Neonatal transfusion practices

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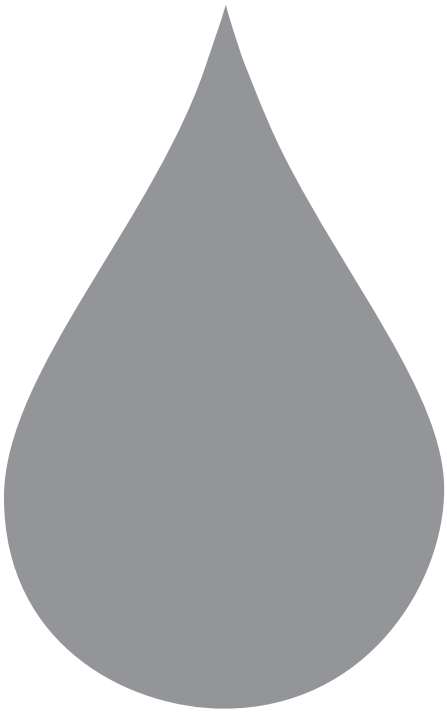
Chapter 1

General introduction and outline of the thesis



General introduction

Neonatology is a fast evolving field in medicine. In recent years great improvements have been made, such as new respiratory support strategies which have greatly improved pulmonary outcome by reducing acute lung injury. Many drugs and therapies used in neonatal medicine have not been tested in randomized trials on young and small infants but are used based on extrapolations of the effects in older children and adults. A treatment mode neonatology can't do without is the use of blood products, especially red blood cell (RBC) transfusions. Over the past few decades the survival rate of (extremely) premature and low birth weight infants has increased, which has led to more emphasis on the long-term outcome in relation to the treatment modalities used during their stay in the neonatal intensive care unit.
Transfusion medicine is a field which has received little interest from pediatricians and neonatologists and it seems difficult to recruit clinical specialists for research on blood products in their patients despite blood products being a life saving treatment.[1]

Red blood cells

In the younger gestational ages blood products are frequently used. Nearly all infants with a gestational age below 28 weeks or <1000 grams will need at least one red blood cell transfusion in the first few weeks of life.[2-4]
Concerns about the effects on the developing immune system, risk of increased oxidative stress and questions about the effect of extra volume loads on the circulation and cerebral perfusion during transfusion have been addressed.[5-7]
It is increasingly known that one of the major reasons for anemia of prematurity is blood drawn for laboratory investigation or loss during procedures. This increased awareness has led to micro-blood testing, a critical view on the amount of testing done and indwelling lines for blood drawing purposes leading to less blood loss.[8-10] Despite these measures many RBC transfusions are still given in clinical practice.

When to transfuse and what volume to transfuse remain important questions, although these have been addressed in various reports. Research has been done to try and establish transfusion thresholds using hemoglobin (Hb) or hematocrit level and transfusion volume, but these studies advise different values and are difficult to compare due to differences in patient groups, used transfusion volumes, transfusion thresholds, transfusion products and outcome measures.

Results of various studies also show conflicting short-term outcome.[11-13] As far as long-term outcome is considered only one study has been done, showing possible detrimental effects of a lower RBC transfusion threshold.[14]
Donor exposure due to transfusion of blood products is a major concern. Effects on the developing immune system, transfer of infectious agents and graft-versus-host disease are only a few of the possible risks. Efforts to reduce the donor exposition comprise amongst others delayed cord clamping, umbilical cord 'milking', critical approach to the necessity of blood testing, micro-blood tests, single-donor programs, and defining a safe lower transfusion threshold.

Platelets

Another issue in transfusion medicine in neonatology is the need for platelet transfusions in newborns with thrombocytopenia (defined as a platelet count below 150 x 10^9/L). Research has been done to find a safe lower threshold for platelet transfusion using various platelet levels for different clinical conditions. However, the severity of thrombocytopenia does not seem to correlate with the severity of the detrimental effects, such as a major bleeding. The negative effects of a low platelet count can be so disastrous that no one dares to suggest a very low transfusion threshold. The question however is not, 'how low should we go?' but 'how low can we go?'. Most international protocols are based only partially on firm evidence. Many guidelines are also expert-based or based on (years of) experience.

Thrombocytopenia occurs in 1–7% of all newborn infants. Among infants admitted to the neonatal intensive care units this percentage is much higher (up to 35%).[15-17] In adults and in children and newborn infants the effects of a low platelet count are not well known. Thrombocytopenia is usually the result of an underlying disease which can also cause deleterious effects. Platelets, next to clotting factors, are needed for the blood clotting process. How many thrombocytes one at least needs remains a question. Severe hemorrhages have been described with a completely normal platelet count and only superficial petechiae in extreme thrombocytopenic conditions as idiopathic thrombocytopenic purpura.

Study objectives

a. To summarize the international literature on the use of red blood cell and thrombocyte products in peri- and neonatal medicine.
b. To find a way to reduce donor exposure in the most vulnerable group of patients by harvesting umbilical cord blood and processing this to an autologous red blood cell product.
c. To reduce donor exposure by transfusing autologous red blood cell products.

d. To compare the short-term and long-term outcome of two different red blood cell transfusion volumes.
e. To study the risk of hemorrhage in thrombocytopenic newborns.
f. To evaluate the erythrocyte and thrombocyte transfusion protocols of the neonatal intensive care units in the Netherlands and compare them to the national and international guidelines.

Outline of the thesis:

In **chapter 2** an overview of the literature on the use of perinatal blood products is given.

Part I describes our studies concerning umbilical cord blood.
In **chapter 3** we describe our pilot study to lower donor exposure by harvesting RBCs after birth from the placenta and umbilical cord of premature born infants and turning this into a red blood cell product for autologous transfusion to be used in the first few weeks of life.
In **chapter 4** our feasibility study on the use of autologous umbilical cord blood RBCs is described.

Part II focuses on red blood cell transfusions in (premature) newborns.
Chapter 5 describes the short-term outcome in two groups of infants born before 32 weeks gestation treated with different RBC transfusion volumes.
Chapter 6 describes the long-term outcome of two groups of extremely premature infants treated with different RBC volumes.
In **chapter 7** we describe the current protocols used in the 10 Dutch neonatal intensive care units (NICUs) regarding RBC transfusions in newborns and compare them to the national guideline 2004, international literature and the revised guideline 2011.

Part III focuses on platelet transfusions in newborns.
The results of our retrospective study on all admitted newborns to our NICU with thrombocytopenia during a three year period are presented in **chapter 8**.
Chapter 9 shows the outcome of two different platelet transfusion strategies on hemorrhage in thrombocytopenic extreme premature neonates admitted to two Dutch NICUs.
Chapter 10 describes the current protocols used in the 10 Dutch NICUs regarding platelet transfusions in newborns and compares them to the national guideline 2004, international literature and the revised guideline 2011.

The results of this thesis are described in **chapter 11** and future research questions are addressed.

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