Effects of early probiotic supplementation in a pediatric setting
Focus on body composition, metabolism and inflammation

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt förvar i Sal E04, målpunkt R-1 (by 6E), Biomedicin, Norrlands Universitetssjukhus, fredagen den 20 maj, kl. 13:00. Avhandlingen kommer att förvars på engelska.

We aimed to determine the short- and long-term effects on growth, body composition, metabolic and inflammatory markers following supplementation with the probiotic *Lactobacillus paracasei* ssp. *paracasei* F19 (LF19) during weaning. **Methods:** One-hundred and seventy-nine healthy, infants in Umeå city, Västerbotten County were randomised to daily intake of cereals with (n=89) or without (n=90) LF19 $10^8$ colony-forming units from 4 to 13 months of age. Weight, length, head circumference and body composition, assessed by skinfold thickness, were examined at 4, 5.5, 6.5, 9, 12 and 13 months of age. Venous blood was drawn at 5.5 and 13 months. In all, 171 infants completed the intervention and were invited to a follow-up at 8-9 years of age between 2009 and 2011, 120 children participated. Weight, height, sagittal abdominal diameter and body composition (using Dual Energy X-ray Absorptiometry-scan) were measured. Data on weight and height at 4 years were collected from medical records. The families filled out a 4-day food record and a food frequency questionnaire, physical activity was assessed using a pedometer for 7 days. At 5.5, 13 months and 8-9 years of age we analysed the serum blood lipid profile. At 8-9 years fasting glucose, insulin, aspartate and alanine transaminases were analysed in serum. Homeostatic Model Assessment index was calculated. At follow-up serum adiponectin, high-sensitivity C-reactive protein and plasma C-peptide, ghrelin, gastric inhibitory polypeptide, glucagon-like peptide 1, glucagon, insulin, leptin, plasminogen activator inhibitor-1, resistin and visfatin were analysed. For characterisation of the plasma metabolome, a subgroup (n=40) was analysed at 5.5 and 13 months of age by gas chromatography time-of-flight mass spectrometry (GC-TOF/MS) analysis and in all (n=112) children at the follow-up using untargeted GC-GC/MS. **Results:** There were no differences between the LF19 and placebo group regarding body weight, length/height at any assessment from 4 months to 8-9 years of age; nor were there any differences between the groups in body composition. In the LF19 group 19 % were overweight/obese, the corresponding number was 21 % in the placebo group (p=0.78). Analysed metabolic and inflammatory markers, both during the intervention and the follow-up did not differ between the two groups. At 13 months of age lower levels of palmitic acid and palmitoleic acid (both $p<0.04$) and higher levels of putrescine (p<0.01) were seen in the LF19 compared to the placebo group. These differences did not persist at 8-9 years of age. At that age, we found statistically stronger models when comparing overweight/obese and normal weight children as well as in relation to sex. **Conclusion:** Early intervention with the probiotic LF19 at the time of weaning exerted transient effects on the metabolome. In a long-term perspective, we found neither benefit nor harm on growth, body composition, metabolic or inflammatory markers following supplementation with LF19 during weaning.

**Keywords:** Probiotics, children, growth, body composition, metabolism, follow-up