A Randomized Controlled Trial of Human versus Bovine-Based Human Milk Fortifiers in Extremely Preterm Infants

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ABSTRACT

Background: Own mother's milk (OMM) provides multiple health benefits, but must be fortified to meet specific nutrient needs of extremely preterm (EP, birth weight 500-1250 g) infants. An entirely human milk (HM)-based fortifier was recently developed.

Objective: To evaluate an entirely HM-based fortifier in EP infants regarding duration of parenteral nutrition (PN), and *a priori* secondary outcomes of length of stay, growth, chronic lung disease (CLD), sepsis, necrotizing enterocolitis (NEC, defined as ≥stage 2), and death.

Design/Methods: We conducted a multi-center randomized controlled trial of 207 EP infants whose mothers intended to provide breast milk comparing an entirely HM-based fortifier (HUM) or a standard bovine-based fortifier (BOV) in 3 arms. The HUM was added to OMM at feeding volumes of 40 (HUM40) or 100 ml/kg/d (HUM100). The bovine fortifier was added to OMM at 100ml/kg/d. If adequate OMM was not available, HUM40 and HUM100 received a nutritionally standardized pasteurized donor HM fortified with HUM while the control group (BOV) received preterm formula.

Results: The groups had similar lengths of stay and rates of growth, CLD, and sepsis. Other results are shown as follows:

	BOV	HUM40	HUM100	p value†
N	69	71	67	
Gestation (wks)*	27.3 ±2.0	27.2 ±2.3	27.2 ±2.2	NS
Birth weight (gm)*	922 ±197	921 ±188	945 ±202	NS
OMM consumed, ml (% of enteral intake)‡	5676 (82%)	4539 (70%)	4048 (73%)	NS
Days of PN‡	22	20	20	NS
NEC, n (%)	11 (15.9)	5 (7.0)	3 (4.5)	**0.05**
Surgical NEC, n (%)	8 (11.6)	1 (1.4)	1 (1.5)	**0.007**
Death, n (%)	5 (7.2)	2 (2.8)	1 (1.5)	NS
Death or NEC, n (%)	14 (20.3)	6 (8.5)	5 (7.5)	**0.04**

*mean ±SD; ‡median; †Chi-Square, Kruskal-Wallis, log-rank test

Conclusions: Predominant use of OMM may have attenuated any effect on days of parenteral nutrition. Fortification of HM feedings at 40 ml/kg/d with an entirely HM-based fortifier is feasible. Significantly lower rates of NEC, surgical NEC, and combined death or NEC were observed in both entirely HM-based groups. For infants under 1250 g, these data strongly support an entirely human milk-based diet, including HM fortifier, through 60 days of age.