

# Cerebral Hemodynamics in Stable Preterm Infants Before and After Packed Cell Transfusion

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## ABSTRACT

**Introduction:** In a year, around 3.5 million preterm deliveries occur in India alone. Some of these babies will require packed cell volume (PCV) transfusion. There is a paucity of robust data on effect of blood transfusions on the cerebral hemodynamic from India. This study was done to see the effect of PCV transfusion on blood flow velocities and resistive index (RI) of anterior cerebral artery (ACA) in stable preterm infants.

**Methods:** A prospective observational study was conducted in a tertiary care hospital in Pune, India. All stable preterm infants (< 37 weeks) receiving PCV transfusion were enrolled. USG Doppler study of ACA was done before and after PCV transfusion. Peak systolic velocity (PSV), end-diastolic velocity (EDV) and RI were measured pre and post PCV transfusion.

**Results:** Thirty infants were included in the study, with median gestation age of 28.8 {interquartile range (IQR), 27-30.55} weeks and median birth weight of 970 {interquartile range (IQR), 869.5 - 1190} grams. There was a significant decrease in PSV pre and post PCV transfusion - 58.46 ( $\pm$  18.44) cm / sec and 46.34 ( $\pm$  13.93) cm / sec respectively (p value < 0.001). Changes in RI and EDV were non-significant.

**Conclusions:** PCV transfusion significantly decreased PSV, reflecting improved cerebral oxygenation, and decreased cardiac output after correction of anaemia. Laboratory threshold for PCV transfusion in stable preterm infants are not known. USG Doppler study has the potential to provide one of the objective criteria for PCV transfusion in these infants though large scale randomized controlled trials are needed to prove its efficacy.

**Keywords:** End diastolic velocity; Packed cell volume transfusion; Peak systolic velocity; Resistive index; Stable preterm



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## INTRODUCTION

An estimated 15 million babies are born preterm every year globally.<sup>1,2</sup> Anaemia is a frequent complication of prematurity and blood transfusions are common in neonatal units.<sup>3,4</sup> One of the principal objectives of blood transfusion is to prevent impaired tissue oxygenation of vital organs and brain.<sup>5</sup> The main variables affecting cerebral oxygen delivery are cerebral blood flow and haemoglobin concentration.<sup>6</sup> Cerebral blood flow can be measured at the bedside by using Doppler ultrasound of contributing arteries.<sup>7</sup> Blood flow can be evaluated by measuring peak systolic velocity (PSV), end-diastolic velocity (EDV) and calculating resistive index (RI).<sup>8-10</sup>

Researchers have shown that blood transfusions improve cerebral oxygen supply and induce a decrease in cerebral blood flow velocity.<sup>11-13</sup> But there is paucity of robust data on effect of blood transfusions on the cerebral hemodynamic from India. Our study is aimed to document the changes in cerebral blood flow after PCV transfusion in stable preterm infants.

## METHODS

A prospective observational study was done from April 2018 to December 2019, in a tertiary level NICU at Pune, India. All stable preterm infants receiving packed cell transfusions for clinical indications and a haemoglobin value of less than 10 gm / dl during the study period were enrolled after obtaining written informed consent from parents. Prior ethics approval was taken from the Bharati Vidyapeeth Medical College Institutional Ethics Committee before starting the study. Preterm infants needing cardio-respiratory support, with major congenital malformations and genetic syndromes were excluded. Transcranial colour doppler ultrasonography was done one hour before packed cell transfusion and 24 hours after post transfusion by a neonatologist who was trained in cranial ultrasonography using a SIEMENS machine (Acuson X 300, SIEMENS Medical Solution) with neonatal probe (5 - 10 Hz transducer). Doppler imaging of the anterior cerebral artery (ACA) was through the anterior fontanelle in the sagittal plane (Figure 1). Pulse doppler was done to measure PSV and EDV (Figure 2). RI was then calculated using the formula:  $RI = (PSV-EDV) / PSV$ .<sup>8</sup> All

measurements were done in thermo-neutral environment ensuring normal body temperature without any pressure provocation in quiet infants, using oral sucrose as pacifier with continuous monitoring of oxygen saturation and vitals. Three measurements were recorded each time and mean was calculated. Protocols followed were according to institutional guidelines. Statistical analysis was done using SPSS software version 25.0. Paired t test was used to test the mean difference between RI, PSV and EDV. Throughout the results 5% level of significance was used. All results are shown with 95% confidence interval, with p-value of less than 0.05 been considered significant.

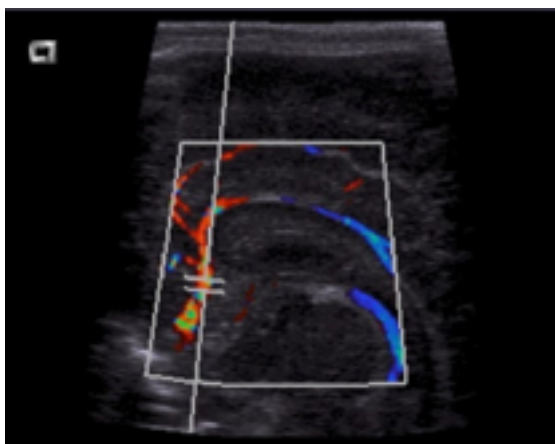
## RESULTS

Thirty infants were included in the study, with median gestation age of 28.8 {Interquartile range (IQR), 27 - 30.55} weeks, median birth weight of 970 (IQR, 869.5 - 1190) grams. Pre-transfusion median haemoglobin was 8.1 (IQR, 7.1-8.7) g/dl (Table 1). Pre and post transfusion mean RI were 0.83 ( $\pm$  0.07) and 0.82 ( $\pm$  0.07) respectively (p value 0.17). Pre and post transfusion PSV were 58.46 ( $\pm$  18.44) cm / sec and 46.34 ( $\pm$  13.93) cm / sec respectively (p value < 0.001) and pre and post transfusion EDV were 9.83 ( $\pm$  6.64) cm / sec and 8.47 ( $\pm$  5.15) cm / sec (p value 0.21) (Table 2).

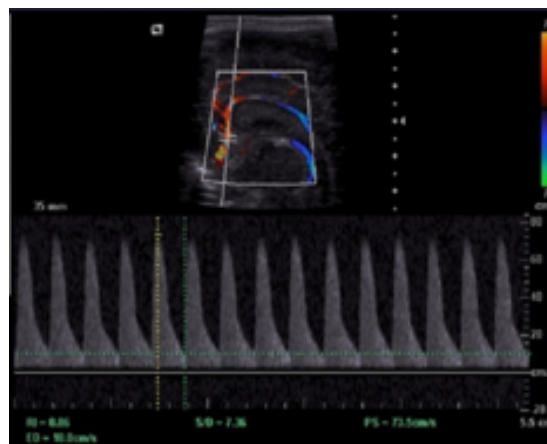
## DISCUSSION

In this study we found a significant decrease in PSV post transfusion but changes in RI and EDV were non-significant. These results are in line with the previously published studies, which showed that blood transfusion decreases the cerebral blood flow velocity.<sup>11-13</sup>

Anaemia may lead to increase in cardiac output and cerebral vasodilation, as a compensatory mechanism to increase the oxygenation of brain parenchymal tissue. Previous studies have documented that blood transfusion decrease cardiac output and heart rate.<sup>14</sup> The decreased cerebral blood flow velocity effect of transfusion can be explained by the reduced cardiac output after the correction of anaemia. Decrease in systolic velocity, may also reflect cerebral vasoconstriction due to improved cerebral oxygenation. Cerebral blood flow is also affected by fetal hemoglobin concentration.<sup>15</sup> On transfusing adult hemoglobin,



**Figure 1.** Identification of ACA (Doppler – Angle of insonation < 15°)



**Figure 2.** Calculation of PSV, EDV and RI using Doppler in ACA

oxygen delivery capacity of blood to the tissues increases, further resulting in decrease of cerebral blood flow.

Caution should be exercised as flow should not be equated with blood velocity measured via Doppler study. Cerebral blood flow velocity also depends on the cross-section area of the vessel. Unfortunately, diameter of the cerebral blood vessels cannot be measured accurately by the currently available USG machines, therefore we have to rely on the

cerebral blood flow velocity to estimate the cerebral blood flow.

Change in only PSV, with no significant change in RI and EDV, may represent ongoing adaptive mechanism after PCV transfusion. Also, PSV and EDV depend on the angle of insonation, whereas RI being a ratio, is not affected by the angle of insonation.<sup>16</sup> The difference in PSV, could be due to the intra-observer bias or due to change of angle of insonation, between the pre and post PCV transfusion velocity readings. However, we tried to minimize the bias, by standardizing the area, where Doppler was acquired. Angle of insonation was always less than 15 degrees. All readings were measured by same individual.

**Table 1.** Baseline characteristics of the population

	Minimum	Maximum	Median (IQR)	Frequency (%) (n = 30)
Birth weight (Grams)	755	1455	970 (869.5 - 1190)	
Gestation age (Weeks)	26.10	34.60	28.8 (27 - 30.55)	
Male				20 (66.7%)
SGA/ AGA				7/23 (23.3%/ 76.7%)
Vaginal delivery				12 (40%)
Pre transfusion Hb (g/dl)	6.70	10.00	8.1 (7.1 - 8.7)	

Inspite of many trials and clinical guidelines the criteria for PCV transfusion in preterm babies are not very clear. Frequently, preterm babies receive PCV transfusion based on clinical signs of inadequate weight gain, tachycardia, tachypnoea, or persistent oxygen requirement.<sup>17</sup> Liberal transfusion increases the risk of transmission of infection, bronchopulmonary dysplasia, necrotising

**Table 2.** Pre and post PCV transfusion RI, PSV, EDV

	Pre PCV Mean (SD)	Post PCV Mean (SD)	p-value
RI	0.83 (0.07)	0.82 (0.07)	0.17
PSV (cm/sec)	58.46 (18.44)	46.34 (13.93)	<0.001
EDV (cm/sec)	9.83 (6.64)	8.47 (5.15)	0.21

enterocolitis and retinopathy and simultaneously increases the cost of NICU stay.<sup>18-20</sup> On the other hand, restrictive regime may increase the chances of chronic hypoxic changes, intraparenchymal brain haemorrhage or periventricular leukomalacia.<sup>21</sup> Some studies showed no difference in neonatal mortality or major morbidity when lower haemoglobin threshold was kept for transfusion, but some showed weak evidence of improved long-term outcome with higher threshold.<sup>22-24</sup>

Researchers have explored the possibility of using cerebral blood flow velocities to define a threshold for transfusion in preterm babies.<sup>14</sup> This approach seems a distant possibility for lack of data from randomised controlled trials. Although we have tried to study the novel topic of correlation of PCV transfusion and cerebral hemodynamics, our study is limited by the fact that it is a relatively small sized, single centric study. Hence, our study needs to be further substantiated with larger, multi centric studies in the future.

## CONCLUSIONS

We conclude that PCV transfusion significantly decreased PSV, reflecting improved cerebral oxygenation, and decreased cardiac output after correction of anaemia. The hemoglobin threshold for the PCV transfusion in stable preterm infants is still elusive. This probably reflects the need of defining blood transfusion threshold by considering not only the clinical and laboratory parameters but also haemodynamic parameters. Doppler studies may provide one such vital parameter.

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