



EDITORIAL

Should human milk for premature children be fortified after discharge to improve neurodevelopmental outcomes? ☆, ☆ ☆



O leite materno deve ser fortificado para crianças prematuras após terem alta para melhorar os resultados de neurodesenvolvimento?

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Preterm children are at higher risk for neurodevelopmental problems.¹ Exclusive breastfeeding for all children, including term infants, has been recommended for the health benefits as well as overall wellbeing.² In addition, improved developmental outcomes have been reported in term children who are exclusively breastfed.³ In preterm children, the advantages of human milk have been well established for protection against necrotizing enterocolitis and sepsis, and trophic effects.⁴ However, it has been recognized that, in preterm children, human milk alone may not support optimal growth because of insufficient nutrient content.⁵ Preterm infants are born at a period of significant organ development and are at risk for deficiency of essential nutrients and trophic factors that promote growth and brain development, such as long-chain polyunsaturated fatty acids and possibly others.⁶ Without fortification, preterm children may have growth retardation, which has been associated with impaired neurodevelopment.⁷ Therefore, it has been recommended that all preterm infants

with birth weight <1800 g should receive fortified human milk, to add supplemental nutrient fortification, focusing on proteins and minerals, and vitamins in particular during the neonatal intensive care unit stay to assure adequate growth.⁸ This fortification has been provided with different commercially available components, and the quality of available products varies. Some units use a more standardized approach while others use a more individualized approach.⁹

Improved neurodevelopmental outcome and the use of human milk in preterm children has been reported in large, mostly observational retrospective studies¹⁰; a more recent review did not conclude that there was improved neurodevelopmental outcome with the use of human milk in preterm children in their meta-analyses.¹¹ However, in that review, studies included did not have much information on fortifier use. A study¹² reported a paradox between preterm infants fed with human milk that grew less during hospitalization compared to formula fed infants, but had better neurodevelopment in the first few years of life; however, the group that was breastfed had higher birth weight, although the authors controlled for growth restriction and socioeconomic status.

Use of fortified human milk during the NICU stay has demonstrated improvement in growth in preterm infants¹²; however, studies on long term neurodevelopmental outcome are not conclusive. A review looked specifically for effects of human milk fortification after discharge on development¹³

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and did not find differences in neurodevelopmental outcome.

There are several human milk fortifiers that had been promoted for use with human milk in premature infants⁵; in addition, some hospitals use powdered preterm formula in order to provide minerals and other needed nutrients for preterm children. The cost of commercially available fortifiers is high, in addition to problems with adding possible contamination or excessive use of fortifiers and effects on long-term health.

The present article from da Cunha et al.¹⁴ reports on a randomized clinical trial of a formula powder (NESTLÉ®, Vevey, Switzerland) human milk vs. human milk with no supplementation on infants born weighing less than 1500g after being discharged from the nursery. This study has multiple strengths, such as using a valid randomized design and blinding developmental evaluators to the intervention group. However, there are several variables that will be difficult to control for. Preterm infants represent a heterogeneous population who may require carefully individualized nutritional care. In addition, there is large variation between the content of breast milk from one mother to another. Although this was a randomized study, human milk content was not analyzed; therefore, a great variability across the different mothers included in the study is possible. If higher-quality fortifiers and maternal vitamin and mineral supplementation were used, the results may have been statistically significant between groups.

Although not described in the study, we can assume that infants were fed directly at the breast, and only supplemented children received expressed breast milk by other means.

This study addresses an important question regarding whether fortification of human milk should be recommended post-discharge for preterm infants for the theoretical advantages of higher protein and nutrient content to improve neurodevelopmental outcomes. This becomes particularly important for infants born at extreme prematurity with longer hospitalization, who may have a significant accumulated deficit in nutrients prior to discharge. It is possible that with newer guidelines of fortification during the NICU stay, children may not be as a disadvantage as we had assumed previously. Several investigations are ongoing, looking into the quality and duration of human milk fortification. In addition, fortification after discharge is not without difficulties, considering the high cost of multicomponent fortifiers; perhaps limited availability; possible contamination during mixing, in particular in areas with limited resources; and, perhaps, even the discouragement of breastfeeding when infants are at home.

We are left with the question of whether we need to fortify breast milk for preterm infants after discharge to improve neurodevelopmental outcomes; however, we can be

reassured from this study that if there is a clinical indication for fortification, it must not interfere with exclusive breastfeeding – the desired method of feeding preterm infants – given all the advantages that breastfeeding provides.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Stephens BE, Vohr BR. Neurodevelopmental outcome of the premature infant. *Pediatr Clin North Am.* 2009;56:631–46.
2. Fewtrell MS, Morgan JB, Duggan C, Gunnlaugsson G, Hibberd PL, Lucas A, et al. Optimal duration of exclusive breastfeeding: what is the evidence to support current recommendations? *Am J Clin Nutr.* 2007;85:635S–8S.
3. Gertosio C, Meazza C, Pagani S, Bozzola M. Breast feeding: gamut of benefits. *Minerva Pediatr.* 2015, May [Epub ahead of print].
4. Johnson TJ, Patel AL, Bigger HR, Engstrom JL, Meier PP. Cost savings of human milk as a strategy to reduce the incidence of necrotizing enterocolitis in very low birth weight infants. *Neonatology.* 2015;107:271–6.
5. Ziegler EE. Human milk and human milk fortifiers. *World Rev Nutr Diet.* 2014;110:215–27.
6. Anderson A, Swank P, Wildin S, Landry S, Smith K. Modeling analysis of change in neurologic abnormalities in children born prematurely: a novel approach. *J Child Neurol.* 1999;14:502–8.
7. Ehrenkranz RA. Nutrition, growth and clinical outcomes. *World Rev Nutr Diet.* 2014;110:11–26.
8. Moro GE, Arslanoglu S, Bertino E, Corvaglia L, Montirosso R, Picaud JC, et al. XII. Human milk in feeding premature infants: consensus statement. *J Pediatr Gastroenterol Nutr.* 2015;61:S16–9.
9. Arslanoglu S. IV. Individualized fortification of human milk: adjustable fortification. *J Pediatr Gastroenterol Nutr.* 2015;61:S4–5.
10. Vohr BR, Poindexter BB, Dusick AM, McKinley LT, Higgins RD, Langer JC, et al. Persistent beneficial effects of breast milk ingested in the neonatal intensive care unit on outcomes of extremely low birth weight infants at 30 months of age. *Pediatrics.* 2007;120:e953–9.
11. Koo W, Tank S, Martin S, Shi R. Human milk and neurodevelopment in children with very low birth weight: a systematic review. *Nutr J.* 2014;13:94.
12. Kuschel CA, Harding JE. Multicomponent fortified human milk for promoting growth in preterm infants. *CDS Rev.* 2004;1:CD000343.
13. Young L, Embleton ND, McCormick FM, McGuire W. Multinutrient fortification of human breast milk for preterm infants following hospital discharge. *CDS Rev.* 2013;2:CD004866.
14. da Cunha RD, Lamy Filho F, Rafael EV, Lamy ZC, de Queiroz AL. Breast milk supplementation and preterm infant development after hospital discharge: a randomized clinical trial. *J Pediatr (Rio J).* 2016;92:136–42.