Impact of two human milk oligosaccharides and lactose on the faecal microbiome of infants with probable cow's milk allergy

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Background:

Early life nutrition is vital for establishing a healthy foundation for infants. Breast milk contains several important components, such as human milk oligosaccharides (HMO) and lactose, which are essential for immune and microbiome development. These immunomodulatory components are particularly beneficial for infants with cow's milk protein allergy (CMPA). These infants are likely to experience intestinal microbial dysbiosis, characterized by low Bifidobacteria levels (and higher Proteobacteria), thought to delay immune maturation and increase the risk of infections. In previous clinical studies, it has been seen that two HMO (2'-FL and LNnT) can enrich all 4 infant-type Bifidobacterial strains and their associated immunomodulating metabolites (e.g., short-chain fatty acids (SCFA) and aromatic lactic acids). Lactose has also been shown to enrich fecal Bifidobacteria and increase the production of SCFA in the colon.

Objectives:

This *ex-vivo* study aimed to investigate the microbiome-modifying effects of 2'-FL and LNnT, in combination with lactose or without lactose, on the dysbiotic gut microbiome of infants with CMPA. Fecal samples from infants with probable CMPA were used in the Systemic Intestinal Fermentation Research (SIFR®) technology.

Study design:

- 12 infant donors were selected aged between 1-7 months (mean age 4.3 months) with a clinical diagnosis of "probable CMPA", with no antibiotic use within 30 days prior to study participation, no consumption of prebiotics and probiotics (except two commonly used and allowed probiotics that are not known to consume 2'-FL or LNnT) within 14 days prior to study participation.
- Four study arms were tested: (1) Control: no added test substrate, (2) 2'-FL & LNnT 1.5 g/l (HMO), (3) Lactose 2.8 g/l (L), and (4) HMO + Lactose.
- Fecal samples were collected from the 12 infants and incubated with the HMO ± lactose mixes, for a 48-hour period using the SIFR® technology.
- Microbiome composition was analyzed using 16S rRNA sequencing.
- SCFA and other metabolic products were measured with gas chromatography and liquid chromatography-mass spectrometry.

Results:

- At baseline, 83.3% (10/12) of infants (all exclusively formula-fed) had low Bifidobacteriaceae in their microbiota.
- HMO ± lactose influenced microbial composition and metabolite production in all fecal samples. An additive effect was observed for HMO + lactose.
- The 2 HMOs enriched HMO-utilizing bifidobacteria species (*B. breve*, *B. longum*, *B. pseudocatenulatum*).
- The 2 HMOs + lactose further increased *B. bifidum.*
- The 2 HMOs ± lactose increased in a diverse range of metabolites (SCFA, aromatic lactic acids and N-acetylated amino acids) associated with immunity, the gut-brain axis, antimicrobial effects, and gut motility.

Conclusions:

- The study found that the combination of HMO (2'-FL/LNnT) and lactose has the greatest bifidogenic effect, which may help correct gut microbial dysbiosis associated with CMPA.
- HMO and lactose individually stimulated the production of health-related metabolites, with the greatest effect observed when both HMO and lactose were used together.
- The findings support the benefits of HMO supplementation in lactose-containing hypoallergenic formula (Althéra HMO) for infants with CMPA, improving gut microbial dysbiosis.
- The effects on gut microbiome composition and metabolomic profile are believed to benefit intestinal mucosal integrity and early immune development.
- Further clinical studies are needed to confirm these health benefits in the host.

Study Summary prepared by Nestlé Health Science