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Morinaga Milk Unveils New Research of *Bifidobacterium longum* subsp. *infantis* M-63 Improving the Intestinal Environment in Healthy Term Infants

TOKYO (Apr. 2023): Morinaga Milk Industry Co., Ltd. (hereafter Morinaga Milk) announced new research entitled “Early Probiotic Supplementation of Healthy Term Infants with *Bifidobacterium longum* subsp. *infantis* M-63 Is Safe and Leads to the Development of *Bifidobacterium*-Predominant Gut Microbiota: A Double-Blind, Placebo-Controlled Trial” in collaboration with Matsumoto City Hospital (Nagano, Japan)¹. This research, published in the peer-reviewed journal *Nutrients* in March 2023, is the first randomized controlled trial (RCT) that demonstrated the beneficial effects of *Bifidobacterium longum* subsp. *infantis* M-63 (hereafter *B. infantis* M-63) as a single probiotic for improving the intestinal environment in healthy-term infants.

Bifidobacteria are predominant bacteria residing in the intestine of infants and are important intestinal bacteria that provide a wide range of health benefits for infants. Since its discovery in 1899, more than 14,000 articles have been published worldwide, extensively evaluating the effects of bifidobacteria in infants and adults. Among the species of bifidobacteria, Morinaga Milk focuses on the research of human-residential bifidobacteria (HRB) based on the idea that these bifidobacteria are suitable for humans in maintaining their health. In its long research journey on bifidobacteria, Morinaga Milk has also elucidated the relationship between bifidobacteria and gut microbiota across all age groups, exploring the potential of HRB species in supporting the health of people of all ages. In this regard, Morinaga Milk is number one in the world* for the number of scientific papers published about the bifidobacteria living in the human intestine.

* According to Metagen, Inc., as of 2019.

Background

B. infantis M-63 is one of the strains of bifidobacteria that harbors infants’ intestines and is expected to promote the intestinal environment in infants and infant health. Previously, a clinical study has shown that administration of three strains of bifidobacteria including *B. infantis* M-63 resulted in earlier formation of *Bifidobacterium*-predominant microbiota in low birth weight infants². However, there are no studies examining the effects of *B. infantis* M-63 as a single probiotic strain in healthy-term infants. Therefore, in this study, in collaboration with Matsumoto City Hospital, we evaluated the safety and efficacy of *B. infantis* M-63 on the gut microbiota and fecal biomarker substances.

Study outline

Subjects: Healthy full-term infants in Japan (n=111)

Study design: A randomized, double-blind, placebo-controlled trial

Primary outcome: Bifidobacteria colonization in infants’ intestines

Secondary outcome: Gut microbiota analysis, fecal physicochemical analysis, defecation frequency and stool consistency, and health status.

Method: Subjects were divided into two groups and given *B. infantis* M-63 (n=56, 1 billion CFU/day) or placebo (n=54) from postnatal age ≤ 7 days to 3 months of age. The test foods were suspended in a small amount of sterile water in a sterilized feeding bottle at room temperature, and mothers fed the suspension to their infants using a feeding bottle. Fecal samples were collected, and fecal microbiota, stool pH, short-chain fatty acids, and immune substances were analyzed. The baby’s health status was recorded daily by the mother in a diary.

Study results

- In the *B. infantis* M-63 group, there was a statistically significant increase in the relative abundance of bifidobacteria in the intestine from the first week of the intake, compared to the placebo group (Fig 1).
- In the *B. infantis* M-63 group, the number of defecations per day decreased from the first week of the intake, and a decrease in “watery” stools was observed in particular.
- In the *B. infantis* M-63 group, infants with higher rates of breastfeeding tended to show higher relative abundance of bifidobacteria in the intestine at 1 month of age.
- In the *B. infantis* M-63 group, stool component analysis at 1 month of age revealed that acetic acid, a type of short-chain fatty acid, and secretory immunoglobulin A (IgA), which plays a pivotal role in the immune function of the digestive tract significantly increased compared to the placebo group (Fig. 2).
- There were no adverse events caused by the supplementation of *B. infantis* M-63, demonstrating its safety in neonates.

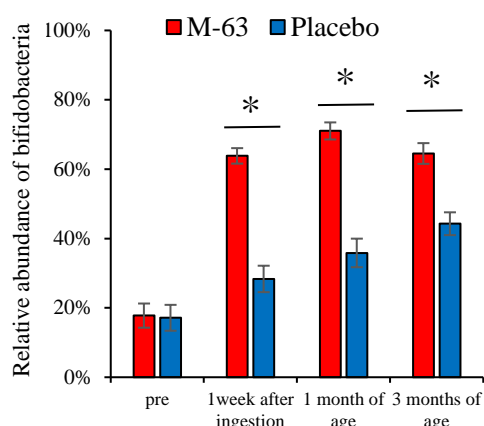


Fig.1 Bifidobacteria occupancy

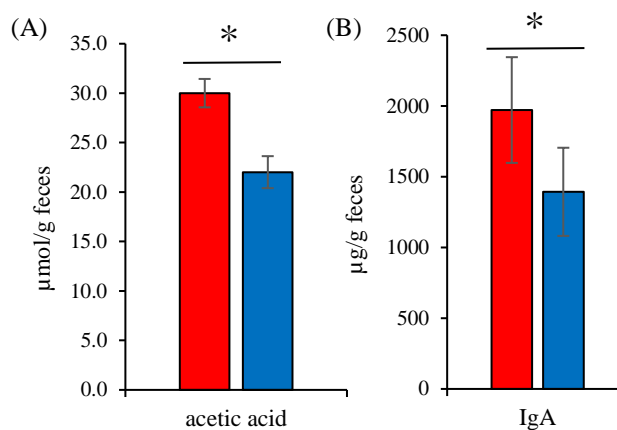


Fig.2 Fecal components at 1 month of age
(A) Acetic acid, (B) IgA

(*P < 0.05; significant difference compared to the placebo group)

Conclusion

This study demonstrated that supplementation with *B. infantis* M-63 in healthy-term infants was safe and positively changed the infant gut microbiota toward higher *Bifidobacterium* levels, and decreased the frequency of watery stools. *B. infantis* M-63 enhanced the secretion of intestinal acetic acid and secretory IgA, conferring beneficial effects on digestive function.

Future prospects

B. infantis M-63 has already acquired GRAS (Generally Recognized as Safe) in the United States in 2022 for general food and infant use, and its safety has been recognized overseas. In the future, we will focus on the global expansion of our probiotic BtoB business for which *B. infantis* M-63 is one of the HRB strains in the pipeline. We will also continue to research how bifidobacteria contributes to the health of both adults and infants.

Reference

- Hiraku, A. *et al.* Early Probiotic Supplementation of Healthy Term Infants with *Bifidobacterium longum* subsp. *infantis* M-63 Is Safe and Leads to the Development of Bifidobacterium-Predominant Gut Microbiota: A Double-Blind, Placebo-Controlled Trial. *Nutrients* **15**, (2023).
- Ishizeki, S., Sugita, M., Takata, M. & Yaeshima, T. Effect of administration of bifidobacteria on intestinal microbiota in low-birth-weight infants and transition of administered bifidobacteria: a comparison between one-species and three-species administration. *Anaerobe* **23**, 38–44 (2013).

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