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A new potential target group benefiting from human milk oligosaccharides?

Wyeth® Nutrition SCIENCE CENTER

Danica Yau Accredited Practising Dietitian (DA), Accredited Dietitian (HKAAD), Full Member (HKDA), MSc, BSc (Hons)

Key messages

- For the first time, safety and efficacy of human milk oligosaccharide (HMO) supplementation have been shown in overweight children aged 6-12 years
- Supplementation of 2'-FL (2'-fucosyllactose) alone and in combination with LNnT (lacto-N-neotetraose) has a beneficial microbiota modulating effect in overweight and obese children

It is evident that commercially produced human milk oligosaccharides (HMOs) are increasingly common on the market, where the safety and gut microbiota modulating effects of these novel ingredients have been tested in infants and adults[1]. For the first time, a double-blind, randomized, placebo-controlled trial in Denmark has **investigated the safety and efficacy of HMO supplementation (2'-fucosyllactose, 2'-FL; lacto-N-neotetraose, LNnT) in overweight children aged 6-12 years**[1].

In the study by Fonvig *et al.* (2021), a total of 75 overweight or obese children aged 6-12 years were randomized to three study groups[1]:

- **Placebo group (*n* = 25):** 4.5 g placebo sachet (which is glucose), once per day for eight weeks
- **2'-FL group (*n* = 25):** 4.5 g 2'-FL sachet, once per day for eight weeks
- **Mix group (*n* = 25):** 4.5 g 2'-FL + LNnT (4:1 ratio) mix sachet, once per day for eight weeks

Key findings[1]:

Gut microbiota diversity

- **The Mix group had an increase in gut microbiota diversity (measured by Shannon index)** from baseline to week 8 ($p = 0.004$)
- No significant changes were observed in the placebo or 2'-FL group

Gut bacterial profile

- **Both the 2'-FL and Mix groups had a significant increase in *Bifidobacterium* abundance** from baseline to week 4 ($p < 0.001$, $p = 0.033$), while the 2'-FL group had a continued increase until week 8 ($p = 0.025$)

Safety

- No serious adverse events were reported
- Differences in reported gastrointestinal symptoms (e.g. abdominal pain, diarrhea) between groups were deemed minor, therefore overall safe and well-tolerated

These study findings showed supplementation of 2'-FL alone and in combination with LNnT has a beneficial microbiota modulating effect in overweight and obese children[1]. Clinical implications of this may be of further research interest based on the potential role that gut microbiota plays in the development of obesity, and also evidence of how the abundance of *Bifidobacterium* species was associated with healthy weight in children[2].

REFERENCES:

1. Fonvig CE. J Pediatr Gastroenterol Nutr. 2021;doi:10.1097/MPG.0000000000003205. 2. Da Silva CC et al. Child Obes. 2020;16(3):204-210.

INFOGRAPHIC

Role of HMOs on Infant Immune Health and Association with Cognition

Access full version here

Prenatal diet – The earliest starting point to prime the neonatal microbiota?

Emily Tai PhD, Mphil, MSc, BSc (Hons)

Key messages

- Prenatal dietary intake including saturated fatty acids, monounsaturated fatty acids, animal and plant proteins was related to diversity and richness of neonatal microbiota
- Prenatal supplementation, but not dietary patterns, was associated with human milk microbiota composition that plays a key role in early-life microbiota

Early-life microbiota has been recognized as a major contributor to long-term health and development[1]. Maternal factors are critical for modelling the neonatal microbiota profile[2,3].

In a nested cross-sectional study including 73 mother-infant dyads, maternal diet during pregnancy was related to both maternal and neonatal microbiota at delivery[2]. **Maternal dietary intake during pregnancy was correlated with diversity and richness of neonatal microbiota in terms of alpha diversity**[2]. Neonatal microbiota richness (measured by Chao index) was positively associated with maternal intake of saturated fatty acids and animal-originated proteins while a negative association with maternal vegetable protein intake was observed[2]. Additionally, maternal intake of fat-related nutrients including saturated fatty acids and monounsaturated fatty acids but not polyunsaturated fatty acids enriched Firmicutes phylum genera and depleted Proteobacteria phylum genera in the neonatal microbiota[2].

Prenatal dietary intake continues to shape neonatal microbiota via its influences on human milk microbiota. Analysis of 771 mothers from the CHILD cohort study demonstrated **maternal supplementation during pregnancy, but not dietary patterns, was correlated with human milk microbiota**[3]. Mothers taking **vitamin D supplements** showed lower abundance of unclassified *Comamonadaceae* whereas mothers taking **calcium-containing antacids** had higher abundance of *Streptococcus*, unclassified *Gemellaceae* and *Rothia* but lower abundance of unclassified *Comamonadaceae* and unclassified *Enterobacteriaceae* when compared with mothers not taking the respective supplements[3]. Taking **fish oil or folate supplement** during pregnancy was associated with a decline in human milk microbial diversity[3]. In addition, taking **vitamin C supplement** during pregnancy increased microbial diversity and relative abundance of *Veillonella* but decreased abundance of *Finegolia* and *Stenotrophomonas* in human milk[3].

Emerging science reinforces the importance of maternal diet and it would be beneficial to follow advices from the International Federation of Gynecology and Obstetrics (FIGO):

"FIGO recommends promotion of a varied and healthy diet as the first step to meeting the nutrient needs of adolescent girls and women, with the provision of supplements or fortified foods when necessary.[4]"

What's NEW— Maternal prenatal gut microbiome helps to predict child development

In a sub-cohort with 215 mother-infant dyads[5],

- Higher maternal alpha diversity during the 3rd trimester was associated with better child behavioral outcomes at 2 years,
  - Primarily because of lower internalizing symptoms that were closely related to subsequent anxiety disorders
- **Healthy maternal dietary pattern may decrease internalizing behavior in children** through higher alpha diversity of maternal fecal microbiome
- Taxa from *Lachnospiraceae* and *Ruminococcaceae* were more abundant in mothers of children with normative behavior
- **Western dietary pattern with high intakes of discretionary food and poor quality was linked to higher internalizing scores**

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1. Stiemsma LT and Michels KB. Pediatrics. 2018;141(4)e20172437. 2. Selma-Royo M et al. Eur J Nutr. 2021;60(3):1429-1442. 3. Chehab RF, et al. Maternal prenatal supplement intake, but not dietary patterns, is associated with human milk microbiota composition in the CHILD cohort study. Presented at: American Society of Nutrition Scientific Sessions and Annual Meeting; June 7-10, 2021 (virtual meeting). 4. Hanson MA et al. Int J Gynaecol Obstet. 2015;131 Suppl 4:S213-S253. 5. Dawson SL et al. EBioMedicine. 2021;68:103400.

INFOGRAPHIC

Maternal Dietary Intake and Human Milk Composition

- **How does maternal diet affect nutrient levels in human milk?**
- **Can maternal diet affect HMO levels in human milk?**

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Summary of the AAP report on probiotics in preterm infants

Emily Tai PhD, Mphil, MSc, BSc (Hons)

Key messages

- The American Academy of Pediatrics (AAP) published a clinical report to provide guidance on use of probiotics in preterm infants
- AAP does not support routinely giving probiotics to preterm infants, especially infants with birth weight < 1,000 g

The intestinal microbiome has been linked to health and disease in preterm infants[1]. Various randomized clinical trials have been performed to evaluate the influences of probiotics on severe necrotizing enterocolitis (NEC), late-onset sepsis and all-cause mortality[2].

In the newly published clinical report, the American Academy of Pediatrics (AAP) discussed differences among commercially available probiotics and regulatory standards in USA, potential risks of the use of probiotics in preterm infants and current evidence in prevention and treatment of NEC, late-onset sepsis as well as mortality[1].

Authors summarized:

- Current evidence **does not support routine universal use of probiotics in preterm infants**, especially whose birth weight < 1,000 g, because:
  - ♦ Most recent clinical trials have not showed a reduction in NEC in infants at the highest risk of NEC
  - ♦ A pharmaceutical-grade probiotic product is not currently available in USA
  - ♦ Long-term safety is still obscure
- Centers that decide to administer probiotics to patients should:
  - ♦ **Discuss the potential risks and benefits of the therapy with parents**
  - ♦ Strongly consider a formalized informed consent process
  - ♦ Develop local guidelines addressing the use of probiotics
  - ♦ Conduct surveillance to assess local influences since administration of probiotics may alter centers' microflora and may affect all infants in the centers
  - ♦ Carefully document outcomes, adverse events and safety
- Clinicians must be aware of **the lack of regulatory standards for available probiotics** in the market

Read the full report online:

https://pediatrics.aappublications.org/content/pediatrics/147/6/e2021051485.full.pdf

REFERENCES:

1. Poindexter B and Committee on fetus and newborn. Pediatrics. 2021;147(6)e2021051485. 2. Dermyshi E et al. Neonatology. 2017;112(1):9-23.

Nutrition News Column

A meta-analysis of risk factors for lactational mastitis

This meta-analysis examined pooled data from 8 cohorts and 10 case-control studies to identify maternal risk factors for mastitis. **Washing nipples before breastfeeding lowered the risk of mastitis** whereas significant risk factors were:

- ☑ Mastitis during previous breastfeeding
- ☑ Cesarean section
- ☑ Breast trauma
- ☑ Anemia
- ☑ Latch problem ≤ 8 weeks postpartum
- ☑ Milk overproduction
- ☑ Blocked duct
- ☑ Cracked nipple, especially ≤ 4 weeks postpartum
- ☑ Use of nipple shields, nipple cream, brassieres or breast pumps
- ☑ Breastfeeding duration > 30 minutes

Read more from:

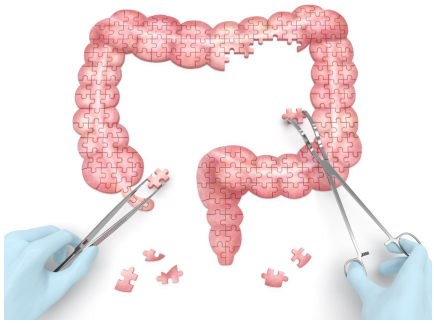
Deng Y et al. Maternal risk factors for lactation mastitis: A meta-analysis. West J Nurs Res. 2021;43(7):698-708.

Local data: Fecal bacteria markers and autism spectrum disorder (ASD) in children

This cohort demonstrated for the first time that **gut microbiome profile of children with ASD was abnormally developed and lagged that of age-matched typically developing peers**, characterized by higher bacterial richness and altered microbiome composition. Five bacteria species were identified as potential biomarkers for differentiating children with ASD from typically developing peers.

Read more from:

Wan Y et al. Underdevelopment of the gut microbiota and bacteria species as non-invasive markers of prediction in children with autism spectrum disorder. Gut. 2021 Jul 26:gutjnl-2020-324015.



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AUTHORS

Danica Yau,
Associate Manager - Medical Affairs

Emily Tai (Editor),
Senior Manager - Medical Affairs & Compliance

PRODUCED BY

Medical, Regulatory & Quality Affairs Department
Wyeth (Hong Kong) Holding Company Limited
42/F, Manhattan Place, 23 Wang Tai Road, Kowloon Bay, Kowloon, Hong Kong
Tel: 852 2599 8230 / Fax: 852 2599 8999
Email: hk.wnsc@wyethnutrition.com