in some cases, successful efforts to eliminate (or reduce) early RBC transfusions should diminish the incidence of IVH.The latest studies have showed that stripping (milking) the umbilical cord blood of small preterm infants before the cord is clamped and cut and also drawing baseline NICU blood tests from fetal blood in the placenta (thus initially drawing no blood from the newborn) do have a lot of benefits:

- more normal blood pressure
- less vasopressor use
- fewer early transfusions
- lower incidence of IVH. It was established cord milkingreduces the need for red cell transfusions in VLBW neonates with 50% and also the IVH is reduced with 50%.

Conclusions

Repeated transfusions of packed red blood cells is a cause of worsening theintraventricular hemorrhage in preterm infants with low birth weight (23%) compared with controls.

Prematurity itself can be a cause of severe anemia corrected only by red blood cell transfusion.

Severe associated pathology increases the degree of the anemia and also the incidence of IV hemorrhage in this category of infants.

Repeated transfusions of packed red blood cells is a cause of worsening of IV hemorrhage in VLBW neonates.

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