Title Page

Impact of red blood cell transfusion on intestinal blood flow and oxygenation in extreme preterm infants during first week of life

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Abstract

Background: Extreme preterm infants are most unstable during the first week of life and hence require frequent blood tests to optimise the intensive care they undergo. This leads to anaemia and need for frequent red blood cell transfusion. Blood transfusion in mature preterm infants has been thought to be associated with intestinal injury and necrotising enterocolitis. The effect of blood transfusion on intestinal blood flow and oxygenation in extreme preterm infants in the first week of life has not been studied.

Methods and Results: The aim of the study was to measure the effect of blood transfusion on intestinal blood flow and oxygenation during the first week of life in extreme preterm infants. Superior mesenteric artery (SMA) peak systolic and diastolic velocities were measured 30-60 minutes before and after blood transfusion to assess intestinal blood flow using Doppler ultrasound scan (Logic P6, GE Healthcare). Intestinal or splanchnic tissue oxy/deoxy-haemoglobin ($sHbO_2$/sHHB) concentrations, Tissue Haemoglobin Index (sTHI) and Tissue Oxygenation Index (sTOI) were measured 15-20 minutes before, during and 15-20 minutes post blood transfusion using a Near Infrared Spectroscopy (NIRS) device (NIRO 300, Hamamatsu Photonics Ltd, Japan).

Heart rate (HR), respiratory rate (RR), arterial oxygen saturation (SaO_2) and blood pressure were recorded continuously during NIRS measurement using a Phillips Intellivue monitor (MP50/MP70). Other data collected: gestational age (GA), birth weight (BWt), pre and post-transfusion hemoglobin (Hb), blood gas (pH, pCO_2 and lactate), and feeding details. Data were analysed using SPSS 22.0 statistical software. Continuous variables were compared using a paired t-test and one way ANOVA. The study was approved by National Research

Ethics Committee (REC no. 12/LO/0527) and adopted as a NIHR Portfolio study (Study ID: 13594); written parental consent was obtained.

20 infants were studied. The median GA was 26 (range 23 - 27) weeks, BWt 762.5 (600 - 1180) grams, age on day of blood transfusion 5 (1 to 7) days and male: female ratio 12:8. 50% of the infants were partially fed (median 18, range 15 - 68 ml/kg/day). There was no significant change in HR, RR and SaO_2, but blood pressure increased significantly ($p<0.01$) following blood transfusion. Hb significantly increased ($p<0.001$; 95% CI 2.12 to 3.04) and lactate decreased ($p=0.02$; 95% CI 0.11 to 1.30) after transfusion, and there was no difference between the pre and post-transfusion pH ($p=0.51$) or pCO_2 ($p=0.47$).

There was no significant change in the mean SMA peak systolic velocity ($p=0.63$) as well as SMA diastolic velocity ($p=0.65$) following blood transfusion. The mean pre-transfusion SMA peak systolic velocity was higher in partially fed (n=10, 0.78 m/s) compared to unfed (n=10, 0.52 m/s) infants ($p=0.06$). The changes in SMA peak systolic velocity ($p=0.72$) and diastolic velocity ($p=0.76$) following blood transfusion was not significantly different between the fed and unfed infants.

NIRS data from 3 infants were excluded from analysis due to motion artefact. There was a significant increase in $sHbO_2$ concentration (mean difference 14.9 µM; $p=0.04$) and sTOI (mean difference 14.6%; $p=0.03$) following blood transfusion. There was no significant difference in $sHbO_2$ or sTOI between the fed and unfed infants and their response to blood transfusion.

Conclusion: Blood transfusion significantly increased systemic blood pressure, intestinal tissue oxygenation but did not alter intestinal blood flow velocities in extreme preterm infants during the first week of life. Partial feeding in extreme preterm infants had no impact on the intestinal blood flow and tissue oxygenation changes following blood transfusion in the first week of life.

Introduction

Extreme preterm infants are most vulnerable in the first postnatal week and need frequent blood tests to monitor their cardiorespiratory status to optimise intensive care. As a result of repeated phlebotomy losses these infants receive frequent transfusions during the first week of life[1,2]. The physiology of intestinal circulation and oxygenation are not clearly documented in human infants. Injecting radionuclide-labelled microspheres in experimental models of newborn lambs has helped us gain insight into this highly complex circulatory system. The oxygen consumption of intestines in these newborn lambs were 1.5 – 3 times higher than that in adults; and this high demand of oxygen consumption was met by increasing blood flow to the intestines [3]. The regulation of intestinal blood flow and oxygenation depends on various intrinsic (myogenic, metabolic factors and endogenous vasodilators) and extrinsic (neural and hormonal) factors which in turn are dependent on the postnatal age of the infant [4]. Apart from physical increase in the length and weight of the intestines following birth resulting in increased metabolic demand as reported in animal models [5], there is also a marked decrease in the intestinal basal vascular resistance following birth which results in a 2-fold increased blood flow to the intestines[6]. Researchers have studied the effect of anaemic hypoxia on newborn lambs by chronic arterial catheterisation. It has been reported that in order to maintain oxygenation in anaemic hypoxic state, the newborn intestinal tissue relies mostly on increases in oxygen extraction [7]. The effect of blood transfusion on splanchnic vasculature is reliant on the balance between mesenteric vasoconstriction and relaxation induced by intestinal endothelial production of nitric oxide. A recent study has shown blood transfusion in enterally fed preterm lambs (n=16) promotes mesenteric vasoconstriction and impairs vasorelaxation by reducing mesenteric arterial endothelial nitric-oxide synthase [8].

Doppler ultrasound scan has been used by researchers to assess intestinal perfusion in preterm infants [9]. Superior mesenteric artery (SMA) blood flow measured by Doppler ultrasound scan has been used to assess blood flow to the gut[10,11]. Changes in tissue oxygenation markers such as oxy/deoxy-hemoglobin (HbO_2/HHb) concentrations, , tissue hemoglobin index (THI) and tissue oxygenation index (TOI) (also known as regional tissue oxygen saturation) of various tissues can be measured using Near-Infrared Spectroscopy (NIRS) [12]. Researchers have used these oxygenation markers to assess the oxygenation status of splanchnic tissues, and as a biomarker to recognize the need for blood transfusion in newborn infants[9]. Intestinal or splanchnic oxygenation can be measured non-invasively by placing the NIRS probe over the hypogastrium[13]. The splanchnic tissue oxygenation measured by NIRS has been used to investigate the effect of feed [14] and blood transfusion[15,16] on intestinal oxygenation in stable preterm infant more than one week of postnatal age.

Despite being most unstable and receiving frequent blood transfusions during the first week of life, the hemodynamic change in the splanchnic tissues following blood transfusion has not been studied in extreme preterm infants. We [17] and others [18] have shown blood transfusion as an independent risk factor of in-hospital mortality in preterm infants. The aim of our study was to measure the effect of blood transfusion on intestinal blood flow and oxygenation in extreme preterm infants in the first week of postnatal life using Doppler ultrasound scan and NIRS.

Methods

The study was conducted in a tertiary level neonatal unit in London, UK. Extreme preterm infants receiving blood transfusion for clinical indication were eligible for the study.

Congenital anomalies, established abdominal pathology such as NEC and infants considered unstable for Doppler ultrasound or NIRS measurements by the attending clinical team were excluded. In accordance with the British Committee for Standards in Haematology (BCSH) guidance [19], blood transfusion was indicated in our neonatal unit for extreme preterm infants in the first week if Hb is less than 12 g/dl or Hct <0.36. The decision for blood transfusion was made by attending clinicians based on infant's Hb, ventilation status and oxygen requirement (FiO_2 >0.35). 15 ml/kg of packed red blood cells were transfused over a period of 3 hours and the ongoing feeding regime was not interfered during the blood transfusion.

Intestinal Doppler ultrasound scan measurements

The Doppler measurements were performed using an ultrasound scanner with a 7 MHz probe (Logic P6, GE Healthcare, US). The superior mesenteric artery (SMA) peak systolic and diastolic velocities were measured 30-60 minutes before and after blood transfusion using a range-gated pulsed wave Doppler ultrasound scan (**Figure 1**). The Doppler measurements were performed by a single operator (JB) to minimise intra-operator variability and utmost care was taken to minimise the angle of insonation to the direction of flow. When this was more than 30° angle correction was performed. The probe was placed in the infra-diaphragmatic region (longitudinal view) to measure SMA blood flow [20]. Cardiac morphology and presence of patent ductus arteriosus (PDA) was also recorded.

Intestinal or splanchnic oxygenation measurements

Intestinal or splanchnic oxygenation was measured using a NIRS device (NIRO 300, Hamamatsu Photonics K.K., Japan) with a sample acquisition rate of 6 Hz (samples/s). It has been reported in a recent study that the reproducibility and mean variability of NIRO 300

is comparable to other NIRS devices currently available [21]. The NIRS probe was placed over the hypogastrium in the midline above the symphisis pubis and held in place using a single use tourniquet (Vygon 'Vene K' Quick Release, Vygon UK Ltd.); utmost care was taken to minimise any movement and the probe was also covered with a diaper to prevent any ambient light interference. To reduce NIRS motion artefacts the infants were minimally handled during the study period. The splanchnic oxy-Hb ($sHbO_2$), deoxy-Hb (sHHb) in micromolar units, tissue Hb Index (sTHI) in arbitrary units and tissue oxygenation index (sTOI) in percentage were continuously measured from 15-20 min before, during and 15-20 min post blood transfusion (**Figure 1**), and downloaded into the research laptop.

Vital parameters measured

The vital parameters such as heart rate, respiratory rate, blood pressure and oxygen saturation were measured using a Phillips Intellivue monitor (MP50/MP70) during NIRS measurements (**Figure 1**), and downloaded continuously using the ixTrend 2.0 software (ixellence GmBH, Halle, Germany) into the research laptop.

Laboratory parameters measured

The pre and post blood transfusion laboratory parameters such as hemoglobin (Hb), hematocrit (Hct) and blood gas parameters such as pH, pCO_2 and serum lactate were also measured (**Figure 1**). Hb and Hct were measured using flow cytometry (Beckman Coulter Inc. US) in the hospital lab and the blood gas parameters were measured by a blood gas analyzer (GEM Premier 4000, Instrumentation Laboratory, UK) in the neonatal unit.

Additional data collected

Antenatal factors: antepartum hemorrhage (APH), maternal pre-eclampsia (PET) and intra-uterine growth restriction (IUGR), chorioamnionitis; and infant characteristics: gestational age, birth weight, Hb at birth were collected. Clinical condition on the day of transfusion: ventilation status and inotropic support were recorded.

The study was approved by the National Research Ethics Committee (REC no.12/LO/0527) and was adopted as an NIHR portfolio study (NIHR Study ID 13594). Informed written parental consent was obtained.

Data analysis

A mean for 15 minute epochs of NIRS and vital parameter measurements were determined for each infant using mathematical software Matlab (Math works, USA) during the following time periods: T1 - 15 to 20 minutes before the start of the blood transfusion, T2 - 1 hour into blood transfusion, T3 - 2 hour into blood transfusion and T4 - 15 to 20 minutes post blood transfusion. The mean of these epochs were then compared using one way ANOVA and t-tests. The pre and post-transfusion values of all other measurements were compared using paired (two-tailed) t-test. A p value of <0.05 were considered significant. The data was analysed using SPSS 22.0 software (IBM Corp., USA).

Results

Infant characteristics

20 infants were studied and infant characteristics were presented in Table 1. The gestational age (GA) and birth weight ranged from 23 to 27 weeks and 600 to 1180 grams respectively. 17 out of these 20 infants received a full course of antenatal steroids. 3 infants were IUGR due to maternal PET. 6 mothers were noted to have APH, 8 had chorioamnionitis and 2 had both. Twelve infants were undergoing conventional invasive ventilation and 8 were receiving non-invasive ventilation (Continuous Positive Airway Pressure – CPAP) at the time of blood transfusion. 10 infants were receiving enteral feed between 15 and 68 ml/kg/day. 19 infants had PDA on echocardiography, otherwise normal cardiac morphology. All infants were receiving antibiotics for presumed sepsis; however, blood culture results were noted to be subsequently negative for all. Three infants were on single inotropic support (Dopamine) because of hypotension, the dose remained unchanged for the duration of the study.

Vital parameters and laboratory measurements

The mean values of pre and post blood transfusion vital parameters and laboratory parameters are presented in **Table 2**. There was a significant increase in systolic, diastolic and mean blood pressure following blood transfusion. The serum lactate levels decreased significantly following blood transfusion. However, the mean pre and post blood transfusion pH and pCO_2 levels in the blood gas remained unaltered.

Doppler measurements

The mean pre-transfusion superior mesenteric artery (SMA) Peak Systolic Velocity (PSV) (0.63 ± 0.32 m/s) did not change significantly post-transfusion (0.60 ± 0.23 m/s; p = 0.63). Similarly the mean pre-transfusion SMA diastolic velocity (0.12 ± 0.05 m/s) did not change significantly post-transfusion (0.11 ± 0.04 m/s; p=0.65). The mean SMA PSV was higher in

partially-fed (0.75 ± 0.22 m/s) compared to unfed (0.52 ± 0.34 m/s) infants (**Figure 2**) but this was not statistically significant (p=0.06). The mean SMA diastolic velocity was similar between the partially-fed (0.14 ± 0.04 m/s) and unfed (0.11 ± 0.04 m/s; p = 0.13) infants. There was no difference between the degree of change in SMA PSV following transfusion between the partially fed and unfed groups (p=0.72) (**Figure 2**).

NIRS measurements

Intestinal or splanchnic tissue oxygenation parameters ($\Delta sHbO_2$, ΔsHHb and sTHI)

The changes in mean intestinal or splanchnic oxy-haemoglobin concentration ($\Delta sHbO_2$), deoxy-haemoglobin (ΔsHHb) concentration and tissue haemoglobin index (sTHI) are shown in **Figure 3**. The mean splanchnic oxy-haemoglobin concentration ($\Delta sHbO_2$) increased from the baseline consistently during blood transfusion and was significantly higher post-transfusion ($p<0.01$). There was a slightly different trend in the ΔsHHb levels during transfusion. There was an initial decrease (p=0.20, 95% CI -5.8 to 25.2 micromolar) within the first hour of transfusion; this lasted for the next one hour and followed by an increase in the ΔsHHb levels in the intestinal tissues. The mean post-transfusion ΔsHHb level was lower than the pre-transfusion ΔsHHb but it was not statistically significant (p=0.93; **Figure 3**). Following an initial drop in sTHI levels in the first hour, there was an increasing trend in sTHI during transfusion which was consistent throughout the transfusion and was present following blood transfusion (**Figure 3**). The mean post transfusion sTHI increased significantly compared to pre-transfusion sTHI (p=0.01).

Intestinal or splanchnic tissue oxygenation Index (sTOI)

The mean pre-transfusion sTOI (35.48 ± 20.31%) increased significantly following transfusion (post-transfusion sTOI 50.07 ± 24.16%; p=0.04). Although there was an increasing trend in mean sTOI over time (35.53% at 1 hour and 38.33% at 2 hours) it did not reach statistical significance until the end of transfusion (**Figure 3**).

NIRS measurements in the partially-fed and unfed groups

There was no difference in mean $sHbO_2$ changes between the partially fed (4.54 micromolar) and unfed (2.25 micromolar) infants in the study population (p=0.76). There was also no significant difference in the mean sTHI between the partially fed (32.18 ± 18.9 arbitrary units) and unfed (45.64 ± 19.4 arbitrary units; p=0.28; CI -12.7 to 39.7) infants. Similarly, there was no significant difference in the mean sTOI between the partially fed (31.78±18.9%) and unfed (38.78±21.8%; p=0.49; CI -14.2 to 28.2) infants. There was also no significant difference in the degree of measurement changes in $sHbO_2$ (p=0.78), sTHI (p=0.76) and sTOI (p=0.72) following blood transfusion between the partially fed and unfed infants.

Discussion

We have demonstrated for the first time that blood transfusion increases splanchnic oxy-haemoglobin concentration ($sHbO_2$), tissue haemoglobin index (sTHI) and tissue oxygenation index (sTOI) in extreme preterm infants during the first week of life. Splanchnic regional tissue oxygenation ($SrSO_2$) (a.k.a sTOI) is a biomarker of tissue oxygenation and they represent the percentage of oxygenated Hb compared to the total Hb in the tissue traversed by the near infra-red light [22]. Similar to the present study Bailey et al reported a significant increase in $SrSO_2$ in preterm infants more than seven days of age (mean postnatal age 31.7±16.2 days) from a baseline 41.3±2.2% to 48.2±2.5% following transfusion[15]. Dani et al studied $SrSO_2$ changes in preterm infants (mean postnatal age

32±23 days) and noted similar changes (pre-transfusion 54±12% to 70±8% post-transfusion)[16]. These studies were performed in more mature preterm infants (gestational age 25 to 31 weeks) with lower pre-transfusion Hb (mean Hb 9.3±1.2 g/dl) compared to the present study. The pre-transfusion splanchnic tissue oxygenation levels (sTOI) noticed in the present study during the first week of postnatal life is comparable to other published reports [13]. Compared to the brain, the baseline pre-transfusion intestinal tissue oxygenation is lower, indicating a lower oxygen requirement and higher oxygen extraction capacities[16]. The increasing trend in the splanchnic tissue oxygenation (sTOI) during transfusion in the current study was apparent as early as one hour into the transfusion but did not reach statistical significance until the end of the transfusion, this pattern is similar to the published reports in older preterm infants [15,16]. There are no published data on blood transfusion and changes in $sHbO_2$, sHHb and sTHI in preterm infants to compare with our findings. Though there were significant increases in $sHbO_2$ and sTHI, the sHHb did not change, resulting in increased sTOI following transfusion in the present study. It is reported that in stable preterm infants receiving full enteral bolus feeds splanchnic tissue oxygenation increase after each feed[14] indicating increased blood flow to the gut. In the current study the degree of change in sTOI, $sHbO_2$, sHHb and sTHI following transfusion between the unfed and partially fed infants remained unaltered which may be due to the lower volume (range 15 - 68 mls/kg/day) of enteral feeds they were receiving.

To better appreciate the effect of blood transfusion on splanchnic perfusion we measured the SMA peak systolic and diastolic velocities before and after transfusion. Our study findings demonstrated no significant change in the SMA flow velocities following blood transfusion in extreme preterm infants which is comparable to reported studies of more mature and older preterm infants[16]. This indicate that transitory haemodynamic changes in the first few days of postnatal life [23] did not alter the effect of blood transfusion on SMA blood flow velocities in the infants studied. Nelle et al reported a significant decrease in blood flow

velocity of coeliac artery following blood transfusion in clinically stable non-ventilated older preterm infants (mean gestational age 29 ± 5 weeks and mean postnatal age 48 ± 21 days)[24]. This is not comparable to the present study as we have measured SMA blood flow as a proxy of intestinal blood flow in extreme preterm infants during the first week of life. Although the blood flow velocities in the SMA remained unaltered following blood transfusion, the blood flow volume to the splanchnic circulation may have a different response to transfusion and this need further investigation.

SMA blood flow velocity has been reported to increase following feeds in older stable preterm infants [20], but we did not find any difference in the SMA peak systolic and diastolic velocities between the partially fed and the unfed groups. There was a noticeable difference of peak systolic velocities between the fed and unfed infants, but it did not reach statistical significance. This could be ascribed to the small amount of enteral feeds these infants received in proportion to total fluids. The effect of PDA and ductal steel on the SMA blood flow is well recognised[25,26], since almost all infants in the current study had PDA, we were not able to analyse the bearing of PDA on the SMA blood flow velocities.

We measured heart rate continuously upto 20 minutes post blood transfusion in the current study and did not notice any changes. It is possible that heart rate would decrease significantly following blood transfusion later and this was more prominent in older clinically and haemodynamically stable preterm infants as reported in some studies[24,27]. Unlike previous studies in older clinically stable preterm infants who did not report any significant difference in mean blood pressure following blood transfusion [16,24], there was a significant increase in the mean blood pressure following blood transfusion in the current study perhaps indicating the haemodynamic effect of increased circulatory volume in the first week of life. We did not notice any change in SaO_2 and respiratory rate following blood transfusion in this

group of infants. In older preterm infants, Fredrickson *et al* also did not notice any difference in the SaO_2, FiO_2 and oxygen consumption between two groups receiving liberal and restrictive transfusion [28]. There was a significant drop in serum lactate levels following blood transfusion in the current study despite normal levels pre-transfusion. It has been reported earlier that blood transfusion reduces serum lactate levels and this have raised the possibility of using serum lactate as a trigger for blood transfusion in preterm infants [9,29].

We carried out the study in a group of extremely premature infants who were receiving either invasive or non-invasive ventilation and were undergoing various circulatory adaptive changes in the first week of postnatal life. The decision to transfuse blood was made by the attending clinical team and was based on the BCSH guidance for transfusion in the first week of postnatal life[19]. Leukocyte depleted, cytomegalovirus negative, Sickle cell negative, plasma reduced packed red blood cells (hematocrit 50-70%), were transfused over a period of 3 hours through an intravenous cannula. This is a standard practice in most neonatal units in the UK. The ventilatory pressures, oxygen requirement, feeding regime, the pre-transfusion pH and pCO_2 remained unchanged during the study period. The mean pre-transfusion Hct (0.31 ± 0.04) is comparable to the reported studies [27,30,31].

Extreme preterm infants receiving blood transfusion during the first week of life for clinical indications were studied, and decision for transfusion was made by the attending clinician. Hence, selection bias cannot be excluded. Since Doppler ultrasound scan measurements are operator dependent, the measurements were performed by a single operator (JB) to minimise intra-operator variability. The splanchnic oxygenation measurements of 3 infants were excluded from the analysis due to motion artefacts, which is comparable to other reported NIRS studies [32,33]. One of the limitations of the study is that we measured the splanchnic tissue oxygenation only upto 20 minutes following transfusion. Other researchers

have measured splanchnic tissue oxygenation at one [34], four and 24 hours [31] post-transfusion , and reported persistence of increased tissue oxygenation state following transfusion in more stable preterm infants. All infants in the current study were receiving intensive care and any alterations in the tissue oxygenation later would be difficult to interpret due to ongoing intensive care management. Three infants were receiving Dopamine and this is unlikely to influence the study findings as the dosage of Dopamine infusion remained unchanged for the duration of the measurements.

Conclusion: Blood transfusion in the first week of postnatal life in extreme preterm infants increased systemic blood pressure, improved intestinal tissue oxygenation but did not alter intestinal perfusion. Partial feeding in these infants had no impact on the intestinal blood flow and tissue oxygenation changes following blood transfusion. Further studies on intestinal perfusion, microcirculation and tissue oxygenation response to blood transfusion in preterm infants of various gestational and chronological age groups are required. The effect of enteral feed on intestinal perfusion and oxygenation during blood transfusion needs to be explored.

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Table 1. Study infant characteristics (n=20)

Infant characteristics	Results
Gestational age at birth (weeks)	25 (1.25)*
Birth weight (grams)	819 (140.6)*
Male : Female	12 : 8[+]
Caucasian : Black : Asian : Mixed	12 : 4 : 3 : 1[+]
Age at transfusion (days)	4 (2)*
Admission Hb (grams/dl)	14.4 (2.28)*
Not-fed: Fed	10:10[+]
Median (range) volume of feeds (ml/kg/d)	18 (15 – 68)

*Mean (standard deviation), [+]Ratio

Table 2. Changes in vital and laboratory parameters following blood transfusion (n=20)

Vital and laboratory parameters	Pre-transfusion Mean (SD)	Post-transfusion Mean (SD)	p values (95% CI)
Heart rate (per min)	159.1 (8.8)	157.9 (15.1)	0.67 (-4.51 to 6.89)
Resp rate (per min)	53.2 (12.3)	50.0 (11.7)	0.13 (-0.99 to 7.28)
Saturation (%)	93.2 (2.9)	93.2 (2.5)	0.96 (-1.71 to 1.63)
Systolic BP (mm of Hg)	46.7 (6.6)	51.6 (4.9)	<0.01 (2.24 to 7.62)
Diastolic BP (mm of Hg)	24.3 (3.1)	30.7 (4.7)	<0.01 (3.17 to 9.11)
Mean BP (mm of Hg)	32.7 (3.8)	37.9 (3.7)	<0.01 (2.61 to 8.01)
Hb (mg/dl)	11.08 (1.30)	13.77 (1.63)	< 0.01 (2.12 to 3.04)
Hct	0.31 (0.04)	0.39 (0.05)	< 0.01 (0.07 to 0.09)
pH	7.28 (0.07)	7.27 (0.05)	0.51 (-0.02 to 0.05)
pCO_2 (kPa)	5.69 (1.21)	5.85 (0.82)	0.47 (-0.63 to 0.31)
Lactate (mmol/L)	2.53 (1.31)	1.78 (0.51)	0.02 (0.11 to 1.30)

Figure 1. Overview of measurements. The numbers in the timeline at the bottom show the various steps of measurements during the process.

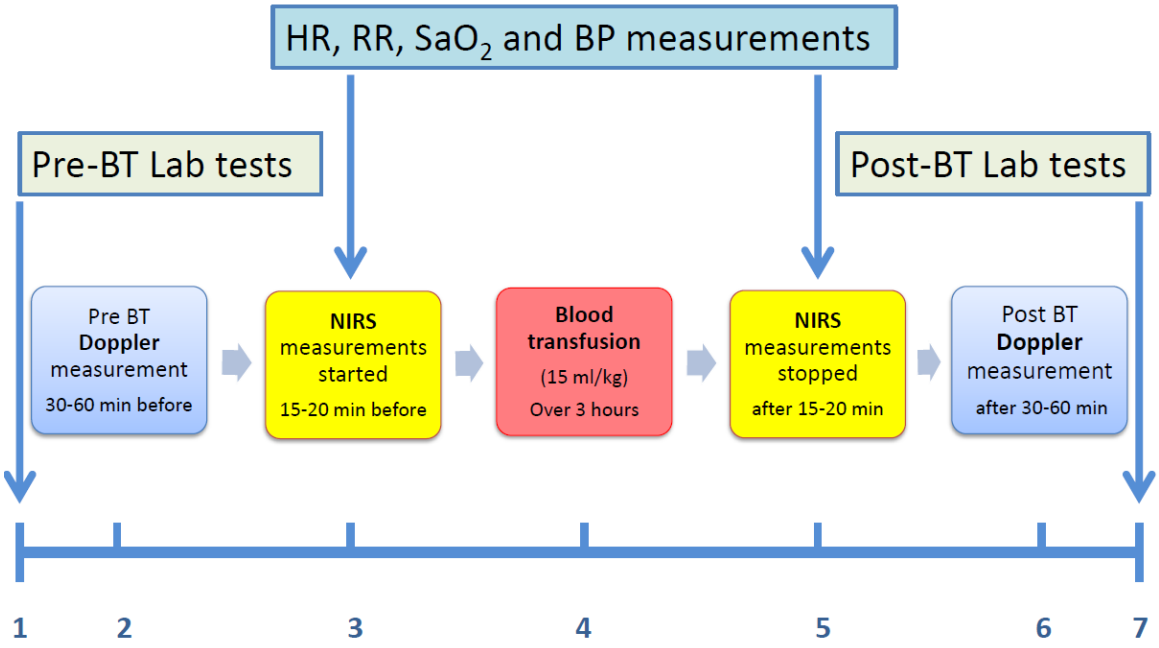

Figure 2: Pre and post blood transfusion SMA peak systolic velocity of partially fed (n=10) and unfed (n=10) infants

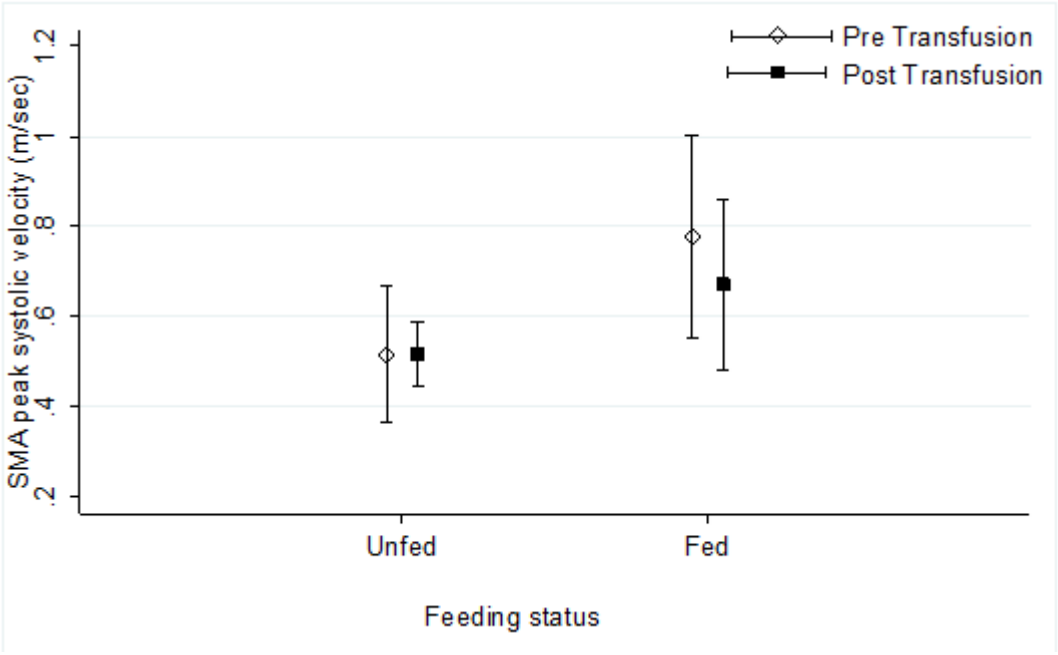

Figure 3: Blood transfusion and changes in splanchnic tissue oxy-Hemoglobin concentration ($\Delta sHbO_2$), deoxy-Hemoglobin concentration (ΔsHHb), tissue Hemoglobin Index (sTHI) and tissue oxygenation index (sTOI) (n=17). *T1 = Pre-blood transfusion, T2 = 1 hour after blood transfusion started, T3 = 2 hours after blood transfusion started, T4 = Post blood transfusion. (* = p<0.05)*