Early Human Development 89 (2013) 683–686

Contents lists available at SciVerse ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Effects of red cell transfusion on cardiac output and perfusion index in preterm infants

H. Gozde Kanmaz [a,*], Y. Unal Sarikabadayi [b], Emre Canpolat [a], Nahide Altug [c], S. Suna Oguz [a], Ugur Dilmen [a,d]

[a] Zekai Tahir Burak Maternity Teaching Hospital; Division of Neonatology, Turkey
[b] Gaziantep Children's Hospital; Division of Neonatology, Turkey
[c] Zekai Tahir Burak Maternity Teaching Hospital, Division of Pediatric Cardiology, Turkey
[d] Yildirim Beyazit University Department of Pediatrics, Turkey

ARTICLE INFO

Article history:
Received 8 November 2012
Received in revised form 29 April 2013
Accepted 30 April 2013

Keywords:
Prematurity
Anemia
Transfusion
Cardiac output
Perfusion index

ABSTRACT

Objective/Aim: The present investigation was designed to study the effect of blood transfusion on cardiac output and perfusion index. The aim was to demonstrate a relationship between hematocrit, lactate, cardiac output and perfusion index in anemic preterm infants and to investigate significant changes in these parameters induced by RBC transfusion.

Methods: Anemic infants who were under 35 weeks of gestational age (GA) and were in a stable clinical condition without respiratory or cardiac problems, signs of sepsis, or renal disease at the time of investigation were enrolled in the study. Enrolled infants received 15 ml/kg pure red blood cells over 4 h. Hematocrit and lactate levels were studied before and after transfusion. Cardiac output was measured by an ultrasound device (USCOM 1A) and perfusion index was monitored by pulse oximeter (MasimoRad7).

Results: Cardiac output decreased by 9% ($p < 0.05$), due to decrease in heart rate by 10% ($p < 0.05$) and stroke volume significantly by 5% ($p < 0.05$) both in left and right sided cardiac measurements. Perfusion index significantly increased and lactate levels significantly decreased after transfusion ($p < 0.05$). Htc was inversely correlated with lactate levels, HR, CI and CO ($r = -0.33$, $p = 0.01$; $r = -0.53$, $p = 0$; $r = -0.37$, $p = 0.004$, $r = -0.28$, $p = 0.03$). PI was not significantly correlated with Htc levels before and after transfusion ($r = 0.07$, $p = 0.7$ and $r = 0.007$, $p = 0.97$).

Conclusion: Our data support that heart rate, CO and CI and lactate levels increased as a response to anemia in preterm infants and RBC transfusion improved perfusion index suggesting better tissue oxygenation.

1. Introduction

Anemia is common after preterm delivery due to blood sampling, rapid growth and insufficient erythropoiesis [1–3]. Red blood cell transfusion in preterm infants is the key treatment modality for anemia of prematurity however clear guidance on the indications for transfusion remains elusive [4,5]. Little is known about the adaptive responses to anemia in VLBW infants and the effects of transfusion at various levels of anemia on the delivery and utilization of oxygen [6–9]. Consequently, transfusion guidelines are inconsistent, and transfusions are administered to premature infants often and repeatedly, using poorly defined indications.

Many symptoms have been attributed to anemia in preterm infants including tachycardia, poor weight gain, apnea, and lactic acidosis, but there is no definitive evidence that when using any current guidelines, transfusion of RBCs results in clinical benefit. Earlier studies show contradictory results about whether transfusions improve cardiorespiratory status [10–13]. Furthermore conflicting results have been reported as to whether blood transfusion results in changes of cardiac output. While Hudson et al. found a reduction of cardiac output with transfusion [2] Alverson et al. [6] and Bifano et al. [11] did not observe a significant change of cardiac output in premature infants.

A variety of minimally invasive hemodynamic monitoring technologies have been developed, which have become attractive as alternative methods of measuring cardiac output. Recently a noninvasive method of transcutaneous, continuous wave Doppler ultrasound measurement of cardiac output was developed, USCOM 1A (Ultrasonic Cardiac Output Monitor, USCO Ltd, Sydney, Australia) Doppler ultrasound device [14,15]. This technology utilizes transaortic or transpulmonary Doppler ultrasound flow tracing to calculate cardiac output as the product of stroke volume and heart rate. Stroke volume is calculated from a proprietary algorithm applying ultrasound principles of blood-velocity time integral measurements in the ventricular aortic outflow tract [14,15]. Perfusion index is an assessment of the pulsatile strength at a specific monitoring site (e.g. the hand, finger or foot), and as such PI is an indirect and noninvasive measure of peripheral perfusion. It is calculated by means of pulse oximetry by expressing the pulsatile signal (during

* Corresponding author at: Neonatal Intensive Care Unit, Zekai Tahir Burak Maternity Teaching Hospital, 06230, Cebeci, Ankara, Turkey. Tel.: +90 312 306 52 70; fax: +90 312 309 47 02.
E-mail address: gzdekanmaz@yahoo.com (H.G. Kanmaz).

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http://dx.doi.org/10.1016/j.earlhumdev.2013.04.018

arterial inflow) as a percentage of the nonpulsatile signal, both of which are derived from the amount of infrared (940 nm) light absorbed. In the neonatal acute care setting, a low PI has been shown to be an objective and accurate measure of acute illness. Additionally, PI measurement represents a more rapid and inexpensive method to assess peripheral perfusion and circulatory status of the patient [16,17].

The present investigation was designed to study the effect of blood transfusion on cardiac output and perfusion index. A Doppler ultrasound device was used to determine cardiac output and pulse oxymeter (Masimo, Radical 7-Rainbow Signal Extraction Technology (SET®) to determine perfusion index. Also we aimed to demonstrate a relationship between hematocrit, lactate, CO and perfusion index in anemic preterm infants and to investigate significant changes in these parameters induced by RBC transfusion.

2. Patients and methods

This study was conducted in Zekai Tahir Burak Maternity Teaching Hospital Neonatal Intensive Care Unit in Ankara, Turkey and was approved by the local ethics committee. Written parental consent was obtained from all participants. Infants who were under 35 weeks of gestational age (GA) and were in a stable clinical condition without respiratory or cardiac problems, signs of sepsis, or renal disease at the time of investigation were enrolled in the study. Infants who were ventilated and/or treated with sedatives, diuretics, vasoactive drugs, who have congenital heart disease including patent ductus arteriosus, suffered from acidosis or hypoxia at the time of investigation were excluded from the study. Enrolled infants received 15 ml/kg pure red blood cells over 4 h. The decision for transfusion was made by the attending neonatologist considering clinical signs of anemia (tachycardia, tachypnea, need for supplemental oxygen, poor weight gain). Demographic data were collected prospectively from medical charts. Hemoglobin, hematocrit, lactate levels, blood pressure, saturation, perfusion index and cardiac output were assessed right before RBC transfusion and within 12–24 h after transfusion.

2.1. Circulatory parameters

The cardiovascular examinations were made at least an hour after previous feeding. Measurements were done when the infants were in a quiet sleep state. Quiet sleep was assumed when the infants' eyes were closed, no movements were observed apart from occasional stable reactions and respiration was regular. The infants were in the supine position. Cardiac output was measured by using USCOM 1A (Ultrasonic Cardiac Output Monitor, USCO Ltd, Sydney, Australia) Doppler ultrasound device. After subject enrollment the set of hemodynamic parameters including cardiac index (CI), stroke volume index (SVI), aortic outflow tract diameter (OTD), velocity time integral (VTI) and heart rate were recorded by two trained investigators before and after RBC transfusion. The mean of pre and post-transfusion USCOM 1A measurements was calculated as average of three measurements performed by the same investigator. Left-sided cardiac measurements (LV-CO) were obtained by placing the transducer at the subject's suprasternal notch and right-sided measurements (RV-CO) were obtained by placing the transducer at the parasternal border as described earlier[14,15].

2.2. Repeatability of USCOM measurements

Repeatability (intra-observer variability) for the experienced user of USCOM measures was assessed by performing five consecutive measurements, of both RV-CO and LV-CO, in 10 infants using the USCOM device.

The PI derived from a pulse oximeter (Masimo SET Radical, Masimo, Irvine, CA, USA) was monitored continuously with the SpO2 sensor placed on right foot. The median PI for each measurement was obtained from the average of PI values recorded at 6-second intervals. For Masimo Radical-7 Rainbow SET the PI upper and lower limits reported by the manufacturer are 0.02–20.00%.

Systolic and diastolic BP was measured indirectly using an oscillometric device (Passport 2, Datascope Corp., MahWah, NJ, USA).

The hemoglobin, hematocrit (Htc) and lactate levels were measured in the hospital's clinical laboratories using standard methods.

3. Statistical analysis

Data are presented as mean (SD). A two tailed paired *t* test was done to test for differences in the measurements before and after blood transfusion; $p < 0.05$ was considered significant. Repeatability (intra-observer variability), for each method, was quantified as coefficient of variation (SD of measurements divided by the mean and expressed as a percentage). Spearman correlation test was performed for correlation analysis; $p < 0.05$ was considered significant.

4. Results

Thirty-five preterm infants were evaluated. The mean gestational age was 28.8 ± 2.1 (range 25–34) weeks and birth weight was 1066 ± 286 g (range 730–1640 g). Infants received RBC transfusion on median 34 day (range 7–95 day) postnatal age. Mean gestational age was 33.8 ± 2.1 (range 29–39) weeks and mean weight was 1375 ± 309 g (range 830–2050) at the time of investigation.

Repeatability of measures (intra-observer variability), by the expert user was 5.3% for LVO and was 6.7%, for RVO.

Changes in the hemodynamic and other laboratory variables after transfusion are summarized in Table 1. Cardiac output decreased by 9% ($p < 0.05$), due to decreases in heart rate by 10% ($p < 0.05$) and stroke volume significantly by 5% ($p < 0.05$) both in left and right sided cardiac measurements. Perfusion index significantly increased and lactate levels significantly decreased after transfusion (Table 1). Systolic and diastolic blood pressures and oxygen saturation did not significantly change before and after transfusion (Table 1).

PI was not significantly correlated with Htc levels before and after transfusion ($r = 0.07$, $p = 0.7$ and $r = 0.007$, $p = 0.97$). Htc was inversely correlated with lactate levels, HR, CI and CO ($r = -0.33$, $p = 0.01$; $r = -0.53$, $p = 0$; $r = -0.37$, $p = 0.004$, $r = -0.28$, $p = 0.03$). Negative correlation was observed between PI and HR ($r = -0.31$, $p = 0.02$) but there was no correlation between PI and CO ($r = -0.04$, $p = 0.74$).

5. Discussion

The results of the present study show that red cell transfusion decreased cardiac output due to decrease in heart rate and stroke volume suggesting that the heart rate before transfusion was increased in response to the anemia. Consistent with our findings Hudson [2] et al. found a decrease in CO by 12% after transfusion of 20 ml/kg of RBC and

Table 1
Changes in the hemodynamic and other laboratory variables after transfusion.

	Pre-transfusion	Post-transfusion	p
Hematocrit %	26.2 ± 3.5	43.1 ± 5.4	0.001
Lactate mmol/L	2.57 ± 0.68	2 ± 0.42	0.001
Heart rate/min	164 ± 15	146 ± 12	0.001
Saturation %	94 ± 3.8	96.8 ± 2.4	0.16
Systolic BP mm Hg	66.9 ± 9.3	67.2 ± 9.6	0.8
Diastolic BP mm Hg	37.8 ± 8.8	37.5 ± 7.3	0.8
Perfusion index	0.84 ± 0.3	1.2 ± 0.4	0.002
LV-CO L/min	0.43 ± 0.09	0.39 ± 0.1	0.003
LV-CI L/min/m^2	3.49 ± 0.59	3.12 ± 0.52	0.003
RV-CO L/min	0.65 ± 0.24	0.56 ± 0.21	0.001
RV-CI L/min/m^2	5.34 ± 1.38	4.59 ± 1.21	0.001