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Milk Fat Globule Membrane: Cognitive Development and Reduced Infections

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Expanded Commentary from the Faculty

The milk fat globule membrane (MFGM) is contained in the lipid fraction of breast milk, and consists of triglycerides and membrane-associated proteins. Both the lipid and protein components of the MFGM appear to have antimicrobial functions, and some MFGM-associated proteins are not found in the whey and casein fractions. In addition, the MFGM contains factors that are likely important in brain development. In addition, the lipid fraction that contains the MFGM is not included in standard infant formulas. The availability of commercially available, bovine-based MFGM that appears to be similar to human MFGM, has made it possible to test whether supplemental MFGM can improve outcomes for formula-fed infants. The clinical trial data that is currently available, although provocative, is limited both in the number of trials and the populations that have been examined.

Zavaleta et al conducted a randomized, double-blind trial of infants 6-11 months old who received either MFGM-supplemented foods or a food containing only skim milk proteins for 6 months.[1] The infants who received MFGM had a lower incidence of diarrhea than infants in the control group (3.84% vs 4.37%, $P<0.05$), and had fewer episodes of bloody diarrhea (odds ratio 0.54, $P=0.025$). This study supports the hypothesis that MFGM has anti-infective properties distinct from those of other components of milk.

Another double-blind study considered neurodevelopmental outcomes in term infants <2 months old, who were randomized to an MFGM-supplemented, low-energy/low-protein diet, or standard formula, until 6 months of age.[2] Breast-fed infants were used as a reference. At 12 months of age, the infants' cognitive, motor, and verbal performance was measured using the Bayley Scales of Infant and Toddler Development. Infants in the MFGM-supplemented and breast-fed groups had similar cognitive test scores, and their scores were significantly better than those infants who received the standard formula. The authors noted that the difference in cognitive scores between the MFGM-protein supplemented group and the standard formula group was larger than those seen in trials of other formula supplements. In a separate analysis, infants in the MFGM-fed group had total serum cholesterol levels that were similar to those seen in the reference group, and fewer infections requiring antibiotics or hospitalization than infants in the standard formula group.[3,4]

Other studies are available, but most are in non-neonatal populations. For example, preschool children ages 2.5 to 6 years of age were recruited into the INPULSE trial, which evaluated both infectious symptoms and behavioral outcomes during a 4-month treatment period with or without MFGM-supplemented formula.[5] This study found that MFGM supplementation was associated with fewer febrile episodes and appeared to improve measures of behavior. No adverse events were reported in the aforementioned studies, and additional studies have evaluated safety in adult populations.[6]

Considerations for MFGM supplementation:

- The MFGM fraction is not well defined, but is removed during the preparation of existing standard infant formulas
- MFGM supplements are not comparable and have differed between studies

- MFGM supplementation may have beneficial effects, including a decrease in infective events and a positive effect on behavioral outcomes
- More studies are needed to better define the effect and safety of MFGM supplementation

Discussion Guide

- Would MFGM supplementation possibly be beneficial?
- Are there specific cohorts of infants who might benefit more from MFGM supplemented formula than others? For example, preterm vs full-term infants.
- Should this information prompt a change in our current practice?
- What are the barriers to adopting this clinical pearl in our institution?
- Are there other concerns or issues we haven't talked about?

Suggested Readings and Resources

1. Zavaleta N, Kvistgaard AS, Graverholt G, et al. Efficacy of an MFGM-enriched complementary food in diarrhea, anemia, and micronutrient status in infants. *J Ped Gastroenterol Nutr.* 2011;53:561-568.

2. Timby N, Domellöf E, Hernell O, et al. Neurodevelopment, nutrition, and growth until 12 mo of age in infants fed a low-energy, low-protein formula supplemented with bovine milk fat globule membranes: a randomized controlled trial. *Am J Clin Nutr.* 2014;99:860-868.

3. Timby N, Lönnerdal B, Hernell O, Domellöf M. Cardiovascular risk markers until 12 mo of age in infants fed a formula supplemented with bovine milk fat globule membranes. *Pediatr Res.* 2014;76:394-400.

4. Timby N, Hernell O, Vaarala O, et al. Infections in infants fed formula supplemented with bovine milk fat globule membranes. *J Pediatr Gastroenterol Nutr.* 2015;60:384-389.

5. Veereman-Wauters G, Staelens S, Rombaut R, et al. Milk fat globule membrane (INPULSE) enriched formula milk decreases febrile episodes and may improve behavioral regulation in young children. *Nutrition.* 2012;28:749-752.

6. Hari S, Ochiai R, Shioya Y, Katsuragi Y. Safety evaluation of the consumption of high dose milk fat globule membrane in healthy adults: a double-blind, randomized controlled trial with parallel group design. *Biosci Biotechnol Biochem.* 2015;79:1172-1177.