Fortification of Breast Milk With Preterm Formula Powder vs Human Milk Fortifier in Preterm Neonates: A Randomized Noninferiority Trial (1)

JAMA Pediatr. 2021 Aug 1;175(8):790-796

Background : Fortification of expressed breast milk (EBM) using commercially available human milk fortifiers (HMF) increases short-term weight and length in preterm very low-birth-weight (VLBW) neonates. However, the high cost and increased risk of feed intolerance limit their widespread use. Preterm formula powder fortification (PTF) might be a better alternative in resource-limited settings.

Objective*:* To demonstrate that fortification of EBM by preterm formula powder is noninferior to fortification by HMF, in terms of short-term weight gain, in VLBW neonates.

Methods:

Design, setting, and participants: Open-label, noninferiority, randomized trial conducted from December 2017 to June 2019 at a level 3 neonatal unit in India. The trial enrolled preterm (born at or before 34 weeks of gestation) VLBW neonates receiving at least 100 mL/kg/d of feeds and consuming 75% of milk or more as EBM.

Interventions: Neonates were randomly assigned to receive fortification by either PTF or HMF. Calcium, phosphorus, iron, vitamin D, and multivitamins were supplemented in PTF and only vitamin D in the HMF group to meet the recommended dietary allowances.

Main outcomes and measures: The primary outcome was the weight gain until discharge from the hospital or 40 weeks' postmenstrual age, whichever was earlier; the prespecified noninferiority margin was 2 g/kg/d. Secondary outcomes included morbidities such as necrotizing enterocolitis, feed intolerance, and extrauterine growth restriction (<10th percentile on the Fenton chart at 40 weeks' postmenstrual age).

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

Can Preterm Formula be used as HMF in Human milk to mitigate the cost and availability issues ?

Results: Of the 123 neonates enrolled, 60 and 63 were randomized to the PTF and HMF groups, respectively. The mean gestation (30.5 vs 29.9 weeks) and birth weight (1161 vs 1119 g) were comparable between the groups. There was no difference in the mean (SD) weight gain between the PTF and HMF groups (15.7 [3.9] vs 16.3 [4.0] g/kg/d; mean difference, -0.5 g/kg/d; 95% CI, -1.9 to 0.7). The lower bound of 95% CI did not cross the noninferiority margin. The incidence of feed intolerance was lower in the PTF group (1.4 vs 6.8 per 1000 patient-days; incidence rate ratio 0.19; 95% CI, 0.04 to 0.95), and fewer neonates required withholding of fortification for 24 hours or more (5% vs 22%; risk ratio, 0.22; 95% CI, 0.07 to 0.75). The incidence of necrotizing enterocolitis stage II or more (0 vs 5%) and extrauterine growth restriction (73% vs 81%) was comparable between the groups.

Conclusion: Fortification with preterm formula powder is not inferior to fortification with human milk fortifiers in preterm neonates. Given the possible reduction in feed intolerance and lower costs, preterm formula might be a better option for fortification, especially in resource-restricted settings.

Key Message: Preterm Formula as a fortifier, can be considered as a safe and cost-effective alternative to standard Human Milk Fortifier (HMF) for fortification of human milk in preterm VLBW Neonates.

Critical Appraisal: A well conducted Randomized Non-inferiority trial with good sample size which has practical implications for Indian scenario where cost of HMF as well as uniform availability are major issues. The jury is still out though as it's an open label trial. A Randomized blinded trial will likely put an end to this issue for ever!

EXPERT COMMENT

"Preterm Formula as HMF can be a useful and cost effective alternative to standard HMF, especially in Indian NICU Setups."

Dr Rohit Arora
M.D (Pediatrics), Clinical-Research Fellow Neonatology (Canada)
Clinical Director & Head - Neonatology
Apollo Cradle Hospital, Sector 14 & 82, Gurgaon

With warm regards,

DR MANINDER S DHALIWAL
Editor – Academic Pearls
pedpearls@gmail.com

DR. PIYUSH GUPTA
IAP NATIONAL PRESIDENT 2021

DR REMESH KUMAR R.
IAP PRESIDENT 2022

DR BAKUL JAYANT PAREKH
IAP PRESIDENT 2020

DR G.V. BASAVARAJA
HON. SECRETARY GEN. 2021 - 22

Reference

1) Arunambika Chinnappan, Akash Sharma, Ramesh Agarwal et al. Fortification of Breast Milk With Preterm Formula Powder vs Human Milk Fortifier in Preterm Neonates: A Randomized Noninferiority Trial**.** *JAMA Pediatr. 2021 Aug 1;175(8):790-796*
2) Vijay Gupta, Grace Rebekah et al: A randomized controlled trial comparing the effect of fortification of human milk with an infant formula powder versus unfortified human milk on the growth of preterm VLBW infants. *J Matern Fetal Neonatal Med; 2020 Aug;33(15):2507-2515*