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SHORT COMMUNICATION

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Improvising neonatal thrombocytopenia management: Insights from split, volume-reduced, single-donor apheresis platelets (NeoVRs-SDAP)

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Abstract

Introduction: Thrombocytopenia is common in neonates, managed with platelet transfusions at defined dose. The product type varies from neonatal-specific units using platelet additive solutions to adult products split into multiple paediatric units. In low-middle-income countries, whole blood-derived random donor platelets (RDP) are common while western countries use split adult single donor apheresis platelets (SDAP). We aimed to assess preliminary effectiveness of split, volume-reduced single donor apheresis platelets (NeoVRs-SDAP) in neonatal thrombocytopenia and observe early post-transfusion outcomes.

Methods: Study was conducted from August 2024 to January 2025 at a tertiary healthcare centre. Persistent thrombocytopenic neonates admitted to the NICU were transfused with NeoVRs-SDAP prepared using Spectra Optia® with modified program yielding an adult dose (300×10^9) in a reduced 100 mL of product volume. These were split into 2–5 aliquots for transfusion. Post-transfusion platelet increments and percentage recovery were assessed after 20–24 h.

Results: Thirteen neonates' 77% preterm, 69.2% VLBW with sepsis received 46 NeoVRs-SDAP. 10 mL of this product contained nearly 3 times more platelets than RDP and 1.5 times more than adult SDAP of same volume. The mean transfused dose was $70.56 \pm 14.21 \times 10^9$ platelets. Median platelet increment was 64 500/μL versus 15 477/μL for RDP ($p < 0.001$). Platelet recovery ranged from 7.5%–52.5%. Split products reduced donor exposure by 56.5%. Survival was 62%, without any transfusion-related adverse events.

Conclusion: NeoVRs-SDAP may be potential alternative in persistent neonatal thrombocytopenia, offering better increments and recovery, reduced donor exposure, and leukoreduction. Further RCTs comparing NeoVRs-SDAP and RDP are recommended.

KEYWORDS

neonate, platelet increments, random donor platelets, single donor apheresis platelets (SDAP), thrombocytopenia, volume-reduced split apheresis platelets

1 | INTRODUCTION

Neonates and adults have similar range of platelet count (i.e. 150 000–450 000/μL) however preterm neonates may have a normal lower limit of 1 20 000/μL according to recent data.[1] If the conventional lower limit is considered, 1% of term neonates and 20–35% of preterm neonates will have thrombocytopenia and, among these preterm neonates 25–38% will have platelet count less than 50 000/μL.[2–6] Platelet transfusions in neonates is given below a specific threshold with a goal to increase platelets by 50 000–100 000/μL.[7,8] The desired platelet increment is achieved by transfusing 10 mL/kg of platelets providing around 10×10^9 platelets from either a whole blood-derived random donor platelet or apheresis-derived platelet product.[6] A threshold of 50 000/μL in preterm neonates has been widely agreed on earlier and now transfusion trigger of <25 000/μL has been recommended for healthy or stable term and preterm infants without other risk factors, whereas some prefer a higher trigger (<30 000–50 000/μL) for very low birth weight (VLBW) neonates within first week of life, clinically unstable neonates, and neonates with NAIT and based on PlaNeT-2 trial.[9–11] This dose is generally recommended to be transfused over 30 min, is now being advocated to be transfused over a period of 2–3 h to avoid the risk of IVH and existing evidence of no difference in platelet recovery between these time frames.[12] American Association of Blood Banks (AABB) recommends a dose of 5–10 mL/kg at a rate of 5 mL/kg/h while some guidelines recommend a dose of 10–20 mL/kg.[13–15] Neonates receiving this 10–20 mL/kg dose would receive a greater volume of platelets and these excess of platelets may not be beneficial if they are in excess to what is immediately needed as platelets last about four days in the human body.[13]

Now, unlike the platelet dose the type of platelet product transfused to neonates varies widely. Some countries provide a specific product for neonatal transfusion, whereas others use a standard adult product and give less of it based on mL/kg dosing. Other countries produce smaller units split from one donation to reduce donor exposure risk by reserving multiple packs from same donor for the same patient.[16–18] In low middle income countries, whole blood derived random donor platelets (RDP) are usually used for neonate and platelet transfusions.[19,20] Paediatric units (pedi-packs) derived from these RDP or a complete 50 mL RDP may be used, discarding the left-over product after dose-based volume is transfused. Role of adult volume apheresis platelets divided into paediatric units has been used in the western countries for neonatal transfusions but literature on volume depleted/reduced apheresis platelets split for neonatal persistent thrombocytopenia is limited to the best of our knowledge.[17,18]

We attempted to modify the adult single donor apheresis platelets (SDAP) into reduced-volume or volume depleted high yield SDAP product customised to neonatal transfusions and evaluate its effect in persistent thrombocytopenia in neonates admitted to neonatal intensive care unit (NICU).

2 | AIM AND OBJECTIVES

We aimed to describe our initial experience with the preparation and clinical use of split, volume-reduced single donor apheresis platelets (NeoVRs-SDAP) for neonatal thrombocytopenia, and to assess their preliminary effectiveness and early post-transfusion outcomes in our setting by evaluating

1. Post-transfusion increment (PI) = (Post-transfusion platelet count) – (pre-transfusion platelet count)
2. Percentage platelet recovery (% PR): ((PI × total blood volume)/(platelet dose)) × 100

3 | MATERIALS AND METHODS

3.1 | Study design

This is a single-centre retrospective observational case series from August 2024 to January 2025 at a tertiary healthcare centre. Neonates admitted to NICU with persistent thrombocytopenia and not responding to whole blood derived RDP transfusions (i.e. failure to achieve >20 × 10^9/L increment on at least two subsequent occasions) included who then received split, volume-reduced single donor apheresis platelets (NeoVR**s**-SDAP) for a pre–post comparison evaluating preliminary effectiveness of split, volume reduced single donor apheresis platelets in persistent neonatal thrombocytopenia.

3.2 | Study Methodology

Details of neonates were retrieved from Hospital information Management system (HIMS, Akhil Diagnostics Pvt Ltd, New Delhi, India). Birth weight categories were defined according to WHO criteria irrespective of the gestational age: very low birth weight (VLBW, <1500 g), low birth weight (LBW, <2500 g), and normal birth weight (NBW, ≥2500–4000 g)[21] NeoVRs-SDAP for neonates were prepared using continuous cell separator (CCS), Spectra Optia® Apheresis System (Terumo BCT Inc., Lakewood, Colo., USA). We used dedicated platelet collection protocol using a customised configuration program that collected adult dose (300 × 10^9 platelets) in a reduced product volume i.e. in 100 mL [NeoVRs-SDAP] and stored for maximum of 5 days in platelet agitators in line with strict quality adherence protocols maintaining temperature of 21.5°C with continuous agitation. The pH of the product was monitored to ensure product quality. This product was then split into 3–5 parts based on the dose according to the weight of the neonate at the time of clinical demand. Details of procedure are given in Figure 1: Preparation of NeoVRs-SDAP for neonates.[22]

Any procedural details were retrieved from departmental records. Post-transfusion platelet count after 20–24 h of split SDAP transfusions were noted emphasising on only the non-immune causes of refractoriness, mostly sepsis in our neonates and to avoid iatrogenic anaemia due to repeated sampling in this susceptible population. Study was approved by Institutes ethical and research committee [SRHU/HIMS/E-1/2025/259].

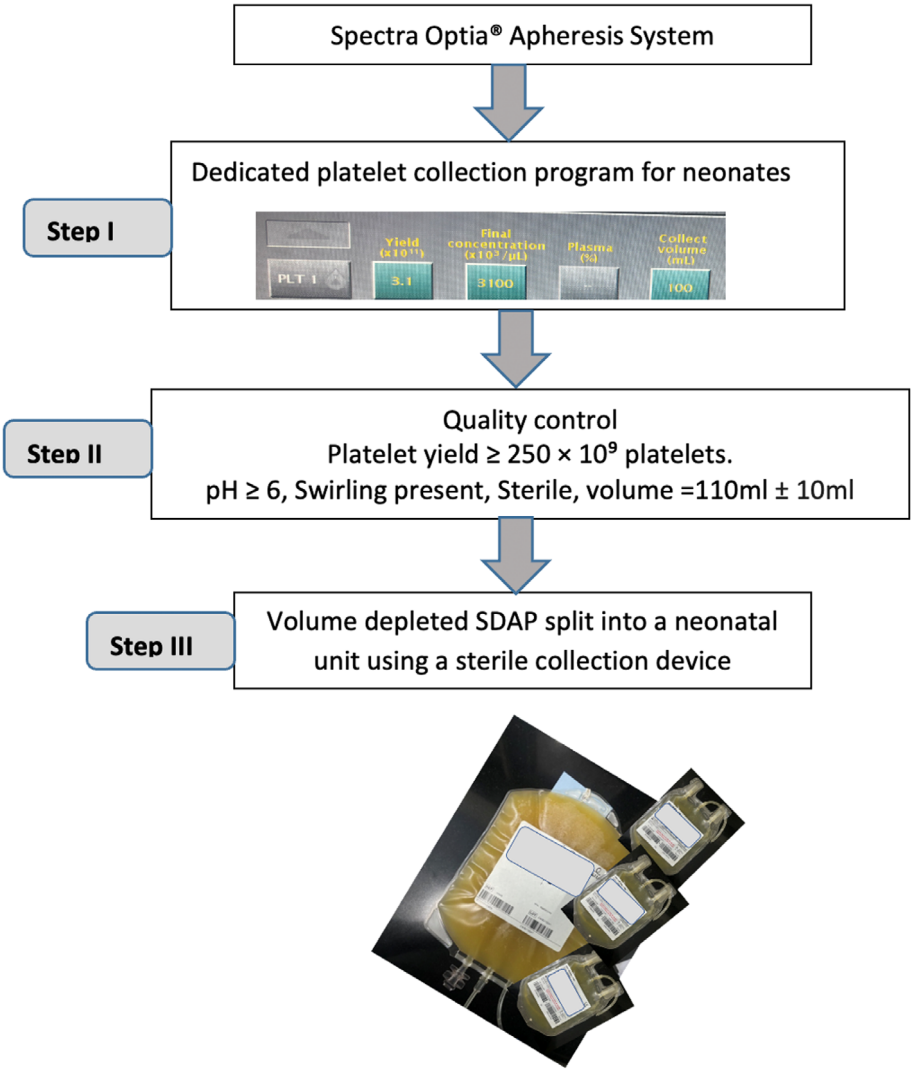

FIGURE 1 Preparation of NeoVRs-SDAP for neonates.

4 | RESULTS

4.1 | Neonate details

Demographic details of admitted neonate is mentioned in Table 1. Our cases include a total of 13 neonates who were admitted in NICU those required SDAP for persistent thrombocytopenia from August 2024 to January 2025. Neonates included were predominantly males (84.6%) and were born preterm (77%) The mean birth weight of neonates was 1.7 ± 0.6 kg of which 69.2% were VLBW, 23.07% were LBW and 7.6% were NBW neonates. Early onset neonatal sepsis was suspected to be the aetiology in all 13 cases, of which six (46%) were culture positive. *Klebsiella pneumoniae* and *Candida* species were the predominantly isolated organism in blood culture.

4.2 | Neo-VRs-SDAP product details

Our Neo-VRs-SDAP product had a mean volume of 110 ± 10 mL and mean platelet yield of 253.07 ± 27.19 × 10^9 platelets. Mean platelets per 10 mL of reduced-volume SDAP were 25.38 ± 2.8 × 10^9 platelets and mean dose of platelets transfused to neonates was 70.56 ± 14.21 × 10^9 platelets based on 25–40 mL of Neo-VRs-SDAP product volumes calculated according to the weight of these neonates. The mean pH on Day 5 was 6.9 ± 0.2. Most of our products were issued by day 3 of collection.

4.3 | Transfusion details

4.3.1 | Random donor platelet transfusions

Total RDP transfused to our thrombocytopenic neonates ranged from 3 to 11, to which the neonates appeared to be refractory and were mostly transfused between 2 and 21 days of life. Total no. of RDP transfused in these neonates prior to split SDAP products was 59 platelets.

4.3.2 | Neo-VRs-SDAP transfusions

Split platelet blood products were prepared from these low volume SDAP in two to four parts ranging from 25 to 30 mL and transfused in a range of two to four transfusions as indicated. Most of our neonates

TABLE 1 Neonates details.

Neonate	Gestational age (weeks)		Gender	Birth weight (kg)	Aetiology of thrombocytopenia	No. of RDP	Day of RDP transfusion	No. of SDAP parts	Days of SDAP transfusion	Outcome
1	Term	37w	male	3.1	Late onset klebsiella sepsis	3	15,19,21	4	27,28,31,34	Discharged
2	Late preterm	36w	male	2.5	Culture negative sepsis, disseminated intravascular coagulation	4	3,9,10,11	3	27,28,31,34	Discharged
3	Moderate Preterm	32w	male	1.3	Culture negative sepsis	4	13,15,17,20	2	21,22	Discharged
4	Moderate Preterm	32w	male	1.27	Culture negative sepsis	5	5,6,16,17	2	11,16	Death
5	Term	37w	male	2.2	Late onset polymicrobial sepsis (Klebsiella and Serratia)	11	29,31,32,33, 38,55,57,58, 59,61,66	12	34,35,39,39,40,43,44,62,53,67,68,69	Discharged
6	Moderate preterm	32w	female	1.25	Late onset fungal sepsis (candida)	0		2	17,18	Discharged
7	Moderate Preterm	32w	male	2.1	Late onset polymicrobial sepsis (Klebsiella and Ralstonia)	5	7,12,16,17,19	2	21,22	Discharged
8	Moderate preterm	32w	male	1.3	Late onset fungal sepsis (candidiasis parapsilosis)	8	7,14,15,16,19,26,39	6	17,18,20,21,27,28	Death
9	Moderate Preterm	33w	male	2.1	Culture negative sepsis	5	2,3,4,8,17	2	37,38	Discharged
10	Very Preterm	30w	male	1.2	Culture negative sepsis	5	5,7,8,12	4	9,10,10,12	Death
11	Very Preterm	28w	female	1	Late onset Klebsiella sepsis	3	5,6,7	1	3	LAMA
12	Late Preterm	35w	male	1.3	Culture negative sepsis	5	4,5,6,8,12	4	9,10,11,12	Death
13	Term	38 w	male	1.6	Culture negative sepsis	1	2	2	3,4	Discharged

were transfused with two to four split SDAP products derived from a single donor, one was transfused with 12 split SDAP products derived from four donors, another was transfused with six split SDAP products derived from three donors and two neonates were transfused four split SDAP products derived from two donors. These split components were mostly transfused between 7 and 67 days of life in these neonates.

The median platelet increment after 20–24 h of RDP and Neo-VRs-SDAP transfusion was 15 477/μL (IQR: 600–17 500/μL) and 64 500/μL (IQR: 35 750–106 250/μL) respectively. The difference was statistically significant ($p < 0001$). The median pretransfusion platelet count in our neonates was 19 000/μL (IQR: 12 000–27 250).

Only three neonates also received red cell transfusion, and no plasma transfusions were given. These products were administered for anaemia and did not influence platelet increments, which were specifically analysed for RDP and Neo-VRs-SDAP exposure.

Platelet recovery in our neonates ranged from 7.5% to 52.5% after split Neo-VRs-SDAP product transfusions.

Exposure reduction

Total no. of split Neo-VRs-SDAP products transfused in our neonates were 46 from 20 reduced-volume SDAP units, resulting in 56.5% reduction in exposure to donors.

4.4 | Outcome

Out of total, 62% neonates survived and discharged between 23 and 56 days of life while mortality was observed in 30% due to either pulmonary haemorrhage or catecholamine-resistant shock. One neonate was discharged against medical advice.

5 | DISCUSSION

In neonatal platelet transfusion choice of platelets, transfusion threshold, dose and rate requires consideration. Use of ABO matched platelets are advised to minimise the incompatible plasma transfusion and improved platelet recovery and survival in vivo. International practice is different between countries. Platelets used in neonatal transfusion are typically collected by apheresis from a single donor, instead of pooled platelets from multiple donors.[15]

In UK, since 2020, 'neonatal platelet' packs are being manufactured by NHS Blood and Transplant (NHSBT; approximately 50 mL in plasma), suitable for neonatal and infant transfusion that include 20% of platelet additive solution (PAS).[16]PAS was already used to prepare platelet products for adults and older children. In addition, the number of platelets per volume of component was reduced ~20% in these new "neonatal" platelet packs. In New York, apheresis platelets are collected from a single donor contain a minimum of 3×10^{11} platelets suspended in 200–300 mL of plasma which is a normal adult dose. These were further split for neonatal and paediatric transfusions.[23] Platelets with additive solution (PAS) and pathogen-inactivated platelets are now available, and may offer advantages for some paediatric patients. In India, the quality requirements of our platelet products i.e., whole blood derived and apheresis are that 10 mL of RDP should contain minimum of 7–10 $\times 10^9$ platelets derived from one RDP containing a minimum of 35×10^9 platelets in 50–70 mL of unit and apheresis derived platelets/single donor apheresis platelet (SDAP) in a full adult dose must contain >300 $\times 10^9$ in 200–300 mL of unit.[22] RDP may or may not be leucoreduced while SDAP are leucoreduced.

In our study, our high yield, volume-reduced SDAP product had a mean platelet yield of 253.07 ± 27.19 $\times 10^9$ platelets in 100 mL, almost reaching an adult dose in only 33.3% of the unmodified adult product volume, which is 200–300 mL. This further led to more no. of platelets per 10 mL of product and eventually in 25 to 30 mL of product that was transfused based on the body weight of the neonate. When evaluated, our 10 mL NeoVRs-SDAP product had 25.38 ± 2.8 $\times 10^9$ platelets compared to 7 $\times 10^9$ and 15 $\times 10^9$ in RDP and normal SDAP respectively. The increase was almost 3 times from an RDP and 1.5 times than a normal adult SDAP. The utility of SDP in neonatal thrombocytopenia was studied by Moser et al. to determine its effect on platelet increment. Their platelet increment was 71 ± 58.6 $\times$ 1000/mm^3 which was correlated with thrombocytopenia aetiology instead of the platelet yield.[24] This may be attributed to the apheresis platelet they used, which was an adult apheresis platelet aliquoted for neonates, in contrast to our study, where we used a volume-reduced, high yield SDAP product customised for our thrombocytopenic neonates. Spectra Optia CCS is widely utilised for plateletpheresis procedures in India, approved by the CDSCO (Central Drugs Standard Control Organization).

Transfusion threshold in preterm non-bleeding neonates is <25 $\times 10^9$/L and <50 $\times 10^9$/L for sick neonates.[10,16] The median pretransfusion platelet count in our neonates was 19 000/μL (IQR: 12 000–27250) for RDP transfusions and 44 500/μL (IQR: 15 000–87 500) for NeoVRs-SDAP. The expected increment with a dose of 10 mL/kg of body weight of platelet is between 50 000 and 100 000/μL and our platelet increments were 64 500/μL (IQR: 35 750–106 250/μL) which was significantly different from RDP transfusions.[25] Our platelet recovery reached 50% in our neonates which is adequate. 62% of our patients transfused with NeoVRs-SDAP exhibited good platelet recovery and survival without any transfusion-related adverse effects and added advantage of leukoreduction. There was 56% reduction in donor exposure that further reduces alloimmunization and risk of transfusion transmitted infections. Another point to highlight in this study is the volume reduction did not involve any further centrifugation of product that usually causes 20% platelet loss. We rather modified an existing program of apheresis to reduce the volume during collection itself and extracting the amount of platelets from donor as in normal adult SDAP. Therefore, it is safe to say that we also prevented platelet loss and open system hence the risk of contamination in this product.

Considering financial implications, although a formal cost-effectiveness analysis was not performed, a pragmatic, context-specific observation was made based on institutional pricing. At our

centre, the billed cost of one SDAP is approximately equivalent to the combined cost of five RDP units. In our cases, the Neo-VRs-SDAP aliquots [billed once at the time of preparation] transfused per patient resulted in an overall expenditure comparable to, or lower than, the cumulative cost of the multiple RDP units [billed with each subsequent RDP unit] these neonates had already received prior to SDAP transfusion. This observation suggests that, in our setting, the use of Neo-VRs-SDAP may be a possible cost neutral option compared to current RDP-based practice, while also reducing donor exposure and providing higher platelet yield. This observation highlights a potentially important consideration for future prospective randomised controlled trials comparing Neo-VRs-SDAP and RDP in neonates incorporating a structured cost-effectiveness component alongside clinical outcomes, as cost may be a key factor influencing product selection in resource-limited settings.

5.1 | Limitations

Our study has certain limitations as our intent was not to present a direct efficacy comparison between RDP and SDAP, but rather to demonstrate the preliminary effectiveness of Neo-VRs-SDAP in thrombocytopenic neonates who showed no increment after RDP transfusions. To address efficacy, we analysed post-transfusion increments separately after RDP and SDAP exposure in pre-post analysis in the same neonate, showing that median increments were significantly higher following Neo-VRs-SDAP transfusions. The absence of a comparative arm, and concurrent or sequential use of both products limits definitive attribution of efficacy is fully acknowledged. Additionally, the process may incur higher costs due to the use of extra bags and sterile connecting device wafers during aliquoting. To address these limitations, a randomised controlled trial comparing RDPs and Neo-VRs-SDAP as separate blinded arms in neonatal thrombocytopenia is highly recommended to comment upon the efficacy including 30-day mortality, logistic and, economic parameters.

6 | CONCLUSION

Neo-VRs-SDAP may prove to be beneficial in neonates with persistent thrombocytopenia in terms of better increment, better platelet recovery and reduced exposure and leukoreduction. This may be attributed to more platelet count or high yield of platelets per 10 mL of product. No transfusion-related adverse events were observed. Although limited by sample size and study design, these findings suggest that NeoVRs-SDAP may represent a practical and potential alternative for persistent thrombocytopenia in neonates. Larger randomised controlled trials are warranted to validate efficacy, safety, and cost-effectiveness.

AUTHOR CONTRIBUTIONS

All listed authors have contributed to the manuscript substantially and have agreed to the final submitted version. **Yashaswi Dhiman:** Design of the article, acquisition, analysis, and interpretation of data for the article. **Saikat Patra:** Design of the article, acquisition, analysis, and interpretation of data. **Chinmay Chetan:** Analysis and interpretation of data. **Manish Raturi:** Acquisition and analysis. **Shoham Majumder:** Analysis, interpretation of data. **Rolika Nautiyal:** Analysis, Interpretation of data. **Tushar Bhardwaj:** Interpretation of data. **Dushyant Singh Gaur:** Manuscript review.

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CONFLICT OF INTEREST STATEMENT

Authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PATIENT CONSENT STATEMENT

As per our hospital policy, an informed consent is obtained from the parent/guardian for neonates prior to any procedure, including transfusion of any blood product.

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