Neonatal transfusion practices

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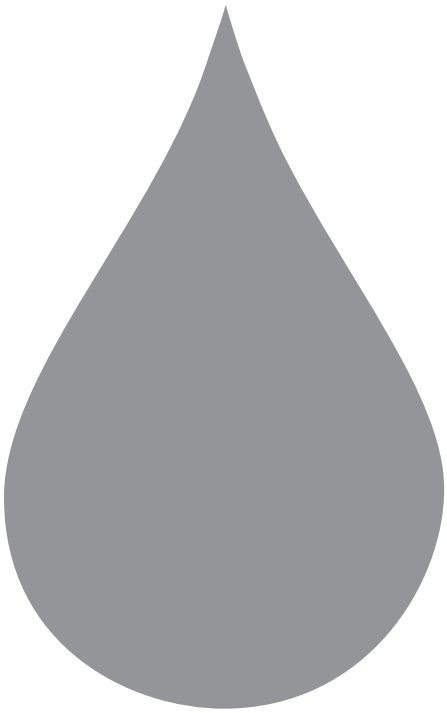
Chapter 12

Summary



In very premature born infants red blood cells are one of the most commonly used products. Nowadays erythrocytes are deemed fairly safe although not enough is known about the effects of an allogenic red blood cell (RBC) transfusion on the still developing immune system of these young infants. Alternatives to allogenic red blood cell transfusions are sought and ways to reduce the amount of transfusions needed, specifically by premature infants, remain a hot topic.
Thrombocytes are the second most used blood product in perinatal medicine. They are of greater concern in regard to transfer of infectious agents.
There is no consensus on the threshold for transfusion for both erythrocytes and thrombocytes. The effects of liberal or restrictive erythrocyte transfusion strategies are still debated. A safe lower threshold for platelet transfusions has still not been established.

In **chapter 1** the problem concerning blood products in neonatal medicine is outlined. The studies performed for this thesis are introduced.

In **chapter 2** a review of the literature is given concerning the various blood products used in perinatal medicine. The different transfusion thresholds are discussed as well as still standing research questions.

Part I Umbilical cord blood

Chapter 3 describes the possibility at birth to predict the need for a RBC transfusion within the first month of life in a premature born infant. Data on 288 infants born between 24 and 36 weeks of gestation were collected. Gestational age of less than 32 weeks and one minute Apgar score of less than 6 were independently associated with the chance of receiving a RBC transfusion in the first thirty days of life. In the newborns with a gestational age of less than 32 weeks, birth weight was also a factor determining the risk of transfusion.
We also looked at the possibility to harvest umbilical cord blood (UCB) in these infants.
The volume harvested was compared to the total erythrocyte transfusion volume in these children, so as to see whether their transfusion needs could have been covered by autologous RBCs.
Sixty-three% of the collected UCB samples was large enough to process and 61% was suitable as a potential RBC transfusion product. For 41% of the infants with a gestational age less than 32 weeks the autologous UCB product would have been sufficient to meet all transfusion needs in the first 30 days of life.

The feasibility to use red blood cells derived from umbilical cord blood for autologous erythrocyte transfusion is described in **Chapter 4**. The aim of the study was to replace 50% of all donor RBC transfusions by autologous RBC transfusions. In 90% of the 195 cases an attempt to collect UCB was done. In 57% of these cases the volume was large enough (≥15 mL) to process, resulting in 64 autologous RBC units (36% of the total population). Due to low collected UCB volumes and subsequent small red blood cell products a transfusion product was available for only 27% of the transfused infants, covering 58% of their transfusion needs within the shelf life time of this autologous RBC product.

Part II Red bloods

In **chapter 5** the results are presented of a prospective study comparing two cohorts of 218 and 241 premature infants born before a gestational age of 32 weeks admitted to two neonatal centers. These centers used the same RBC transfusion trigger but a different transfusion volume (15 vs. 20 mL/kg). The effects of the transfusion volume on the number of RBC transfusion episodes, total transfusion volume and neonatal complications are described. In the lower-transfusion-volume unit we found a significantly lower amount of infants transfused than in the higher-transfusion-volume unit (59% vs. 77%, $p<0.001$). In the group of infants with a gestational age between 24 6/7 and 27 6/7 weeks both units showed a similar percentage of infants with a RBC transfusion and a similar transfusion frequency per infant leading to a significantly higher total transfusion volume in the higher transfusion volume unit (77 mL/kg in the lower-transfusion-volume unit versus 104 mL/kg in the higher-transfusion-volume unit, $p<0.01$). In the group of infants with a gestational age between 28 0/7 and 31 6/7 weeks the total transfusion volume was comparable, given in 3 episodes in the lower-transfusion-volume unit and 2 episodes in the higher-transfusion-volume unit. This resulted in a greater donor exposure in the lower-transfusion-volume unit compared to the higher-transfusion-volume unit, as we did not use reserved single-donor pedipacks for these infants. The composite clinical outcome in regard to bronchopulmonary dysplasia, intraventricular hemorrhage (IVH), retinopathy of prematurity and mortality was similar in both units, showing no detrimental effects of a different total transfusion volume on short term outcome.

Chapter 6 shows the neurodevelopmental outcome, post discharge mortality, blindness and deafness at the corrected age (CA) of 24 months in the subgroup infants born before a gestational age of 28 weeks described in chapter 5. Both units transfused an equal percentage of infants in this age group. The infants in both units received a mean number of RBC transfusions of 5.5. Unit A transfused with a volume of 15 mL/kg, Unit B 20 mL/kg. This led to

a significant difference in total transfusion volume of respectively 79 ± 47 mL/kg and 108 ± 47 mL/kg (p=0.02). There was no significant relationship between the composite outcome at 24 months CA and the total transfusion volume received during the post natal hospital stay.

Chapter 7 shows that despite a national guideline for the transfusion of RBCs, most neonatal intensive care centers (NICUs) in the Netherlands have their own transfusion protocol taking gestational age and degree of illness into account. The international literature shows a variety of guidelines with no definite thresholds either. The following thresholds are advised: Hb 8.0 mmol/L in case of endotracheal ventilation, Hb 7.0 mmol/L in stable infants with cardiopulmonary problems and extra oxygen need, Hb 6.0 mmol/L in stable infants less than 4 weeks old and Hb 4.5 mmol/L in stable older infants. We recommend 15 mL/kg of RBCs per transfusion. Indications for irradiating blood products and administering Parvovirus B19 safe blood are given.

Part III Platelets

Chapter 8 describes the frequency of thrombocytopenia and the risk of IVH in our tertiary care NICU in Leiden, The Netherlands. We retrospectively studied all infants (n=1727) admitted to our ward during a three-year period (January 2006–December 2008). The risk of persistent thrombocytopenia, defined as a platelet count below 150 x 10^9/L found at more than one measurement, was 27% (n=422), comparable to the frequency reported in the literature. The difference in the risk of IVH ≥ grade 2 in infants with thrombocytopenia compared to a normal platelet count was significant, 12% versus 5% (p<0.01) respectively. The severity of thrombocytopenia in relation to the incidence of severe IVH, however, showed no correlation.

In **Chapter 9** the number of very premature thrombocytopenic infants with intracranial hemorrhages and other severe bleedings in two Dutch NICUs with a different platelet transfusion guideline are compared. In the restrictive-platelet-transfusion-guideline unit transfusions were given only in case of a major hemorrhage (IVH > grade 2, mucosal, pulmonary or gastro-intestinal bleeding), severe bruising or massive petechiae, surgery or the need for an invasive procedure *and* a platelet count <50 x 10^9/L. In the liberal-platelet-transfusion-guideline unit the indications for a platelet transfusion were based on platelet counts: 1) platelet count <30 x 10^9/L in clinically stable infants, 2) platelet count <50 x 10^9/L in unstable infants and/or before planned surgery, 3) platelet count <100 x 10^9/L in neonates with active bleeding and/or at start of exchange transfusion. In the restrictive-transfusion

unit the number of thrombocytopenic infants transfused was significantly lower compared to the liberal-transfusion unit (15% (21/145) versus 31% (44/141), p=0.001). Despite the more restrictive transfusion strategy the number of infants with a (severe) intracranial hemorrhage was comparable (p=0.38). Our conclusion is that more liberal platelet transfusion guidelines do not diminish the number of hemorrhages in very premature thrombocytopenic infants.

Chapter 10 describes the difference in platelet transfusion protocols in the Dutch NICUs despite a national guideline. These guidelines are compared to the national guideline and the revised guideline 2011. International guidelines are presented. Internationally no safe lower threshold has been established. We propose to administer platelets in all infants with a platelet count <20 x 10^9/L. For ill infants younger than 32 weeks of gestation or with a bodyweight below 1500 gram, or for infants with an active major hemorrhage, in need of surgery or an invasive procedure or after an exchange transfusion a minimum platelet count of 50 x 10^9/L is advised. In case of extra corporal membrane oxygenation (ECMO) or before an exchange transfusion platelet counts should be maintained ≥100 x 10^9/L. A platelet concentrate acquired through apheresis of a single donor containing at least 10 x 10^9 platelets/kg should be given. Indications for irradiation of products and Parvovirus B19 safety are similar to those for RBCs.

In conclusion, preventative measures for anemia should be used to reduce the number of RBC transfusions needed. Alternatives for allogenic RBC transfusions should be further explored and implemented.
The effect of platelet transfusions on the risk of bleeding is not always evident and needs to be studied further.
We state that both for RBC and platelet transfusions in (premature) newborn infants safe thresholds are still not established. Transfusions may have (late) detrimental effects. Safe thresholds for both erythrocytes and platelets need to be found by large prospective randomized trials focussing not only on the direct effects but also on the long-term effects.