



CORRESPONDENCE

Response to: “Letter to the Editor: Effect on splanchnic oxygenation of breast milk, fortified breast milk and formula milk in preterm infants”

Pediatric Research (2021) 89:6; <https://doi.org/10.1038/s41390-020-01164-0>

We want to thank Embleton and co-workers¹ for their valuable remarks and interest on our research.² We agree that birth weight of infants who received mother's own milk (MOM), fortified human milk (FHM) or preterm formula (PTF) were rather different, but we carried out a prospective study and this design does not always allow an optimal balance of population variables. On the other hand, we could not plan a randomized controlled study for ethical reasons since in our centers PTF is administered only when human milk is not available because of better effects of HM on preterm infants' outcomes.^{3,4} Infants were studied when they were clinically stable and tolerating full bolus enteral feeding for 1 week with a total daily amount between 140 and 160 mL/kg, without intravenous support. These criteria were chosen to avoid clinical bias and to guarantee a similar functional and physiological gastrointestinal maturation in study groups, despite the different gestational age at near-infrared spectroscopy (NIRS) measurement. However, birth weight and postnatal age did not statistically differ between the groups. Our aim was to evaluate changes of splanchnic regional oxygenation in infants fed MOM, FHM or PTF, and we could not have assessed their effect on the NEC occurrence due to the small size of our population. Infants who were fed with PTF had more frequently bronchopulmonary dysplasia, patent ductus arteriosus (PDA) and retinopathy of prematurity than infants who were fed with FHM, but differences were not statistically significant and, therefore, these variables did not require statistical adjustments. Moreover, none of the infants had PDA and all were clinically stable at NIRS measurement and this excludes that the clinical severity may have affected our results. We did not report hematocrit data, but they did not differ between the groups since we applied the guidelines of Italian Society of Neonatology on transfusions,⁵ and this allowed to avoid significant differences. In our study, decisions about whether to increase feeding volume, halt feeding advancement and fortification were made by the clinical team based on local protocols. This can explain why the achievement of full enteral feeding and starting of fortification occurred later than expected, although without significant differences between the groups. We regret because data were reported as mean values and standard deviations in tables and as median values and interquartile ranges in figures, while *P* values were calculated using median values and interquartile ranges in both tables and figures. We submitted an Erratum to correct this inaccuracy. We performed NIRS measurement with INVOS 5100® (Somanetics Corporation, Troy, MI, USA), which uses two wavelengths, 730 and 810 nm. These wavelengths are included in the near-infrared optical window, namely, the range of wavelengths where the light has its highest capacity of penetration in tissues. Within this window, melanin, blood, water and fat can essentially absorb light, while protein and calcium

light absorption is negligible. In detail, absorption of fat is thousands of times lower than that of melanin, about hundred times lower than that of oxy- and deoxy-hemoglobin, and lower than that of water.⁶ Furthermore, considering that the self-adhesive transducer for NIRS measurement was placed on the infra-umbilical abdomen region above the small intestine, it is rational to assume that digestive processes may have reduced the differences in composition between MOM, FHM and PTF and their potential effects on NIRS measurement. Therefore, our opinion is that milk components cannot alter NIRS absorptive capacity.

AUTHOR CONTRIBUTIONS

C.D., C.C., S.M., G.R., C.P., C.S., E.M. and M.S. read and approved the final manuscript.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

Statement of consent: Patients were enrolled after informed parental consent.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Carlo Dani^{1,2}, Caterina Coviello², Simona Montano², Giulia Remaschi², Chiara Petrolini², Chiara Strozzi³, Elena Maggiora³, Miriam Sabatini³ and Diego Gazzolo⁴
¹*Division of Neonatology, Careggi University Hospital of Florence, Florence, Italy;* ²*Department of Neurosciences, Psychology, Drug Research, and Child Health, University of Florence, Florence, Italy;* ³*AO SS Antonio, Biagio and C. Arrigo Hospital, Alessandria, Italy and* ⁴*Neonatal Intensive Care Unit, G. D'Annunzio University of Chieti, Chieti, Italy*
 Correspondence: Carlo Dani (cdani@unifi.it)

REFERENCES

- Embleton, N., Berrington, J., Bloomfield, F. & Martin, C. Letter to the Editor: Effect on splanchnic oxygenation of breast milk, fortified breast milk and formula milk in preterm infants. *Pediatr. Res.* <https://doi.org/10.1038/s41390-020-1043-y> (2020).
- Dani, C. et al. Effect on splanchnic oxygenation of breast milk, fortified breast milk, and formula milk in preterm infants. *Pediatr. Res.* <https://doi.org/10.1038/s41390-020-0935-1> (2020).
- Miller, J. et al. A Systematic review and meta-analysis of human milk feeding and morbidity in very low birth weight infants. *Nutrients* **10**, E707 (2018).
- Quigley, M., Embleton, N. D. & McGuire, W. Formula versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst. Rev.* **7**, CD002971 (2019).
- Girelli, G. et al. Recommendations for transfusion therapy in neonatology. *Blood Transfus.* **13**, 484–497 (2015).
- Mustafa, F. H., Jones, P. W. & McEwan, A. L. Near infrared spectroscopy for body fat sensing in neonates: quantitative analysis by GAMOS simulations. *Biomed. Eng. Online* **16**, 14 (2017).

Received: 9 July 2020 Revised: 5 August 2020 Accepted: 10 August 2020
 Published online: 12 October 2020