IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 10 Ser.4 (October. 2021), PP 22-24
www.iosrjournals.org

Changes in the Use of Fresh-Frozen Plasma Transfusions in Preterm Neonates

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Abstract
Background- Preterm neonates are a highly vulnerable group of patients at risk of severe bleeding complications such as intraventricular hemorrhages (IVH). Various treatments are used to try to prevent the occurrence of hemorrhages, including the administration of platelets, vitamin K and fresh frozen plasma (FFP).
Methods- We conducted a retrospective analysis in the NICU of the S M S Medical College Jaipur. All neonates with a gestational age at birth between 24 weeks and 37 weeks, admitted to our NICU were included.
Results- A total of 21 patients (4.20%) received one or more FFP transfusions during admission. Among these 21 patients, the median number of FFP transfusions per neonate was 1.
Conclusion- In conclusion, we found that abnormal coagulation was the most frequent indication for FFP transfusion. Further research is needed because the use of coagulation values in preterm neonates is not well-validated, and whether FFP transfusion can effectively correct coagulation abnormalities or decrease bleeding risk is unknown.

Keywords- *FFP, Preterm, IVH*

Date of Submission: 29-09-2021 Date of Acceptance: 12-10-2021

I. Introduction

Preterm neonates are a highly vulnerable group of patients at risk of severe bleeding complications such as intraventricular hemorrhages (IVH). Various treatments are used to try to prevent the occurrence of hemorrhages, including the administration of platelets, vitamin K and fresh frozen plasma (FFP).[1] Although FFP transfusions are often given 'prophylactically' in non-bleeding neonates, their use is not based on robust evidence. [2]

To date, randomized trials have failed to show a beneficial effect of FFP transfusion on bleeding risk. Despite the lack of evidence, international guidelines often recommend the use of FFP in neonates with clinically significant bleeding and those who have abnormal coagulation tests, or prior to invasive procedures.[3] Since these guidelines are mainly based on expert opinion and extrapolate findings from studies in adults, international consensus on the use of FFP is lacking, with wide variation in the use of FFP transfusion among Neonatal Intensive Care Units (NICUs). Reports on the proportion of neonates receiving FFP during admission to the NICU vary from 2 to 11% . [4]

Not much is known on the variation of the use of FFP between neonatal centers or per indication, nor on the variation throughout the years. Neonatal coagulation ranges are different from those for older children and adults, and since it is unclear whether mild/moderate prolongation of PT and aPTT values predict clinical bleeding, interpreting neonatal coagulation test results can be difficult, which can contribute to variation and inappropriate use of FFP.[5]

II. Material And Methods

We conducted a retrospective analysis in the NICU of the S M S Medical College Jaipur. All neonates with a gestational age at birth between 24 weeks and 37 weeks, admitted to our NICU were included.

The main outcome measures were the percentage of neonates receiving FFP transfusion and the percentage of neonates in whom coagulation testing was performed per epoch. Additionally, we examined the primary indications for FFP transfusion as described in the patient records; abnormal coagulation was defined as at least one prolonged aPTT or PT test result and disseminated intravascular coagulation (DIC) was defined as the combination of a platelet count below 100 × 109 platelets per liter, activated partial thromboplastin time (aPTT) >90 s, prothrombin time (PT) ratio >1.5, fibrinogen concentration below 150 mg/dl, no improvement after administration of vitamin K and absence of liver disease.

As an additional outcome, we assessed the occurrence of major hemorrhage per epoch. Major hemorrhage was defined as intraventricular hemorrhage ≥ grade 3, severe gastrointestinal hemorrhage (any amount of fresh visible rectal bleeding except for mild bleeding caused by necrotizing enterocolitis (NEC)) and pulmonary hemorrhage (defined as fresh bleeding through an endotracheal tube with increased ventilatory requirements) [19,20]. We also evaluated if undergoing coagulation testing was associated with higher odds of receiving FFP transfusion. Other additional outcomes included the number of neonates with abnormal coagulation, the percentage of neonates receiving FFP transfusion and the percentage of neonates undergoing coagulation testing per gestational age at birth in weeks. Baseline characteristics included gender, gestational age at birth, birth weight, small for gestational age (SGA) (birth weight < 10th centile), multiple birth and delivery mode. We also collected the following neonatal outcome variables: NEC ≥ stage 2, proven sepsis defined as a clinically ill neonate with a positive bacterial blood culture, symptomatic patent ductus arteriosus (PDA) requiring medical treatment (indomethacin or ibuprofen) or surgical closure, respiratory distress syndrome (RDS) defined as respiratory failure requiring ventilator support and surfactant treatment, length of hospital stay in days and neonatal mortality during admission.

III. Results

Table 1. Baseline Characteristics

Mean age	35.2±0.36 weeks
Male	312 (62.4%)
Female	188 (37.6%)
Multiple birth	202(40.4%)
Received one or more FFP	21(4.20%)

A total of 21 patients (4.20%) received one or more FFP transfusions during admission. Among these 21 patients, the median number of FFP transfusions per neonate was 1.

Table 2. Indications for FFP Transfusion (n=21)

Abnormal coagulation, n (%)	10(47.62%)
Prolonged PT and aPTT	11(52.38%)
Prolonged aPTT	11(4.76%)
DIC, n (%)	5(23.81%)
Clinical bleeding, n (%)	4(19.04%)
Surgery	2(9.52%)

Overall, 500 neonates underwent coagulation testing: aPTT and PT were prolonged in 11 (52.38%) and 11 (52.38%) of these neonates, respectively. A total of 21 neonates received FFP transfusion. Coagulation was determined in 10 out of the 21 (47.26%) FFP-transfused neonates.

IV. Discussion

To our knowledge, this is the first study assessing changes in the use of FFP over the years, as most studies on the use of blood products in neonates have focused on red blood cells (RBC) and platelet transfusion. It is therefore uncertain whether a similar decrease also occurred in other NICUs. In the past few decades, the use of RBC and platelets has decreased, after studies showed that restrictive transfusion guidelines were non-inferior to liberal guidelines.[6] The reduced use of blood products (RBC and platelets) may have contributed to a concomitant decrease in the use of FFP transfusion. Overall, we found that 21 (4.20%) preterm neonates admitted to our NICU received at least one FFP transfusion.

A study by Keir et al. reported much higher use of FFP in 11% of the neonates.[7] This could be explained by the fact that they excluded neonates with a gestational age of >30 weeks. We found that the use of FFP and coagulation tests was lower in neonates with a gestational age at birth of 30 to 32 weeks. Importantly, we also saw a decrease in the percentage of neonates undergoing coagulation testing per epoch, decreasing from 24.3% to 8% over the years. We speculate that this is probably partly due to the increased awareness of

iatrogenic anemia in preterm neonates resulting from cumulative blood loss due to frequent blood draws for laboratory tests.[8]

Health professionals may, therefore, have had a more conscious attitude towards the reduction in coagulation testing. In addition, it has been recognized that neonatal coagulation test results can be ambiguous and difficult to interpret in the absence of evidence-based reference values. Some guidelines express the aim to reduce routine neonatal coagulation testing, which may have made neonatologists more inclined to skip coagulation tests.

V. Conclusion

In conclusion, we found that abnormal coagulation was the most frequent indication for FFP transfusion. Further research is needed because the use of coagulation values in preterm neonates is not well-validated, and whether FFP transfusion can effectively correct coagulation abnormalities or decrease bleeding risk is unknown.

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Dr. Sunita Ranwa, et. al. "Changes in the Use of Fresh-Frozen Plasma Transfusions in Preterm Neonates." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(10), 2021, pp. 22-24.