Factors Associated with Platelet Transfusions in Neonates Admitted in Intensive Care Unit in a Tertiary Care Centre

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ABSTRACT

Introduction: Neonatal thrombocytopenia (TP) is a commonly encountered problem in intensive care unit during hospital stay and platelet transfusion remains a mainstay of treatment. No study has clear data on the prevalence, causes of TP and effect of platelet transfusions in neonates. Present study was undertaken to investigate the cause for neonatal TP and transfusion practice in our institute. This would be helpful in improving guidelines and thereby reducing unnecessary transfusions and multiple donor exposures.

Material and methods: 220 neonates who received platelet transfusions are analyzed prospectively during the study period of 24 months. Both neonatal and maternal factors which leads to neonatal TP was evaluated and indication for platelet transfusion was analyzed.

Results: Low birth weight (74.5%), preterm babies (64.5%), pregnancy induced hypertension (PIH) (34.5%), maternal infections (28.2%) are major factors which contributed to the development of neonatal TP. 58.2% of neonates received single (128/220) and 41.8% received multiple platelet transfusions (92/220). Multiple platelet transfusions were more in necrotizing enterocolitis (NEC) ('p' value=0.010), intrauterine growth retardation (IUGR) ('p' value=0.026), hospital stay ('p' value=0.001), maternal infection ('p' value=0.003) and gestational diabetes mellitus ('p' value=0.002) and neonates belongs to severe and very severe ('p'=0.001) TP categories.

Conclusion: Single or multiple neonatal and maternal factors were involved in causing neonatal TP which in turn led to platelet transfusions. Most of the neonates in our study had bleeding manifestations and received platelet transfusions within 1 to 5 days of birth and mortality was higher with neonates who receives multiple transfusion.

Keywords: Platelet Transfusion, Neonatal Thrombocytopenia, Intensive Care Unit, Single and Multiple Transfusion, Bleeding Manifestation.

INTRODUCTION

In modern neonatology units, platelet transfusions are integral and indeed lifesaving at many occasions. 95% of neonates admitted in intensive care unit (ICU) receives platelet transfusions as prophylactically and/or therapeutically with the hope that they will reduce the risk of spontaneous bleeding.[1,2] This is commonly seen in neonates who encountered TP during treatment period in ICU and it usually resulted in unnecessary transfusions.[3]

TP was the most common hematological problem encountered in the neonatal intensive care unit (NICU).[4] It is defined as platelet count less than 150×10^9 /L, and is not uncommon among neonates.[3] A large population study showed that more than 98% of term neonates born to mothers with normal platelet counts had platelets above 150×10^9/L at birth.[5-7]

Preterm and sick neonates are more prone to develop TP and in most cases it will be mild to moderate and resolved without intervention. Neonates usually present with petechiae, hematoma, gastrointestinal, mucosal or umbilical bleed.[8]

Intracranial hemorrhage appeared to be the significant cause of morbidity and mortality in the sick pre and full term infants and those with low platelet count and so most platelet transfusions in these groups were with no bleeding or minor bleeding only.[9,10]

Majority of extremely low-birth-weight (LBW) infants require at least one transfusion and at times many receive multiple platelet transfusions.[11] The time of onset of TP is important for the diagnosis and subsequent therapy of neonatal TP. TP present within the first 72 hours of life (early onset TP) typically resulted from different causes.[8]

In addition, no study had yet proved clinical benefits of platelet transfusions in Neonatal TP. So improved guidelines are required to fix safe lower limit for platelet transfusions in stable and sick neonates, effective platelet transfusion protocols in sick neonates and improved therapy for conditions which precipitate TP.[12,13]

Present study was undertaken to investigate the existing paucity of data on causes of TP and platelet transfusion in neonates. This would have been helpful in developing guidelines and/or protocols for appropriate platelet transfusions and thereby reducing multiple donor exposures.

MATERIAL AND METHODS

It's a descriptive study conducted in the Department of Transfusion Medicine Government Medical College, Thiruvananthapuram in collaboration with Neonatology division of department of pediatrics in Sree Avittom Thirunal (SAT) Hospital for women and children. Total of 247 neonates who received platelet transfusions, while admitted in the ICU which consisted of inborn nursery (IBN) and outborn nursery (OBN). Of which 27 neonates were excluded due to chromosomal abnormalities, congenital diseases, life threatening conditions leading to death within 24 hours and those cases in which consent was not obtained. Study was approved by Human Ethical Committee and review board of our institution for a period of 24 months from 01-01-2013.

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Both neonatal and maternal factors which contributed in the development of neonatal TP and their platelet transfusions were analyzed in detail. The guideline for platelet transfusions formulated by National Neonatology Forum (NNF) is being followed in our institution where the study was conducted.[14]

STATISTICAL ANALYSIS

Statistical data were analyzed using SPSS software version 16. Continuous variables were expressed as mean of standard deviation and qualitative data were expressed as frequencies and percentages. The characteristics associated with platelet transfusions were identified using chi-square test for qualitative and t-test for quantitative variables.

RESULTS

Table-1 shows demographic details and characteristics of the neonates in the study. 220 neonates who received platelet transfusions was analyzed, majority (89.10%) belonged to 1-2 days of age. Since majority of our study group are belonged to LBW (74.5%) and preterm (64.5%) category, this proves their presence associated with significant relationship with neonatal TP.

The mean gestational age of neonates was 34.16 weeks and their standard deviation was 3.101. The minimum gestational age of neonates was 26 weeks and the maximum was 39 weeks. The median and mode were 34 and 37 respectively.

Incidence of late onset thrombocytopenia (occurred > 72 hours of birth) are more (61.8%)in our study it may be due to increased incidence of sepsis and NEC. Following TP majority (70%) of neonates received their first platelet transfusion within 1 to 5 days after birth.

Neonatal factors which are associated with neonatal TP either alone or in combination with other factors are showed in Table-2. 128 neonates received single transfusion and 92 had received multiple transfusion. Following single/multiple platelet transfusion there is shift of neonates from one category (very severe category) to another category (severe category) due to platelet count increment during the course of study (Figure-1). i.e. 21.80% of neonates in very severe category before transfusion is reduced to 8.20% after transfusion. Similar shifts are seen in other categories also during the course of study. The mean platelet count before and after transfusion was 43,118 and 54,109 respectively and their standard deviation was 1.945 and 2.369.

Depends on weight and number of transfusion, the volume of transfusion received by each neonate differs. i.e. 3.6% of neonates received platelet concentrate of 1-10 ml, 32.7% 11-20 ml, 25.5% 21-30 ml, 11.8% 31-40 ml, 10.9% 41-50 ml, 11.8% 51-100 ml, 2.7%101-150 ml and 0.9% 151-200 ml.

In addition to platelet transfusion, 54.5% received packed red cell transfusions and 83.6% received fresh frozen plasma. Number of transfusion episodes increases with number of days of ventilator support. Increase in duration of hospital stay (21.8% for 1-5 days, 17.3% for 6-10 days, 14.5% for 11-15 days, 20% for 16-20 days, 6.4% for 21-25 days, 20% for 26-70 days), usage of inotropes (68.20% for maximum of 6 days), incidence of caesarian section (60%) results in increased episodes of TP and therefore increase in number of platelet transfusion.

PIH (34.5%), maternal infections (28.2%), HELLP syndrome

Demographic details and neonatal characteristics	
Age of neonates	1-2 Days: 196 (89.1%) 3-4 Days: 06 (2.7%) 5-6 Days: 06 (2.7%) 7-28 Days:12 (5.5%)
Gender	Male: 128 (58.2%) Female: 92 (41.8%)
Gestational age of neonates	25-28 weeks: 14 (6.4%) 29-32 weeks: 44 (20%) 33-36 weeks: 84 (38.2%) 37-40 weeks: 78 (35.4%)
Birth weight	≥ 2500 Grams: 56 (25.4%) 1500-2499 Grams: 84 (38.2%) 1000-1499 Grams: 58 (26.4%) < 1000 Grams: 22 (10%)
Term of baby	Preterm: 142 (64.5%) Term: 78 (35.5%)
Onset of thrombocytopenia	< 72 Hours: 84 (38.2%) > 72 Hours: 136 (61.8%)
Day of first platelet transfusion	01-05 Days: 154 (70%) 06-10 Days: 36 (16.4%) 11-15 Days: 14 (6.4%) 16-20 Days: 10 (4.5%) 21-25 Days: 00 (0.0%) 26-28 Days: 06 (2.7%)

Table-1: Demographic details and characteristics of the neonates in the study

Neonatal factors	Frequency	Percentage
NEC	86	40%
Sepsis	96	43.6%
Respiratory distress	178	80.9 %
IUGR	86	39.1%
Respiratory distress and IUGR	70	31.8%
IUGR and sepsis	36	6.4%
Respiratory distress and sepsis	72	32.7%
Hypoglycemia	28	12.7%
Coagulopathy	64	29.1%
DIC	62	28.5%
Shock	56	25.5%

Table-2: Associated neonatal factors in the study group

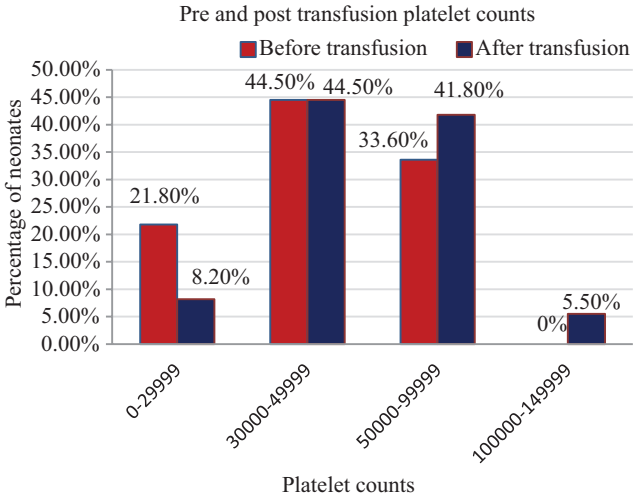

Figure-1: Neonatal shift between TP catoregory due to increment in their platelet counts

(14.1%), premature rupture of membrane (16.4%), anemia (16.2%), GDM (13.6%), thyroid disorder (8.2%), antepartum hemorrhage (5.5%) and Eclampsia (7.3 %) are the maternal factors which led to neonatal TP. 67.3% of mothers had adequate amniotic fluid whereas 28.2% had oligohydramnios and 4.5% had polyhydramnios.

DISCUSSION

In our institute 9036 neonates were admitted in NICU during the study period in which only 247 received platelet transfusions. Out of this 27 were excluded from the study due to various reasons mentioned earlier.

It was noted that TP was commonly seen among LBW babies that account for 74.5%. Among LBW neonates 37.5% falls under birth weight of < 1500 grams had TP and received platelet transfusions frequently when compared to neonates with birth weight of ≥ 2500 grams. Almost similar results were observed by Stanworth et al. in their study where 44.4% of LBW babies having < 1500 grams had TP.[12] Anil K Gupta el al. found that platelet count was significantly lower in LBW neonates having a weight of < 1500 grams than neonates with birth weight > 2500 grams.[3] Similarly reports from other studies from other places.[15,16]

In present study 64.5% of neonates were preterm (i.e. gestational age < 37 weeks) but statistical analysis showed no significance in relation between the gestational age and neonatal TP (p=0.092). An analysis by Gupta AK et al. also reported that gestational age had no effect on neonatal TP. Statistical analysis showed no significance ('p' value=0.054).[3] Median gestational age of neonates in our study was 34.16 weeks (interquartile range [IQR]: 33-36 weeks). Whereas study by Stanworth et al. had narrated that the median gestational age of 169 enrolled neonates was 27 weeks (interquartile range [IQR]: 24-32 weeks).[17]

Late onset TP was more (61.8%) in our study when compared to early onset TP (38.2%) which might be due to increased incidence of NEC 40%, sepsis 43.6%, pre-eclampsia 34.5% and gestational diabetis mellitus (GDM) 13.6%.

Also noted that majority of neonates in our study group (70%) had the first platelet transfusion within first five days of life. Simon J. Stanworth et al. observed in their study that most of the initial platelet transfusions (61%) were given before postnatal day 14. However other studies had indicated that a large number of platelet transfusions were required even after postnatal day 14.[17]

40% of neonates in our study (86/220) developed NEC as a complication of prematurity and LBW. Among 86 neonates, 40 neonates fall in category of severe TP (30,000-49,999/µl). Similar data was reported previously by Hutter et al., Patel et al., O'Neill et al., and Kenton et al.[18-20] More recently Baer et al. identified severe TP in 2.4% of neonates with NEC.[16]

We observed various bleeding manifestations such as intra-cranial bleeding, bleeding from nasogastric tube, umbilical stump, oral mucosa and heel stick in the neonates. Of these bleeding from heel stick injury (88/220) and nasogastric tube (76/220) are commonly observed.

In our study 58.2% of neonates received single platelet transfusion (128/220) and 41.8% received multiple platelet transfusions (92/220). Similarly in the study by Anil K Gupta et al. more number of neonates received single platelet transfusions which for accounted for 56.5%.[3] In contrast Del Vecchio A et al. found that neonates received multiple platelet transfusions (52%) was more compared to neonates received single unit platelet transfusion (48%).[21]

Neonates in our study categorized has moderate (50,000-99,999), severe (30,000-49,999) and very severe TP (0-29,999). When comparing single and multiple transfusions in these three groups separately it was found that multiple platelet transfusions were more in severe and very severe categories. Similarly, high rate of platelet transfusions (70%) in severe TP group.[2,21]

On considering birth weight of neonates, 64.3% of normal birth weight neonates had received single platelet transfusion and only 35.7% received multiple platelet transfusions whereas in case of LBW group 56.1% received multiple transfusions and only 43.9% received single platelet transfusion. Similarly in a research by Del Vecchio A et al. found that LBW neonates had received more number of platelet transfusions when compared to normal birth weight neonates.[21]

Table-3 shows neonatal factors which led to single and multiple platelet transfusion. Significant association was observed between NEC and multiple platelet transfusions ('p' value=0.010) in our study. Alexander B et al. noticed that a large number of platelet transfusions were given in neonates with NEC.[22]

Among total platelet transfusions Single transfusion = 128 Neonates (58.2%) Multiple transfusions = 92 Neonates (41.8%) (50 neonates received two unit transfusion, 28 three transfusions and 14 four or more than four transfusions)
Neonates with bleeding manifestation (Total = 160 Neonates) Single transfusion = 84 (52.5%) Multiple transfusions = 76 (47.5%)
Neonates with intrauterine growth restriction (Total = 86 Neonates) Single transfusion = 52 (60.5%) Multiple transfusions = 34 (39.5%)
Normal birth weight (Total = 56) Single transfusion = 36 (64.3%) Multiple transfusions = 20 (35.7%)
In low birth weight babies (Total = 164) Single transfusion = 72 (43.9%) Multiple transfusions = 92 (56.1%)
Term babies (Total = 78) Single transfusion = 52 (66.7%) Multiple transfusions = 26 (33.3%)
Pre-term babies (Total = 142) Single transfusion = 76 (53.5%) Multiple transfusions = 66 (46.5%)
Grades of thrombocytopenia Moderate thrombocytopenic neonates Single transfusion = 56 (25.5%) Multiple transfusions = 18 (8.2%) Severe thrombocytopenic neonates Single transfusion = 44 (20%) Multiple transfusions = 54 (24.5%) Very Severe thrombocytopenic neonates Single transfusion = 18 (8.2%) Multiple transfusions = 30 (13.6%)

Table-3: Comparison between single and multiple platalet transfusions

Neonates with IUGR also showed a significant association with neonatal TP ('p' valve=0.024). Gupta AK et al. noticed a similar relation in their study group ('p' value=0.022).[3]

There was ample evidence in our study to suggest that various systemic diseases had showed its influence in the development of TP in neonates. Among which respiratory distress accounted for a maximum of 80.9%, followed by cardiovascular diseases (19.1%). Statistically there was no significant association between TP and respiratory problems/mechanical ventilation ('p' value =0.629 and 0.770). similarly, Gupta AK et al. also reported the same.[3]

Maternal factors which contributed to the development of neonatal TP were infections, GDM, PIH etc. Eslami Z MD et al. and Payne SD et al. described that similar factors could contributed to neonatal TP.[4,23]

Significant association were seen between TP in neonates and other variables like bleeding manifestations ('p' value=0.004), hospital stay ('p' value=0.001), maternal infection ('p' value=0.003) and GDM ('p' value=0.002). similar maternal factor association was observed by Maayan-Metzger et al.[24]

The strength of the study includes descriptive design and follow up. It was a hospital based study. So it did give an idea of burden on blood bank facilities at our center. This also gave us profile of the patients requiring platelet transfusions following neonatal TP.

The limitation of the current our study was it lacked the case-control design and neonatal alloimmune thrombocytopenia was not assessed in neonates with poor platelet increment due lack of facility.

CONCLUSION

In our study the major neonatal factors that led to TP and platelet transfusions were prematurity, LBW, IUGR, NEC and neonatal sepsis. Single or multiple neonatal and maternal factors were involved in causing neonatal TP which in turn led to platelet transfusions. Most of the neonates in our study had bleeding manifestations and received platelet transfusions within 1 to 5 days of birth.

In our center we strictly adhere to NNJ transfusion guidelines and unnecessary transfusions are avoided. Still defining the causes of TP and following effective transfusion protocols would help to develop appropriate and novel treatment modalities.

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