Extremely low birth weight infants supplemented with probiotic *Lactobacillus reuteri* DSM 17938 had higher gut microbiota diversity during the neonatal period

Jie Xu¹, Maria Tärnberg¹, Erik Wejryd^{1,2}, Giovanna Marchini³, Baldvin Jonsson³, Eva Sverremark Ekström⁴, Magalí Martí¹, Maria Jenmalm¹ and Thomas Abrahamsson^{1,2}

¹Department of Clinical and Experimental Medicine and ²Department of Paediatrics, Linköping University, Linköping, Sweden, ³Astrid Lindgren Children's Hospital, Karolinska University Hospital, Karolinska Institute, Department of Neonatology, Stockholm, Sweden
⁴Department of Molecular Biosciences, The Wenner-Gren Institute, Stockholm University, Stockholm, Sweden

Background and aims

Dysbiosis, with a reduced microbial diversity, has been associated with multiple diseases, including necrotizing enterocolitis, in pre-mature infants. It is hypothesized that probiotics may counteract the dysbiosis and hence promote health. The aim of the current study was to investigate the effect of probiotic supplementation on the gut microbiota in extremely low birth weight (ELBW) infants.

Methods

In a randomized, double-blind, multicenter, placebo-controlled trial, ELBW infants with a birth weight < 1000g, born at gestational week <28, were supplemented with either probiotics (*L. reuteri* DSM 17938) or placebo (n=67 and 65, respectively) from birth until gestational week 36. A total of 551 stool samples were used for profiling the gut microbiota with next generation sequencing of the 16s rRNA gene at 1 (n=54/54), 2 (n=54/53), 3 (n=51/51) and 4 (n=52/48) weeks of age, at gestational week 36 (n=50/37) and at 2-years (n=20/27) of age.

	probiotics n=67	placebo n=65
<i>Demographic data</i>		
gestational age at birth, weeks, median (IQR)	25.7 (24.6-26.4)	25.7 (24.6-26.5)
birth weight, grams, median (IQR)	726 (630-814)	760 (615.5-864)
girls, n (%)	36 (54)	23 (35)
infants from multiple pregnancy, n (%)	28 (42)	19 (29)
<i>Perinatal factors, n (%)</i>		
premature rupture of membranes	24 (36)	16 (25)
chorioamnionitis	20 (30)	10 (15)
Caesarean section	49 (73)	37 (57)
maternal antibiotics	41 (61)	31 (48)
<i>Clinical outcomes, n (%)</i>		
onset of NEC during the study period	7 (10)	8 (12)
onset of sepsis during the study period	38 (57)	34 (52)
<i>Antibiotic treatment and mechanical ventilation</i>		
antibiotics 1st week of life, n (%)	67 (100)	65 (100)
antibiotics 2nd week of life, n (%)	57 (85)	50 (77)
antibiotics 3rd week of life, n (%)	48 (72)	44 (68)
antibiotics 4th week of life, n (%)	49 (73)	39 (60)
antibiotics until end of gw36, days, median (IQR)	26 (19-37)	26 (12.5-37.5)
mechanical ventilation, days, median (IQR)	14 (6-31)	15 (4-33)

Table 1. Background data.

Figure 1A. Average abundance of bacterial genera in the probiotics group.

Figure 1B. Average abundance of bacterial genera in the placebo group.

Figure 2. Linear discriminant analysis effect size, showing bacterial taxa that significantly differed in abundance between groups.

Figure 3 Alpha-diversity, in terms of Shannon's index of diversity.

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Conclusions

The main finding of this study is that supplementation of *L. reuteri* DSM 17938, in ELBW preterm infants, affects the microbiome during the neonatal period in terms of altered composition and increased alpha-diversity.