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Study of Blood Component Therapy in Neonates

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Abstract: ***Objectives: Blood components which are used in modern day practice include, apart from whole blood, a variety of other products like Packed Red Blood Cells , Platelets, Leucocytes, Plasma, Cryoprecipitate and individual factor concentrates . Blood component therapy is a very common intervention practiced in new-borns. The objective of this research was to study the Indications, Pattern of usage & Acute Non-infectious Transfusion Reactions (ANITR) of Blood Component therapy in neonates in Mahatma Gandhi Medical College & Research Institute (MGMCRI), Puducherry and to have an overview of evaluation of component therapy in neonatal practice. Materials and Methods: In this study 210 neonates who received various blood component transfusion like Packed Red Blood Cells, Random Donor Platelets, Fresh Frozen Plasma, Cryoprecipitate and Whole Blood (as comparator) in MGMCRI during the period of APRIL 2012 - MARCH 2015 were followed and studied in this cross sectional study. Observation and result: Neonatal Blood Component Therapy in 210 neonates, Indications: Neonatal anemia in 60%, Thrombocytopenia in 52%, Others - 42% were observed. Pattern of usage: Platelets - 42%, Packed Red Blood Cell's - 34%, Fresh Frozen Plasma - 23% and Cryoprecipitate - 1% were observed. Acute Non-infectious Transfusion Reactions were observed in 7.5% of cases. The study was extended to the other parameters like gestational age (term), sex and birth weight of the neonates also. Conclusion: There is increased usage of all Blood Component for appropriate indication for the transfusion in neonates during the period of study. Minimal transfusion reactions mainly Acute Non-infectious Transfusion Reactions not warranting stoppage of transfusion were seen. Most frequently used component was Platelets and maximum usage of components was seen in preterm and very low birth weight babies.***

Keywords: Whole Blood, Packed Red Blood Cells, Platelets, Fresh Frozen Plasma, Cryoprecipitate.

1. Introduction

Transfusion of whole blood creates hazards to the patients which was noted in the past few decades. So transfusion of blood components has been considered, to be a low risk and safe procedure [1]. Consequently an increasing need for stricter guidelines for transfusing blood products has been recognized.

Blood components can be prepared in a licenced blood bank which has the required space, specialized equipments, storage facilities and trained personnel. Advent of blood component therapy was by use of factor VIII for haemophiliacs commenced in U.K in 1980, which was prepared by fractionation of human plasma. Its not just for checking infections, but also to minimize the other side effects of blood transfusion[2].

In United Kingdom and other western countries, whole blood is not used for transfusion for the patients routinely [3,4]. With development of PVC bags with integral tubing separation of components could be done safely without risk of infections. It is processed into various components and only that are specifically needed by the patient are used. Preterm neonates are the most frequently transfused group of patients. In that 85% of extremely low birth weight newborns receives a transfusion by the end of their stay in hospital [4,5,6].

Use of Blood Components ensures added advantages:
i] Maximized use of one unit of blood for a number of patients with same unit. ii] Shelf life of each component is longer than in whole blood. iii] Better patient care with specific components without danger of overloading/ side effects of other unwarranted components. iv] Cost effective blood bank system wherein cost & processing a unit of blood is shared by a number of patients compared to as if given as whole blood to only one [7-10].
Blood components used in modern day practice include, apart from whole blood, a variety of other products, like Red Blood Cell products, Leukocyte products, Platelet Concentrates and Plasma is shown in the **Table 1** [11].

Table 1: Various Blood products

Red blood cell products	Platelet products	Leukocyte products	Plasma	Plasma derivatives
Packed red cells	Platelet rich plasma	Granulocyte rich plasma	Fresh frozen plasma	Factor VIII Concentrate
WBC poor red cells	Platelet concentrate	Lymphocyte rich plasma	Frozen plasma	Factor IX Concentrate
WBC depleted red cells	Frozen platelets		Cryoprecipitate	AT-III Concentrate
Washed red cells			Cryo removed plasma	Factor XIII Concentrate
Frozen deglycerolized red cells				Albumin
				IV Immunoglobulin
				Rh Immunoglobulin

The Guidelines for the transfusion of Packed Red Blood Cells (PRBCs) varies according to age, level of sickness and haematocrit is shown in the **Table 2** [12].

Table 2: Guidelines for transfusion of PRBCs in neonates

i] Hematocrit <20% with low reticulocyte count with symptoms
ii] Hematocrit <30% and any of the following: a. On <35% oxygen hood b. O2 by nasal cannula. c. On CPAP* and/or on ventilation d. With significant tachycardia or tachypnea (heart rate >180 beats/min or respiratory rate >80 beats /min for 24 hours). e. With significant apnea or bradycardia (>6 episodes in 12 hours or 2 episodes in 24 hours requiring bag and mask ventilation) f. With low weight gain (<10 g/day over 4 days).
iii] Hematocrit <35% and either of the following: a. On >35% oxygen hood. b. On CPAP pressure ≥6-8 cm of water.
iv] Hematocrit <45% and either of the following: a. On extracorporeal membrane oxygenation. b. With congenital cyanotic heart disease

* **CPAP - Continuous positive airway pressure**

The Guidelines for Platelet transfusion in neonates varies according to the platelet value range and shown in the **Table 3** [13,14].

Table 3: Guidelines for transfusion of Platelets in neonates

i] Platelet count less than 30,000/cubic mm: transfuse all neonates, even if asymptomatic.
ii] Platelet count 30,000 to 50,000/cubic mm: consider transfusion a. Sick or bleeding newborns b. Newborns weighing less than 1000 gm or less than 1 week of age c. Previous major bleeding tendency (Intraventricular Hemorrhage grade 3-4) d. Newborns with concurrent coagulopathy e. Requiring surgery or exchange transfusion
iii] Platelet count more than 50,000 to 99,000/cubic mm: transfuse only if actively bleeding.

The Indications for the use of Fresh Frozen Plasma (FFP) in neonates is shown in the **Table 4** [15].

Table 4: Indications for transfusion of FFP in neonates

i] Congenital coagulopathies – rare
ii] Acquired coagulopathies a. Vitamin K deficiency; b. Disseminated intravascular coagulation (DIC); c. Liver disease – liver failure; d. Anticoagulant reversal e. Massive transfusion and DIC

The Indications for the use of Cryoprecipitate are congenital factor VIII deficiency, congenital factor XIII deficiency, afibrinogenemia & dysfibrinogenemia and Von Willebrand disease [16].

The common Acute Non-Infectious blood Transfusion Reactions that occurs in first 24 hours of transfusion in neonates are [17-21]:

i] Acute immune mediated reactions
a. Immune mediated hemolysis
b. TRALI (Transfusion related acute lung injury)
c. Febrile non-hemolytic transfusion reactions (FNHTR)
d. Allergic reactions

ii] Acute non immune reactions
a. Fluid overload
b. Metabolic complications
1. Hyperkalemia
2. Hypoglycemia
3. Acid- base derangements
4. Hypocalcemia and hypomagnesaemia.

2. Materials and Methods

To study the Indications, Pattern of usage & Acute Non-infectious Transfusion reactions of Blood Component therapy we included 210 neonates who received various blood component transfusion like Packed Red Blood Cells, Random Donor Platelets, Fresh Frozen Plasma and Cryoprecipitate in Mahatma Gandhi Medical College & Research Institute, Puducherry during the period of APRIL 2012- MARCH 2015 were followed and studied in this cross sectional study. The neonates who received whole blood in the same study period was included as a comparator. The study was approved by the institutional Thesis and Human Ethics Committee.

Blood Bank of MGMCRI: Our Institute runs Blood Bank, licensed for the whole blood transfusion by the Department of Drug Controller, India since 2001. Since then Whole blood transfusion has been in routine practice. Blood Component separation and transfusion has commenced since 2012 when we upgraded our infrastructure and duly licenced by Drug Controller of India under the relevant act. The Blood Components that we prepare includes Packed Red Blood Cells, Random Donor Platelet Concentrate, Fresh Frozen Plasma and Cryoprecipitate.

Statistical analysis: Statistical methods such as Pie chart and Bar diagram were used for the descriptive purpose.

3. Observation and Result

The parameters which we included in our study were compared between the Whole Blood & Blood Component Transfusion in neonates as shown in the **Table 5.** The component which was used more in the neonatology group transfusion was Platelets which is shown in the pie chart **Fig.1**. The comparison between the Whole Blood & Blood Component Transfusion in neonates is shown in the statistical bar diagram **Fig.2.**

Table 5: Whole Blood versus Blood Component Transfusion in neonates

Parameters	Whole blood transfusion	Blood component transfusion
Number of Units	73	**650** PRBC - 223 (34%) Platelet - 273 (**42%**) FFP - 148 (23%) Cryoprecipitate - 6 (01%)
Number of Neonates	50	**210**
Sex : Male Female	 **62%** 38%	 **66%** 34%
Term: Full term Preterm Late Preterm Very Preterm Extreme Preterm	 36% **64%** **40%** 24% 0%	 31% **69%** **32%** 22% 15%
Birth Weight: Normal Low Birth Weight Very Low Birth Weight	 34% **42%** 24%	 17% 37% **46%**
Acute Non Infectious Transfusion Reactions: Yes No	6 % (3 babies) i] FNHTR – 1 (2%) ii] Hyperkalemia – 1 (2%) iii] Volume Overload – (2%) **94%**	7 % (15 babies) i] TRALI – 1 (0.5%) ii] FNHTR: a. PRBC transfusion – 2 (1%) b. Platelets transfusion – 3 (1.5%) c. FFP transfusion – 2 (1%) d. Cryoprecipitate – 1 (0.5.%) iii] Hypoglycaemia –3 (1.5%) iv] Hypomagnesaemia – 1 (0.5%) v] Volume overload – 1 (0.5%) vi] Immune mediated Haemolysis – 1 (0.5%) **93%**

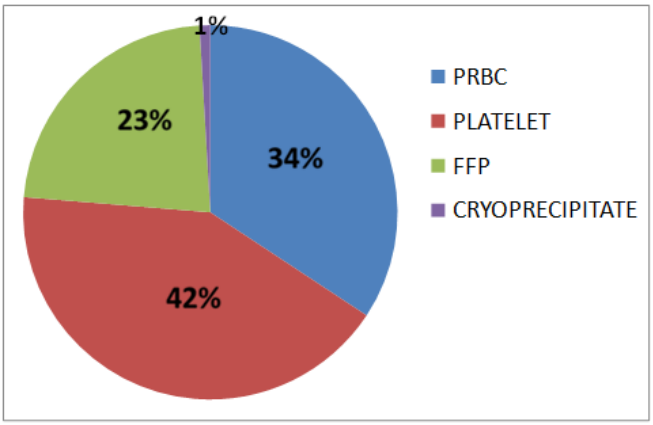

Figure 1: Pattern of usage of Blood Components

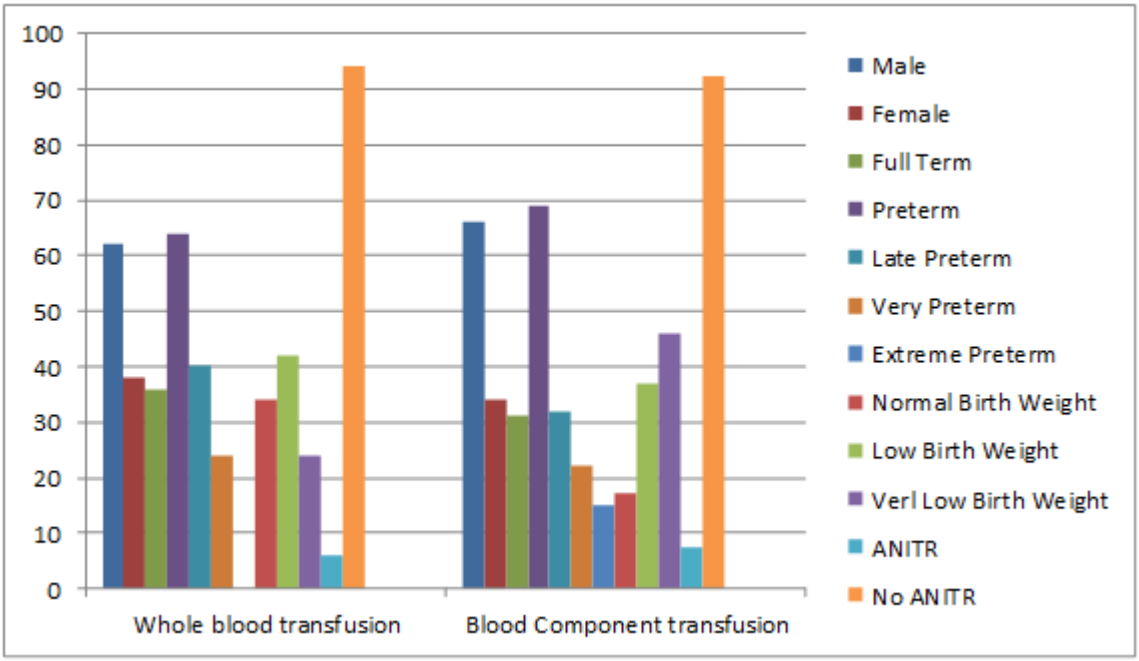

Figure 2: Whole Blood versus Blood Component Transfusion in neonates

The Indications for Packed Red Blood Cells that we transfused in 124 out of 210 neonates is tabulated in the **Table 6.** The Indications for Platelet concentrate that we transfused in 111 out of 210 neonates is tabulated in the **Table 7.** The Indications for Fresh Frozen Plasma that we transfused in 87 out of 210 neonates is tabulated in the **Table 8.** The Indications for Cryoprecipitate that we transfused in 3 out of 210 neonates is tabulated in the **Table 9.** The Indications for the whole blood transfusion for the neonates is tabulated in the **Table 10.**

Table 6: Indications for Packed Red Blood Cells transfusion in neonates

INDICATION	**No. of babies 124/210 (60%)**
Hematocrit <20%	**11 (9%)**
Hematocrit <30% -Hematocrit <30% and on ventilation -Hematocrit <30% and significant tachycardia -Hematocrit <30% and significant tachypnea -Hematocrit <30% and significant bradycardia - Hematocrit <30% with low weight gain	**74 (60%)** 22 06 03 04 **39**
Hematocrit <35%	**23 (19%)**
Hematocrit <45% -With Congenital heart disease -Non specific	**16 (12%)** 03 **13**

Table 7: Indications for Platelet concentrate transfusion in neonates

INDICATION	**No. of babies 111/210 (52%)**
Platelet count less than 30,000/cubic mm	**15 (14%)**
Platelet count 30,000 to 50,000/cubic mm -With CHD – ASD Surgery -With congenital diaphragmatic hernia surgery -With Sepsis -Non specific	**80 (72%)** 01 02 02 **75**
Platelet count more than 50,000 to 99,000/cubic mm	**16 (14%)**

Table 8: Indications for Fresh Frozen Plasma transfusion in neonates

INDICATION	**No. of babies 87/210 (41%)**
Sepsis	**42 (48%)**
DIC	08 (9%)
Pulmonary Haemorrhage	05 (6%)
IV Haemorrhage	02 (2%)
HMD	02 (2%)
Hypovolemia	01(1%)
NG Bleeding	04 (6%)
Melena	03 (3%)
Respiratory distress	03 (3%)
Other bleeding diathesis	**17 (20%)**

Table 9: Indications for Cryoprecipitate transfusion in neonates

INDICATION	**No. of babies 3/210 (1.5%)**
Von Willebrand disease	01 (33%)
Factor VIII Deficiency	02 (67%)

Table 10: Indications for the Whole Blood Transfusion in neonates

CRITERIA	**NUMBER OF BABIES**
Anemia Hb - <12g% - Anemia in 1st 24 hours Hb - 8 to 10g% - Oxygen dependency Hb - ≤7g% - Late anemia	16 (**32%**) 02 (13%) 11 (68%) 03 (19%)
Exchange transfusion	21 (**42%**)
Surgery	04 (8%)
Pulmonary hemorrhage	03 (6%)
Melena	02 (4%)

Sepsis	01 (2%)
Hemolytic disease of Newborn (HDN)	03 (6%)
Total	**50**

4. Discussion

The Pattern of usage of Blood Components in neonatal transfusion from APRIL 2012 – MARCH 2015 showed frequency of usage of Platelets > Packed Red Blood Cells > Fresh Frozen Plasma > Cryoprecipitate in that order. The most frequently used component was Platelets (42%). Second most frequently used component was Packed Red Blood Cells (34%) followed by Fresh Frozen Plasma (23%) and Cryoprecipitate (1%).

Most frequently used component was Platelets (42%) which was most often indicated in the Platelet counts of 30,000 to 50,000/ cu.mm (72%) and premature babies (69%). Neonatal thrombocytopenia could be early (<72 hrs) or late (>72 hrs). Early type could be due to placental insufficiency (Pre-eclampsic Toxaemia, Intra Uterine Growth Retardation, diabetes), asphyxia, perinatal infection, maternal autoimmune (Idiopathic Thrombocytopenic Purpura, Systemic Lupus Erythematosus) and severe Haemolytic Disease of Newborn. Late manifestations could result from congenital infections (Cytomegalovirus, toxoplasma, rubella and maternal autoimmunity (Idiopathic Thrombocytopenic Purpura, Systemic Lupus Erythematosus) Second most frequently used component was Packed Red Blood Cells which was most often used in the haematocrit range of 20-30% (34%) which was more pronounced in premature neonates weighing less than 11.5kg. Phlebotomy loses due to frequent blood sampling and expected decline in haematocrit in neonates during first week could have contributed to lower levels. Leukodepleted Packed Red Blood Cells with additive are the product of choice. Irradiation and prolonged storage increases K^+ and diminishes 2,3 DPG levels, hence in exchange / massive / intrauterine transfusions < 5days old irradiated Packed Red Blood Cells are transfused within 24 hours. Post transfusion hypoglycaemia may ensure due to stimulation of insulin secretion. Of the 50 neonates who received whole blood transfusion, 21 (42%) cases were for exchange transfusion and reminder for massive transfusions due to miscellaneous other causes.

Third most frequently used component in this series was Fresh Frozen Plasma (23%). Most cases comprises of bleeding in various sites associated with sepsis (48%) and miscellaneous other causes (32%). Some (20%) were due to various coagulopathies including congenital as well as acquired. Acquired coagulopathies include vitamin K deficiency, Disseminated Intravascular Coagulation, liver disease and exchange/ massive transfusion.

Least frequently used component was Cryoprecipitate (1%). Out of total two cases one was von Willebrand disease and the other one was haemophilia A (factor VIII deficiency). Indications for use of cryoprecipitate include hypofibrinogenemia/ dysfibrinogenemia, haemophilia A (when factor VIII concentration not available) and von Willebrand disease with active bleeding when not responding to DDAVP (1-deamino-8-D-arginine vasopressin).

Incidence of Febrile Non Haemolytic Transfusion Reactions in our series revealed total of 8 cases (4%) including all types non of which warranted stoppage of transfusion. Frequency of individual type FNHTR and other reactions and other reactions includes FNHTR in PRBC's transfusion - 2 (1%), in Platelet transfusion -3 (1.5%) cases, in FFP transfusion -2 (1%), in cryoprecipitate transfusion -1(0.5%), Transfusion Related Acute Lung Injury – 1 (0.5%), hypoglycaemia – 3 (1.5%), hypomagnesaemia – 1 (0.5%), volume overload – 1 (0.5%) and immune mediated haemolysis – 1 (0.5%) are comparable to all other works (Table 5).

5. Summary & Conclusion

Neonates, more often premature babies often need blood transfusions. Relatively large number are transfused with possibility of passive transfer of antibodies. Therefore individual component transfusion is preferable compared to whole blood. Because of lack of isohemagglutinins in neonates, immature immune system with risk of TAGVHD and considering their long life expectancy, possibility of sensitization to HLA antigens the long term consequences of which remains significant. Use of only required components is prudent. This also ensures economy of the donor blood in a limited donor programme. Citrate, K^+, volume and temperature regulation needs special requirements. Testing of maternal serum for antibodies is strongly advocated. Leukodepleted / Irradiated PRBC's must be used for extreme premature babies and for exchange / massive transfusion in neonates. Increased transfusion of components than the whole blood was achieved in our study.

6. Future Scope

The highest achievement in this new modern era in the field of Transfusion medicine is the separation of one unit of blood into its various components for the transfusion. So that more Blood component transfusion must be encouraged than the whole blood transfusion, to minimise avoidable transfusion reactions, allogeneic sensitization, volume overload and to use one unit of blood to save many lives. So further extension of this study to the patients of all age groups who got admitted in various departments and receiving various blood component transfusions is recommended in order to know the pattern of usage and the common indications of the blood components among all age groups and to increase the preparation and storage of the blood components which is used more and to minimise immediate as well as long term sequelae of transfusions. This simple cross sectional study can be done in all the institutions to know the common indications, transfusion reactions that encountered, pattern of usage of blood components of Blood transfusion in various geographical areas and to promote economy of voluntarily donated blood to save many lives with one unit of blood.

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