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Effects of red blood cell transfusion on neonatal cerebral hemodynamics: a TD-NIRS and DCS study

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ABSTRACT

Anemia is a common problem in preterm neonates, and red blood cell transfusion (RBCT) is used to improve oxygen delivery. In order to limit the risk of possible complications new strategies to minimize the need for RBCTs are needed, as assessment of hemoglobin concentration in blood ([Hb]) alone appears to be an inadequate biomarker. In this study, we search for hemodynamic and metabolic thresholds to help define the need of RBCT in anemic newborns. The effect of RBCTs on cerebral tissue oxygen saturation (S_tO_2) and blood flow (measured as Blood Flow Index, BFI) was estimated using a non-invasive hybrid diffuse optical device that combines Time Domain NIRS (TD-NIRS) and Diffuse Correlation Spectroscopy (DCS) techniques (BabyLux device). We enrolled 18 clinically stable neonates receiving RBCT at Neonatal Intensive Care Unit (NICU) of Ospedale Maggiore Policlinico in Milan. Tissue oxygen extraction (TOE) and the cerebral metabolic rate of oxygen consumption index ($CMRO_2I$) were computed, the Wilkinson signed rank test for paired data was performed to compare data before and after RBCT. Preliminary results are in accordance with previous publications as regards cerebral oxygenation: a significant increase in S_tO_2 (from 56.62 ± 5.20% to 63.85 ± 4.95%, $p<0.05$) and reduction in TOE (from 41.35 ± 5.9 % to 31.04 ±5.41%, $p<0.05$) were observed. The response in cerebral blood flow was smaller (only 10%) but also more variable, so conclusions regarding the effect of transfusion on cerebral oxygen metabolism are still uncertain.

Keywords: transfusion, neonates, time-domain NIRS, diffuse correlation spectroscopy, cerebral metabolic rate of oxygen consumption

1. INTRODUCTION

Up to 90% of extremely preterm neonates receive at least one RBCT during their hospitalization in NICU [1]. RBCTs are needed in many cases such as acute bleeding, cardiorespiratory compromise or anemia of prematurity. However, RBCT could generate some risks (e.g., infections, intra-ventricular hemorrhage) that are particularly dangerous for preterm neonates [2] and up to now the hemoglobin level in the blood is the only biomarker used to evaluate the need for a transfusion, but this method might be insufficient since very often ill preterm newborns do not benefit from RBCT [3,4]. Several works have already been published exploiting NIRS to study the effects of RBCT on neonates [5]. Most of these studies made use of commercial CW-NIRS devices, which only give access to tissue oxygen saturation (S_tO_2). No studies have been conducted up to now combining TD-NIRS with DCS, which instead allow for retrieving absolute hemoglobin concentration, metabolic information, and blood flow index.

2. MATERIALS AND METHODS

The effect of RBCT on cerebral hemodynamics of preterm neonates was investigated by exploiting biophotonic techniques, following the protocol described in this section. Cerebral oxygenation was recorded with a commercially available spatially resolved CW-NIRS device (INVOS 5100C, Covidien Inc., USA). The sensor was placed on the prefrontal region of neonate's head. Also, hearth rate and arterial saturation (S_pO_2) were continuously monitored with a commercial pulseoxymeter. The recording started about 30 min before the transfusion and ended about 30 min after the end of the transfusion. Conversely, TD-NIRS and DCS measurements were performed with the BabyLux device only before and after the transfusion (repositioning the probe). The measurements were performed on the prefrontal region with a source-detector separation of 1.5 cm, as five repetitions of 60 s (with an acquisition time of 1 s). The TD-NIRS and DCS data were analyzed with semi-infinite homogeneous model. Finally, all hemodynamic and metabolic

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parameters were averaged and compared with the Wilkinson signed-rank test. The protocol was approved by the local research ethics committees. The protocol was registered at ClinicalTrials.gov, identifier NCT03983694.

3. RESULTS

We enrolled 18 preterm neonates, but of them only 14 were eligible due to unstable hemodynamic parameters during the measurements and incorrect probe positioning. The average gestational age at birth of enrolled neonates is 30.9±3.1 (at the enrollment 35.1±3.1), and the average weight 1690 g. The results of this study are summarized in Fig. 1.

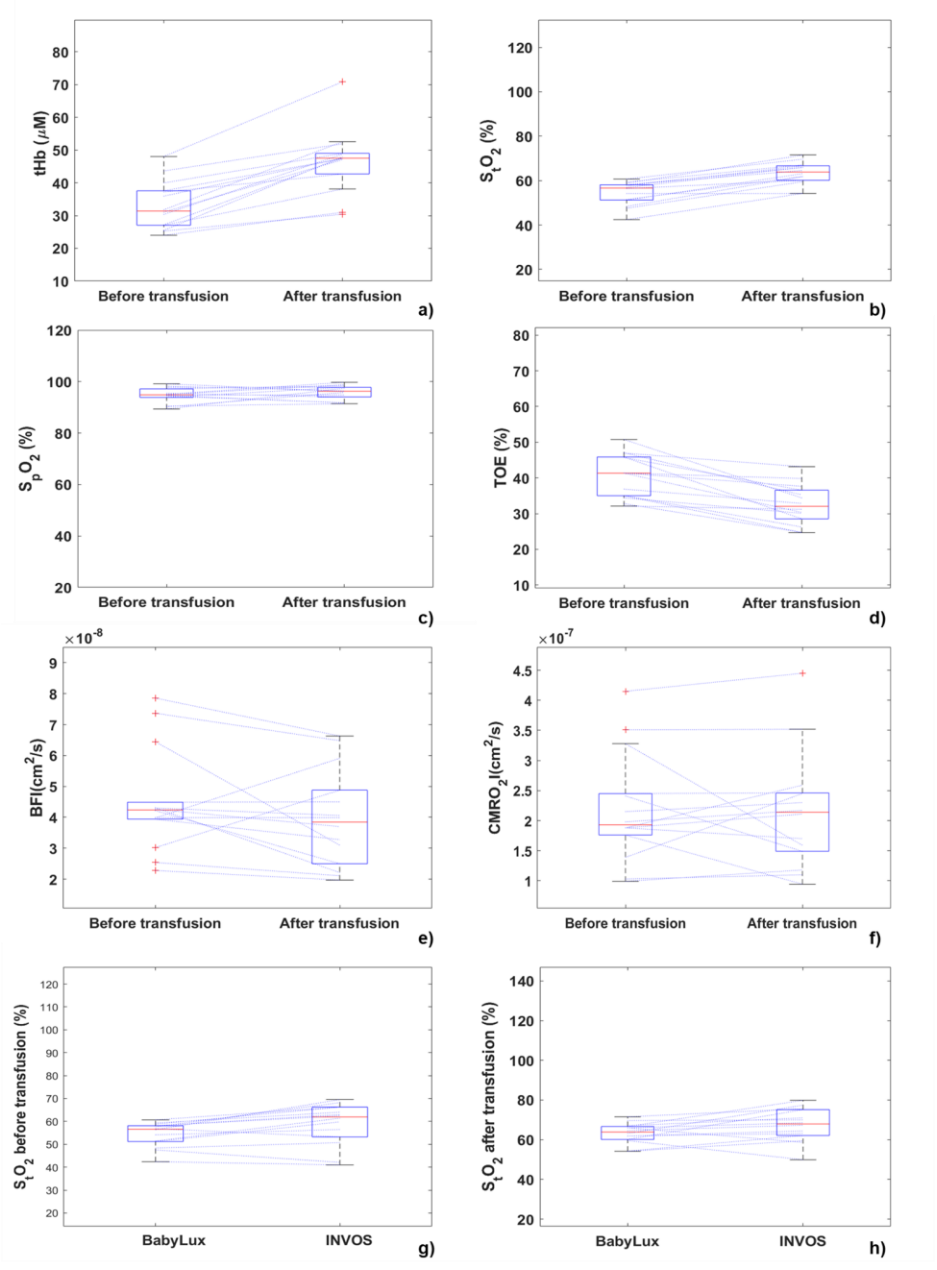

Figure 1. Box plot of tHb (panel a), S_tO_2 (panel b), S_pO_2 (panel c), TOE (panel d), BFI (panel e), $CMRO_2I$ (panel f), measured with the BabyLux device, before and after RBC transfusion (Y-axis scaled approximately to image a factor of 4). The red lines inside the box represent the median, the bottom and top edges of the box indicate the 25th and 75th percentiles, respectively. The whiskers extend to the most extreme data points not considered outliers, and the outliers are plotted individually in red. Dashed lines connect values measured before and after the transfusion for the same patient. In panel g) and h) the S_tO_2 measured with the BabyLux device is compared to the one measured with the INVOS device before and after transfusion.

tHb (panel a), and S_tO_2 (panel b) show a clear increase in their values after RBCT. In particular, the median among all the patients increases from 31.4 μM to 47.53 μM for tHb (with an increment of 51.4%, $p<0.05$), and from 56.62% to 63.85% for S_tO_2 (with an increment of 12.8%, $p<0.05$). These variations are far higher than the error performed when the probe is repositioned (about 10 % for tHb, and 5.7% for S_tO_2) [6], suggesting that the hemodynamic variations measured with the BabyLux are related to real physiological changes after RBCTs. Accordingly, TOE show significant reduction ($p<0.05$, from 41.35±5.90 to 31.04±5.41). On the contrary, S_pO_2, BFI and $CMRO_2I$ do not show significant variations after RBCTs. Finally, we compared the S_tO_2 estimated with the BabyLux device to the one estimated with the INVOS device before (panel g) and after (panel h) RBCTs. The results obtained with the INVOS device show a higher median value, but also a wider dispersion.

4. DISCUSSION AND CONCLUSIONS

The results suggest that RBCT increases brain oxygenation as well as cerebral hemoglobin concentration. These results agree with previous works [5] where an increase of brain oxygenation was observed after RBCT. With respect to previous studies, we were able to compare the results obtained with a CW-NIRS device and TD-NIRS device. Differences among S_tO_2 retrieved were observed: wider dispersion was shown in case of CW-NIRS measurements, probably due to the stronger influence of superficial tissues compared to TD-NIRS technique, suggesting that TD-NIRS technique allows for a more accurate and precise estimation. The smaller dispersion of S_tO_2 values retrieved with the BabyLux device may suggest that TD-NIRS hemodynamic parameters could be better biomarkers compared to the ones measured with CW-NIRS devices. The use of a hybrid device allowed us to also estimate brain metabolism of preterm neonates. However, the metabolism does not seem to be affected by the RBCT, as suggested by the non-significant change of $CMRO_2I$. Unfortunately, the statistical precision of the estimate of the effect on $CMRO_2I$ was poor, mainly due to the scatter of the BFI data.

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