Developing Evidence-Based Practice Guidelines for Neonatal Blood Transfusions

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Abstract

Premature infants receive packed red blood cell (PRBC) transfusions to maintain a hemoglobin threshold, replace laboratory losses, or treat symptoms such as tachycardia, tachypnea, apnea, or growth failure (Kasat, Hendrickson-Munoz & Mally, 2011). There are no widely established parameters for PRBC transfusions in neonates, which leads to variations in practice. Some institutions have established unit specific guidelines, but the overall practice is based on the provider discretion. The development of an evidence-based practice guideline is intended to set a consistent, lower hemoglobin threshold at which neonates in the neonatal intensive care unit (NICU) receive PRBCs with a goal of decreasing the frequency of PRBC transfusions. Preventing short term and long term problems in the neonate is the ultimate desired outcome. This review will give an overview of the pathophysiology of the neonate receiving PRBCs, short and long term problems associated with neonatal PRBC transfusions, and restrictive versus liberal transfusion criteria. A retrospective chart review was performed describing the indications for patients that had received transfusions in the NICU at Mayo Clinic-Rochester during 2012. A Hemoglobin Threshold Transfusion Guideline was developed after extensive literature review.

Developing Evidence-Based Practice Guidelines for Neonatal Blood Transfusions

Premature infants are among the most frequently transfused population of patients. There are 38,000 premature infants weighing less than 1,500 grams born annually in the United States and up to 80% of these infants will receive multiple blood transfusions (Ringer, Richardson, Sacher, Keszler & Hallowell Churchill, 1998). Frequent laboratory testing, anemia, and critical illness contribute to the need for packed red blood cell (PRBC) transfusions in this population. Premature infants weighing less than 1,500 grams can have a weekly blood loss 10-30% of their total blood volume due to frequent laboratory samples (Wildness, Madan, Grindeanu, Zimmerman, Wong & Stevenson, 2005). This is significant since the volume of blood transfused is highly correlated to the total blood volume removed (Wildness et al., 2005). Unfortunately, there is no clinical parameter to determine when to transfuse PRBCs in a neonate. The decision to transfuse PRBCs is ultimately done by provider discretion, which results in a wide variation of neonatal transfusion practices. Indications for PRBCs can be to maintain a set hemoglobin threshold, replace laboratory losses, or treat symptoms such as tachycardia, tachypnea, apnea, or growth failure (Kasat, Hendrickson-Munoz & Mally, 2011).

Significance

An evidence-based practice guideline that will establish a lower, consistent hemoglobin level is a possible solution to decreasing the number of PRBC transfusions. The development of an evidence-based practice guideline for PRBC transfusions is important because it will provide guidance for neonatal nurse practitioners and other providers. It will standardize the practice and decrease the number of PRBC transfusions for this population. Neonates managed without transfusion guidelines are twice as likely to receive blood transfusions compared to neonates who are managed with a transfusion guideline (Kasat et al., 2011).

Problem Statement

The current practice for PRBC transfusions at Mayo Clinic-Rochester lacks guidance and suggests there is a need to standardize the practice and set consistent lower hemoglobin levels to decrease PRBC transfusions among this population. There is much variation in transfusion practices among the neonatologists and providers within this facility.

Literature Review

Multiple problems exist for neonates who receive PRBC transfusions. The standardization of criteria to be used by providers to decrease the number of PRBC transfusions is needed. This review gives an overview of the pathophysiology of the neonate receiving PRBCs, short and long term problems associated with neonatal PRBC transfusions, restrictive versus liberal transfusion criteria and finally short and long term outcomes associated with neonatal PRBC transfusions. Appropriate indications and thresholds were able to be identified by reviewing the current literature.

Pathophysiology of Blood Transfusion in Neonates

The main function of the red blood cell is to transport oxygen from the pulmonary bed to other tissues for release. The oxygen-carrying capacity is diminished and tissue oxygenation can be comprised in cases of anemia. PRBC transfusions can be indicated to restore tissue oxygenation and expand blood volume in neonates (Luchtman-Jones & Wilson, 2011). Premature infants are vulnerable to anemia because the postnatal decrease in hemoglobin is more pronounced, reaching a nadir of 7-9 mg/dL at 4-8 weeks (Gomella, 2009). These infants are also more prone to develop severe cardiorespiratory illness and infection which requires frequent laboratory assessment and blood loss from laboratory sampling (Wideness, 2008). The

combination of decreased hemoglobin, laboratory sampling, short lifespan of red blood cells, and inadequate erythropoietin production contribute to need for PRBC transfusions in neonates.

Clinical Problems Associated with Neonatal Blood Transfusion

Chronic lung disease, retinopathy of prematurity, and intraventricular hemorrhage are clinical problems that have been associated with PRBC transfusions along with an increased risk of necrotizing entercolitis during PRBC transfusions (Kasat et al., 2011). Incompatibility, transfusion reactions, and infections such as hepatitis B, hepatitis C and human immunodeficiency virus are also associated clinical problems connected with neonatal PRBC transfusions (Ringer et al., 1998).

Prevention of Blood Loss in Neonates

Studies have shown that delayed cord clamping, decreasing laboratory testing and laboratory losses, autologous placental blood transfusion, erythropoietin use and the introduction of more conservative transfusion guidelines can decrease transfusions in extremely low birth weight neonates (Madan, Kumar, Adams, Benitz, Gaeghan & Wideness, 2005).

Restrictive or Liberal Hemoglobin Thresholds.

The Premature Infants in Need of Transfusions (PINT) study was a randomized control trial conducted by Kirplani, Whyte, Andersen, Asztalos, Heddle, Blajchman…& Roberts (2006). Kirpalini et al. (2006) reported the primary outcome of death or survival with ROP, BPD, or brain injury defined as presence of cystic periventricular leukomalcia, intra-parenchymal echodensity, porencephalic cyst, or ventriculomegaly on ultrasound prior to discharge was demonstrated in 74% percent of the restrictive group compared to 69.7% of the liberal group; which was not significantly different. There were no significant differences demonstrated among any of the secondary outcomes of hemoglobin level, number of PRBC transfusions,

number of donor exposures, rate of growth, serum ferritin change, cases of necrotizing entercolitis, apnea requiring treatment, use of xanthines or doxapram, culture proven infections, post-natal steroids, time on oxygen, time to extubation, and time to discharge (Kirpalani et al., 2006). Kirpalani et al. (2006) reported that in the first four weeks of life the liberal group maintained a mean hemoglobin concentration about 10 mg/dL higher the restrictive group, which provides evidence that the transfusion thresholds can be moved downward by 10 mg/dL in ELBW infants without a clinically important increase in the risk of death or neonatal morbidity. Whyte et al. (2009) evaluated the consequences of the previously mentioned PINT study by investigating the neurodevelopmental outcomes of the ELBW infant's that were randomly assigned to the restrictive versus liberal hemoglobin transfusion threshold groups. Whyte et al. (2009) enrolled the same 451 infants from their original research study and obtained outcomes on 421 of those infants 18 to 21 months' corrected age. Thirty infants were lost due to previous deaths or lost contact prior to follow-up. The infants were evaluated for death or the presence of cerebral palsy, cognitive delay, and severe visual and/or hearing impairment. Neonatal follow-up physicians and certified psychologists evaluated these infants using the Bayley Scales of Infant Development. Whyte et al. found some "weak evidence of benefit from a higher hemoglobin threshold for transfusion primarily through a secondary analysis of cognitive delay" (p. 212). The study report continues by saying it is a "borderline statistical significance" and "not conclusive in its own right but is hard to dismiss as simply the play of chance"; therefore, additional investigation is encouraged (Whyte et al., 2009, p. 212).

The Bell et al. Study (Iowa). In a randomized trial by Bell et al. (2005), the focus was similar to the PINT study. The trial was designed to review liberal versus restrictive guidelines for red blood cell transfusion in preterm infants (Bell et al., 2005). This study is referred to as the

Iowa Trial. The study was designed to include infants weighing less than 1300 grams and more than 500 grams. The infants were further stratified into three groups based on weight. The groups were infants weighing 500 grams to 750 grams, 751 grams to 1000 grams, and 1001 grams to 1300 grams (Bell et al., 2005). Within each of these three groups, the infants were then assigned to the liberal or restrictive hemoglobin programs for red blood cell transfusion thresholds. There were a total of 100 infants enrolled in this study after filtering through the exclusion criteria, declined parental consent, and other reasons (Bell et al., 2005). The exclusion criteria included infants that had alloimmune hemolytic disease, congenital heart disease, other major birth defects requiring surgery, or a chromosomal abnormality (Bell et al., 2005). The study also excluded the infants if death was thought to be imminent, familial, religious or philosophical objections were present, or if they had received prior transfusions before they were enrolled in the study (Bell et al., 2005). Infants were also excluded if they were taking part in another study that may interfere with the results of this study or the already noted study. Each of the participants did require parental consent prior to enrollment.

The study was further developed to determine the intervention thresholds for each patient and transfusions were only administered when hematocrit level fell below the assigned value (Bell et al., 2005). The patients' hematocrit thresholds were altered based on respiratory support. The infant's threshold would be altered based on respiratory support that was broken into three phases. The three phases included infants requiring endotracheal intubation (phase 1), nasal continuous positive airway pressure (NCPAP) or supplemental oxygen (phase 2), and requiring neither positive pressure nor oxygen (phase 3) (Bell et al., 2005). Transfusions were administered at 15 ml/kg when the infant would reach or fall below their hematocrit threshold based on the phase the infant was in at that time. The infants may have received an additional

transfusion based on other pre-determined criteria (i.e. preoperative per surgeon request, increased respiratory support, apnea of prematurity requiring intervention, treatment of hypovolemia, etc.) (Bell et al., 2005).

The results of the study were evaluated based on criteria for "number of transfusions received, number of RBC donors, survival to discharge, occurrence of a patent ductus arterious (PDA), germinal matrix or intraventricular hemorrhage, periventricular leukomalcia, ROP, BPD based on 2 criteria (oxygen dependence at postnatal age 1 month and postmenstrual age 36 weeks), duration of assisted ventilation, duration of supplemental oxygen, number and frequency of apnea to various degrees, evaluation of growth in regards to weight and length, and number of days hospitalized (Bell et al., 2005, p. 1686)."

After review of the Bell Study criteria, the 51 infants enrolled in the liberal transfusion group received more RBC transfusions than the 49 infants in the restrictive transfusion group (5.2 to 3.3, respectively) (Bell et al., 2005, p. 1688). The study identified no difference in survival or risk of PDA, ROP, BPD, along with no difference in time on assisted ventilation, time on supplemental oxygen, time to double birth weight, or time spent in the hospital (Bell et al., 2005). The study identified no difference in risk of a germinal matrix or intraventricular hemorrhage (IVH) of all grades. The study did note that there was increased incidence of IVH, parenchymal brain hemorrhage, and periventricular leukomalcia (PVL) in the restrictive blood transfusion group, but it was not statistically significant (P=.115) (Bell et al., 2005, p. 1689). The study did also reveal that the restrictive transfusion group had significantly more apnea with varying degrees of intervention required than those in the liberal transfusion group (Bell et al., 2005).

The study concluded that in a comparison of the restrictive versus liberal transfusion groups, the number of transfusions can be reduced by utilizing lower restrictive thresholds. The question was raised in regards to the increase in apneic episodes and brain insults (i.e. PVL, IVH) in the restrictive blood transfusion group and their possible negative effect on neurologic outcomes. Overall the investigators of this study suggest that utilizing restrictive transfusion thresholds in clinical practice should be evaluated carefully, because they are not without cost (Bell et al., 2005).

Bell, Strauss, Wildness, Mahoney, Mock, Seward…& Zimmerman (2005) conducted a randomized trial of restrictive versus liberal guidelines for PRBC transfusions 103 preterm infants with birth weights of 500-1300 grams admitted to the Children's Hospital of Iowa NICU. Bell et al., (2005) reported that there were no difference in survival, risk of patent ductus arteriosus, retinopathy of prematurity, or bronchopulmonary dysplasia, time on assisted ventilation, time on supplemental oxygen, time required to regain birth weight, time to double birth weight, or length of hospitalization. The study demonstrated that restrictive guidelines may be harmful due to likelihood of intraparenchymal brain hemorrhage or periventricular leukomalacia and more frequent episodes of apnea (Bell et al., 2005). Infants in the liberal group received more PRBC transfusion, but the number of exposed donors was not significantly different among the two groups (Bell et al., 2005).

Nopoulos, Conrad, Bell, Strauss, Widness, Magnotta… & Richman (2011) conducted a study to assess the long-term outcome of brain structure of premature infants at 12 years of age. Participants of this study were recruited from the Iowa trial, of which 55 agreed to participate. Forty-four of the participants were able to complete magnetic resonance imaging. A control group was formed for comparison. General linear model procedures were used to analyze brain

measures. Nopoulos et al. (2011) reported that intracranial volume in the restricted group was not different from the controls and the intracranial volume in the liberal group was substantially smaller compared to the control group.

The Bifano et al. Study. Bifano in 2001 was the first to evaluate neonatal transfusion guidelines in a prospective manner (Bishara & Ohls, 2009). The goal of the study was to establish two groups to be treated as a high (liberal) vs. a low (restrictive) group related to transfusion thresholds. The research study included a small population of 50 randomized infants that had birth weights of 650 grams to 1000 grams (Bishara & Ohls, 2009). The study divided the two groups based on hematocrit thresholds. The high group had a baseline hematocrit of greater than 32% while the low group would have a baseline hematocrit of less than 30% (Bishara & Ohls, 2009). The high group was treated with Epo and blood transfusions while the low group was treated with transfusions only. At the conclusion of the study the infants in the high group obtained statistically significant differences in maintaining a higher hematocrit threshold than those in the low threshold group (Bishara & Ohls, 2009). However, this study did demonstrate outcomes for these infants at 36 weeks post menstrual age and at 12 months of life, resulting in no significant differences of outcomes between the two groups. The populations were similar in growth, weight gain, head circumference, and no significant differences were identified in neurological outcomes. The researchers in this trial concluded that, in the ELBW infants, that there was an additional cost to those in the high hematocrit group with no additional benefit. They also concluded that the restrictive population was not associated with adverse outcomes.

The Chen et al. Study. A randomized trial of restrictive versus liberal thresholds was also conducted on premature infants with birth weights of less than 1500 grams at Kaohsiung

Medical University Hospital by Chen, Tseng, Lu, Yang, Fan and Yang in 2008. The restrictive group kept hematocrits above 35% for infants with assisted ventilation, above 30% for infants with nasal continuous positive airway pressure support, and above 22% in spontaneously breathing infants (Chen et al., 2009). The liberal group kept hematocrits above 45% for infants with assisted ventilation, above 40% for infants nasal continuous positive airway pressure support, and above 30% in spontaneously breathing infants (Chen et al., 2009). Chen et al. (2009) demonstrated no significant difference in the percentage of infants with patent ductus arteriosus, respiratory distress syndrome, severe intraventricular hemorrhage, retinopathy of prematurity, oxygen dependence at 28 and 36 weeks, and length of hospital stay. Chen et al. also demonstrated that infants in the liberal group received a greater volume of PRBCs over 30 days compared to the restrictive group and the reticulocyte count in the restrictive group was significantly higher than the liberal group at day 30. The restrictive group had more episodes of apnea, but the finding was not significantly different (Chen et al., 2009). The study also demonstrated that there was no statistical difference in the proportion of cases of chronic lung disease between the groups (Chen et al., 2009).

The Valieva et al. Study. Valieva, Strandjord, Mayock, & Juul (2009) conducted a retrospective chart review to determine the risks and benefits with PRBCs in ELBW infants. The chart review measured detailed patient information such as weight, respiratory support, heart rate, apnea number and severity of episodes before and after transfusions, and blood volumes both in and out of the infant. The researchers also documented intraventricular hemorrhage (IVH), NEC, ROP, and BPD as secondary outcomes. Differences between the individual patient's average in the "2 days before transfusion and the average in the 3 days after transfusion" were examined (Valieva et al., 2009, p. 332). In analyzing the statistical data Valieva et al., (2009) found during the 12 month period a total of 60 ELBW infants were admitted. The research team was able to analyze 52 of the infants and determine "47

(90%) underwent transfusion" with the average number of PRBC transfusions being "3.8 +/- 3.0 per patient" and the number and volume of transfusions decreased as both birth weight and gestational age decrease (Valieva et al., 2009, p. 333).

In further findings the study did not discover a relationship between transfusions and weight again, higher hematocrit levels protecting infants from IVH, or clinical improvement of cardiorespiratory status post transfusion. A small, but statistically insignificant, decrease in moderate and severe apneic episodes was found in infants with very low circulating hemoglobin levels. They did find necrotizing enterocolitis (NEC) was associated with PRBC transfusions within 7 days and bronchopulmonary dysplasia (BPD) was found to be associated with the number of transfusions at DOL 28, but "correlation disappeared by 36 weeks corrected gestational age" (Valieva et al., 2009, p. 335). Valieva et al. were able to say that their study did not identify any clinical benefits of their current transfusion guideline. A significant number of babies required additional respiratory support after the PRBCs and there were new concerns of NEC and BPD associated with the infusions (2009). The transfusion guidelines at University of Washington Medical Center's Neonatal Intensive Care Unit were made more restrictive.

Summary of Findings

Infants in the liberal group were more likely to receive a higher volume of PRBCs and have a higher hemoglobin level while the restrictive group maintained a higher reticulocyte count after 30 days. Kirpalani et al., (2006) and Chen et al., (2009) reported no significant difference in the number of apnea and brain injury between both groups. The Bifano et al. study incorporated Epo and blood transfusions into their liberal threshold group and found there were no significant differences in outcomes between the two groups. Valieva et al., (2009) study's statistical analysis did provide evidence to support a relationship between PRBC transfusions and the morbidities of NEC and BPD.

In contrast, Bell et al. (2004) reported an increased likelihood of intraparenchymal brain hemorrhage or periventricular leukomalacia and more frequent episodes of apnea among the restrictive group and Nopoulos (2011) reported that the intracranial volume of the liberal group was substantially smaller compared to a control group. Three of the studies found that the restrictive groups received their first transfusion at a later age and that the length of stay was not statistically significant among the restrictive and liberal groups. PINT, Bifano, and Nopoulos were the only studies that reported outcomes after hospital discharge.

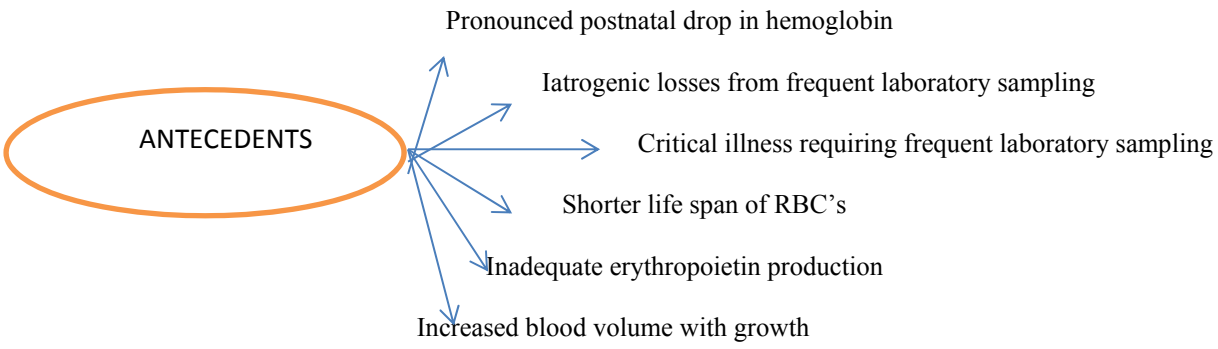
Limitations of the studies included the different enrollment criteria, inconsistent transfusion volumes, and sufficient differences in thresholds used and indications for transfusions. Only one of the studies evaluated the use of Epo in their trial. All of the studies used different thresholds for their restrictive and liberal groups and indications were also based on level of respiratory support. Different definitions were used when defining outcomes as well. Kirplani et al. (2006) defined apnea requiring intervention as bag-mask ventilation or intubation, Bell (2005) defined it as infants requiring methylxanthines, and Chen (2009) defined it as infants with absence of breathing for more than 20 seconds or a shorter pause associated with oxygen desaturation or bradycardia. Transfusion volumes varied among studies from 10 ml/kg to 15 ml/kg and the birth weights varied among the three studies. Both Chen (2009) and Bell (2005) used a single hospital for their study and Kirplani (2006) enrolled patients for 10 different hospitals.

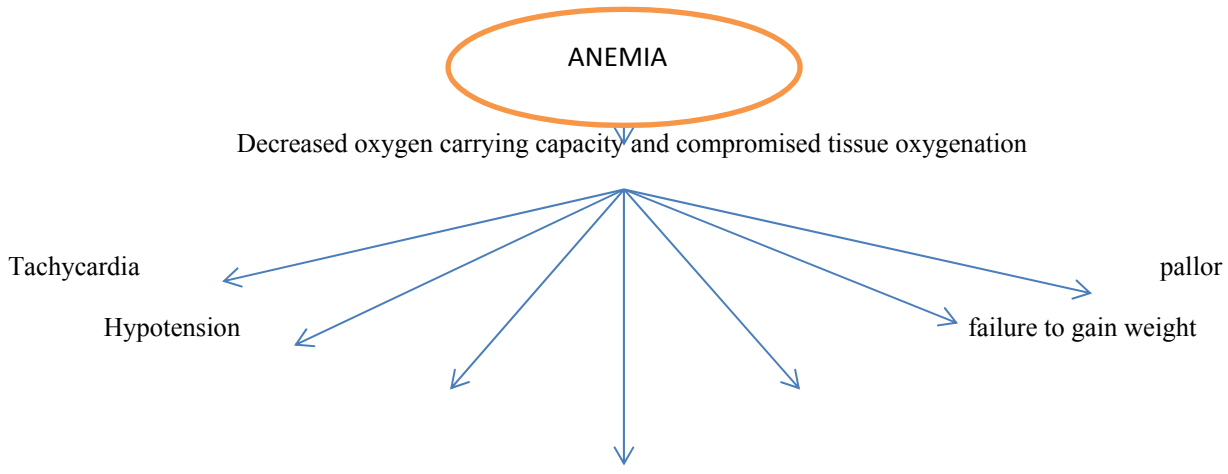
Further Considerations

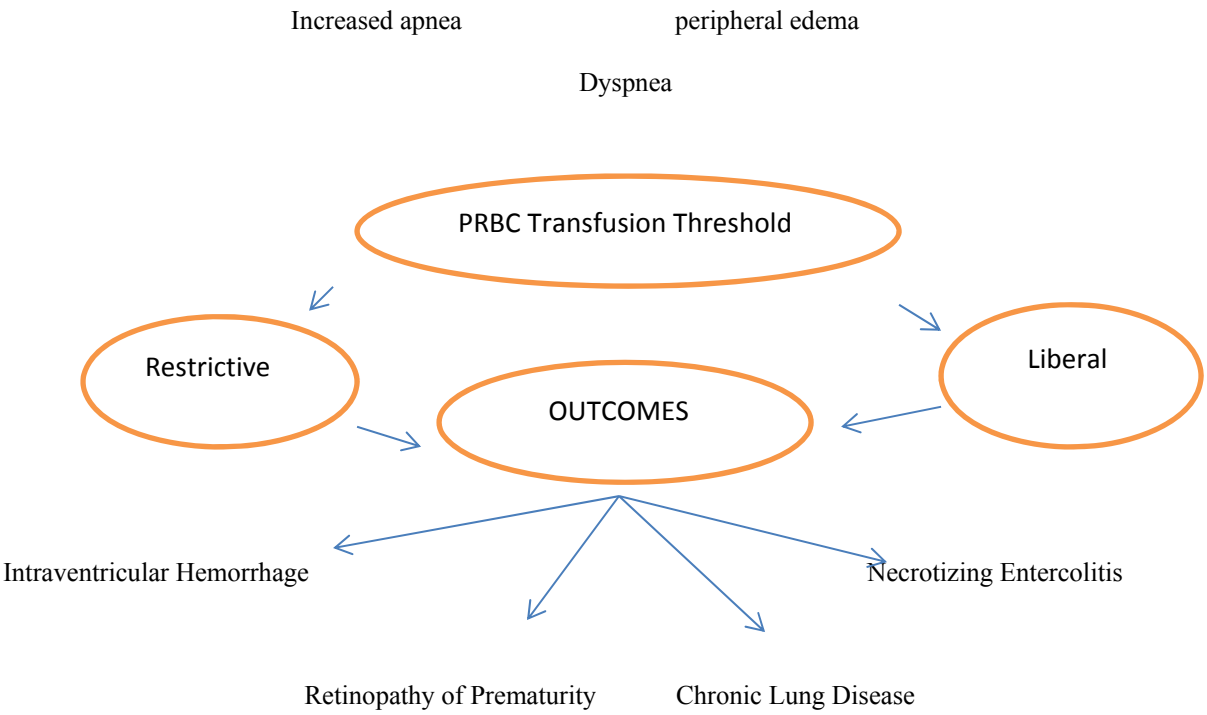
Several countries have developed evidence-based practice neonatal transfusion guidelines to decrease the number of transfusions in neonates. The Canadian Paediatric Society (2002) has identified strategies to prevent anemia and reduce donor exposure along with the risks associated

with PRBC transfusions. The strategies include delayed cord clamping, restrictive blood sampling, use of erythropoietin, use of iron supplementation and vitamins, and use of appropriately identified recommendations for red blood cell transfusions. Their literature recommends identifying: hemoglobin concentration between 10-12 mg/dL in extreme illness conditions for which RBC transfusion may improve oxygen delivery to vital organs; hemoglobin concentration between 6-10 mg/dL or hematocrit between 20-30% and the infant is severely ill and/or on mechanical ventilation; hemoglobin concentration 6.0 mg/dL or less or hematocrit falling 20%; hypovolemic shock associated with acute blood loss; and for clinical signs such as failure to thrive or no weight gain, tachycardia, tachypnea, supplemental oxygen needs, and lethargy. An evidence based guideline for Mayo Clinic-Rochester's NICU was developed considering literature findings and the NICU neonatologists' considerations.

Model of Anemia







Description of Conceptual Framework

Walker and Avant's linguistic, pragmatic concept analyzes explicit and implicit concept definitions in the literature to identify criteria, antecedents, and consequences for pragmatic purposes in research and practice (Grove, Burns & Gray, 2013). The defining attributes of the pathophysiology of anemia will provide a means to distinguish concepts and identify the characteristics that give meaning to the concept of anemia and PRBC transfusions.

Middle Range Theory

The concept of middle range theories can be summarized as less abstract theories that can be applied directly to practice and focus on clarification and application (Grove, Burns, & Gray, 2013). The Theory of Health Promotion for Preterm Infants according to Levine's Conservation Model of Nursing (Mefford, 2004) can be applied to the neonatal population, especially related to the ELBW population. This theory offers direction to restore health once the infant has been exposed to the external environment eliminating the safety of the internal environment. The

theory correlates the internal and external environment by addressing the possible threats to "energy balance, structural integrity, personal integrity, and social integrity" by addressing the adaptations required to maintain the health of the whole being (Mefford, 2004). The infant that is born prematurely is required to adapt to extrauterine life that is less than optimal to support the physiological changes necessary for life and requires effort to support the psychosocial requirements of the infant and family.

An infant weighing less than 1,000 grams requires multiple interventions to maintain structural integrity in the extrauterine environment including therapeutic treatment of PRBC transfusions to maintain homeostasis. This theory supports the problem that is being addressed in this proposal. The treatment of anemia in the ELBW infant is management of the physiologic state that is necessary to sustain life. The medical team and families understanding of the physiologic needs of the ELBW infant would require a delicate balance of weighing risks and benefits of transfusions. This threat to energy balance and the structural integrity of the infant necessitates intervention to conserve energy and integrity utilizing Levine's Model (Mefford, 2004). The interventions will improve the outcomes of the infant as evidenced by physiologic stability and growth, minimal structural injury, neurodevelopmental competence, and stability of the family system with integration of the infant into the family (Mefford, 2004).

Methods

Research Design

The design for this project was non-experimental using a retrospective chart review of patients weighing less than 1,000 grams who were admitted to the NICU at Mayo Clinic-Rochester who received PRBC transfusions in 2012. A comparative descriptive design was used

to compare Mayo Clinic-Rochester's variables to the previously mentioned literature review to develop an evidence-based guideline for PRBC transfusions.

Sample, Sampling Procedure

The convenience sample was all neonates born with a birth weight of less than 1,000 grams who were admitted from January 1, 2012 to December 31, 2012. This sample was shown to be the highest risk population to receive PRBC transfusions during their NICU stay.

Setting

The setting was a twenty-six bed level III Neonatal Intensive Care Unit at Mayo Clinic-Rochester. The unit consisted of four separate nurseries located on the third floor of the children's hospital within a hospital. Care was provided by six neonatologists, a group of rotating pediatric residents, and neonatal nurse practitioners with one hospitalist.

Ethical Considerations

The protection of human rights is extremely important in this population. Neonates are an extremely vulnerable population since they are considered legally and mentally incompetent subjects (Grove, Burns & Gray, 2012). This project was considered a research benefit since it contributed to the acquisition of knowledge for evidence-based practice. Mayo Clinic's Institutional Review Board (IRB) found this project to be exempt since the research involved the collection or study of existing data, documents and records. The HIPPA Privacy Rule applied to all subjects and data was collected in a manner that the subjects could not be identified.

Data Collection Procedures

Three primary investigators completed the data collection. Each infant in the chart review was assigned a number and data was collected on the following variables: current hemoglobin prior to the PRBC transfusion; level of respiratory support prior to the PRBC

transfusion; FiO2 prior to the PRBC transfusion; indication for the PRBC transfusion; day of life for the PRBC transfusion; and number of PRBC transfusions received during NICU stay. The data was recorded in an excel spreadsheet.

Data Analysis

Descriptive analyses of data were done to identify the mean number of PRBC transfusions, the mean day of life for PRBC transfusions, mean FiO2 prior to the PRBC transfusion, and the indications given for PRBC transfusions. A primary analysis of data was performed by the three primary investigators to develop the Hemoglobin Threshold Transfusion Guideline.

Results

Data were reviewed on 23 patients who were admitted to the NICU at Mayo Clinic-Rochester during the year of 2012. One patient was excluded for congenital anomalies. The mean hemoglobin for PRBC transfusions was 10.3 mg/dL with a range of 6.9 mg/dL to 12.3 mg/dL. The mean FiO2 was 0.37 with a range of .21 to 1.0. The mean day of life for PRBC transfusions during the first 28 days of life was found to be 6.5. The mean number of PRBC transfusions was 6.86 with a range of 1-15. The level of respiratory support was recorded as the following options: room air, incubator O2, low –flow nasal cannula (LFNC), high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP), mechanical ventilation, or high frequency oscillation (HFOV). The indications for PRBC transfusions were recorded as anemia, hypotension, spells, volume replacement, post-surgical, respiratory distress or other. Another indication was to provide a blood prior to removal of a central line which would be an issue of convenience or prophylactic transfusion. A majority (49.3%) of the PRBC transfusions were given for anemia. There was no indication documented for 24% of the PRBC transfusions and

about 7% of the infants received PRBC transfusions prior to line removals (see Figure 1). Fifteen percent of these PRBC transfusions would have qualified for PRBC transfusions according to the newly developed Hemoglobin Threshold Transfusion Guideline (see Figure 2). Six of the PRBC transfusions had other considerations and one was excluded for going to the operation room.

Discussion

The process for the development of the unit based transfusion guideline started with the extensive literature review from the three primary investigators. The investigators met to review and analyze the literature in order to provide a concise presentation to the Mayo Clinic-Rochester Neonatology fellow and clinical nurse specialist (CNS). The fellow and CNS were assigned to the investigators as support staff in the development of the guideline. The group (CNS, fellow, and investigators) developed the guideline based off the literature. The guideline was brought to the Mayo Clinic-Rochester Neonatal Quality and Safety Committee for approval by consensus. The document was approved and was brought to the Neonatal Division Practice meeting for final approval. This meeting included the six neonatologists for the Neonatal ICU at Mayo Clinic-Rochester. Consensus was obtained and approval for implementation starting January 1st, 2014 (See Table 1). The chart review was performed after the guideline was developed due to time constraint and physician preference.

The findings of this study further supported the need for the standardized guideline for neonatal PRBC transfusions at Mayo Clinic-Rochester. The mean hemoglobin of 10.3 mg/dL and mean FiO2 of 0.37 were significant findings in support of the Hemoglobin Threshold Transfusion Guideline created after comprehensive literature review. In addition, the hemoglobin threshold for infants less than or equal to seven days of life requiring an FiO2 of ≥

40% and mechanical ventilation or CPAP ≥ 8 was determined to be 11 mg/dL while the threshold for infants greater than 7 days of life requiring an FiO2 ≥ 40% and mechanical ventilation or CPAP ≥ 8 was determined to be 10 mg/dL. The hemoglobin threshold for infants less than or equal to 7 days of life requiring an FiO2 less than 40% if mechanically ventilated or CPAP ≥ 8 was determined to be 9 mg/dL and 8 mg/dL for infants greater than 7 days of life. The mean day of life for PRBC transfusions during the first 28 days of life was found to be 6.5.

These findings suggested that patients were transfused during the first week of life and further support the Hemoglobin Threshold Transfusion Guideline's grouping of patients into categories of being less than or equal to 7 days of life or great than 7 days of life. (see Table 1). The mean number of PRBC transfusions was 6.86 which were statistically significant because patients received an average of seven transfusions, confirming that they received multiple PRBC transfusions during their initial admission. This project revealed a wide variety of indications for PRBC transfusions. Seven percent of these patients received PRBC transfusions prior to removal of central lines. The Hemoglobin Threshold Transfusion Guideline identifies exclusion criteria for patients which includes: infants with critical congenital heart disease, acute blood loss/shock, hemolytic disease, and planning for surgery. There is no indication for "removal of central of lines" and this would not a justified indication for a PRBC transfusion.

The development of the Hemoglobin Threshold Transfusion Guideline is relevant to the neonatal nurse practitioner because it standardized the practice for PRBC in the neonatal population. Standardization of PRBC transfusions is an evidence-based practice. The relevance to advanced practice nursing includes the knowledge that evidence-based practices involve high levels of clinical reasoning skills and linking these best scientific practices result in better patient health outcomes (Sebastian et al., 2000). By establishing a unit guideline, the advance practice

nurse would be able to use evidence-based practice in managing their patients daily, specifically in regards to PRBC transfusions.

Limitations of Study

This study was conducted in one hospital and compared to data identified in the previously mentioned literature review. The chart review was performed after the guideline was developed due to time constraint and physician preference. Indications were not documented in all of the electronic medical records.

Future Research

The findings of this study demonstrate a need for future research in regards to neonatal PRBC transfusions. Erythropoietin, iron supplementation, and iatrogenic blood loss are areas for potential research on this subject. Increasing the number of participants and evaluating the results of the study after implementation of the new guidelines would assist in evaluating short and long term problems associated with neonatal PRBC transfusions.

Conclusion

The development and establishment of an evidence-based practice Hemoglobin Threshold Transfusion Guideline for neonatal PRBC transfusions required an extensive literature review and data analysis. The literature review included the pathophysiology of the neonate receiving PRBCs, short- and long-term problems associated with neonatal PRBC transfusions, restrictive versus liberal transfusion criteria, and short- and long-term outcomes associated with neonatal PRBC transfusions. The data analysis, although performed after guideline development, supported the previously identified criteria for the Hemoglobin Threshold Transfusion Guideline. Specifically by identifying the variable indications and lack of consistency noted in the transfusions administered to patients in the year 2012. The guideline has been implemented at

Mayo Clinic-Rochester and a planned retrospective chart review will be performed in 2015 to evaluate the effectiveness of the guideline.

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Table 1

Hemoglobin Threshold Transfusion Guidelines

≤7 days of life	Respiratory Status	>7 days of life
11	▪ FiO2 ≥40% **AND** mechanically ventilated **OR** CPAP≥8	10
9	▪ FiO2 <40% **IF** mechanically ventilated **OR** CPAP≥8 ▪ CPAP <8, HFNC, LFNC (any FiO2)	8
8	▪ No respiratory support	7

- Guidelines should NOT apply to infants with CCHD, acute blood loss/shock, hemolytic disease, or are planning for surgery
- Transfuse 15 cc/kg of PRBCs over 3 hours
- Make infant NPO for duration of PRBC transfusion
- Removal of a central line is NOT an indication for PRBC transfusion

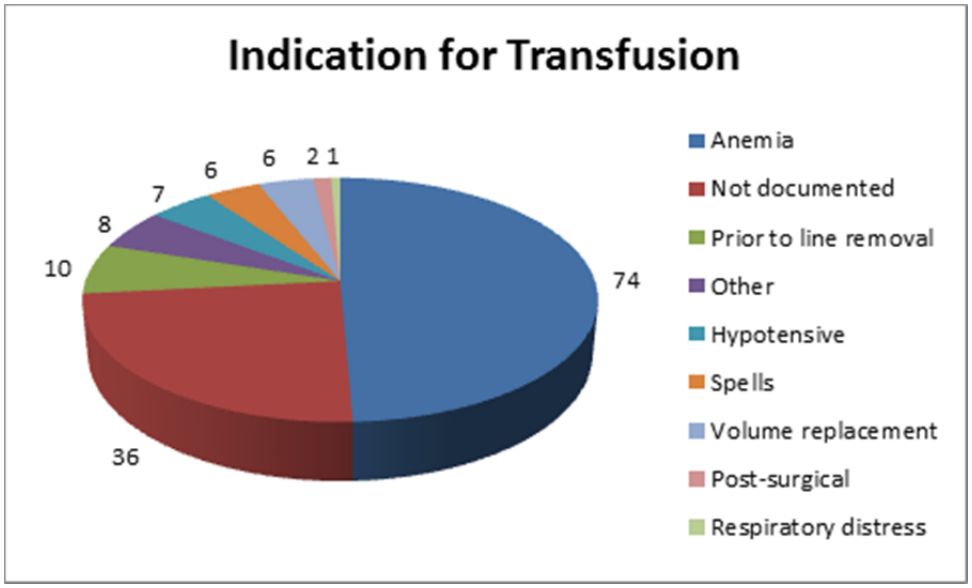
Indication for Transfusion
74
36
10
8
7
6
6
2
1
Anemia
Not documented
Prior to line removal
Other
Hypotensive
Spells
Volume replacement
Post-surgical
Respiratory distress

Figure 1.

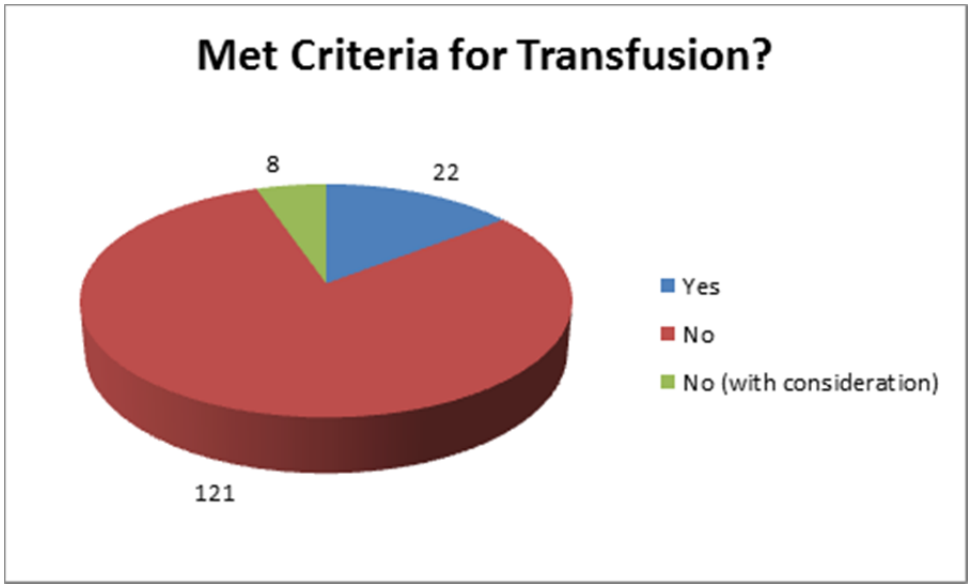
Met Criteria for Transfusion?
8
22
121
Yes
No
No (with consideration)

Figure 2.