Editorial Material: Transfer of Probiotic Bacteria From Mother to Child: A Matter of Strain Specificity? in JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION, vol 61, issue 2, pp 157-158

Christina E. West and Maria Jenmalm

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Transfer of probiotic bacteria from mother to child: a matter of strain specificity?

Christina E West¹, Maria C Jenmalm²

1. Department of Clinical Sciences, Pediatrics, Umeå University, Umeå, Sweden

2. Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden

Primary prevention is key to avert the allergy epidemic and strategies to favorably modify early intestinal colonization have included administration of probiotic bacteria in pregnancy and/or infancy. In meta-analyses, a combined perinatal intervention, given either to the mother in pregnancy and during breastfeeding, or to the pregnant mother and then to the child postnatally, has shown the most consistent preventive effect on eczema, but not on any other allergic outcomes (1). Many expert bodies do not recommend probiotics for allergy prevention, but in their recently launched guidelines, the World Allergy Organization (WAO) now suggests using probiotics for allergy prevention in pregnant and breastfeeding mothers at high risk for having an allergic child and in infants at high risk of developing allergic disease (based on a history of allergic disease in parents or siblings). The WAO guideline panel underscored that the recommendation is conditional and based on low quality evidence, however, when they considered all critical outcomes they found that there is a plausible net benefit of probiotics for eczema prevention (1). No recommendations on which strains to use, timing or dosages were given, and they stressed that there is call for well designed and adequately powered randomized controlled trials in both high and low risk populations.

It also remains to be unravelled how probiotics mediate their clinical effects. In the animal kingdom, maternal to fetal transmission of microbes is an evolutionary conserved phenomenon and emerging evidence suggests that bacterial transfer begins already *in utero* also in humans (2-4). When the probiotic is given solely to the mother, it is thus theorized that the probiotic is transmitted from the mother to the fetus, or from the mother to her infant via breast milk. To date, studies examining if the probiotic consumed by the mother is present also in infant stool are scarce, and studies examining the effect of maternal probiotic ingestion on gut microbial composition and diversity in their infants are even scarcer (5).

Dotterud and colleagues have previously reported that maternal probiotic ingestion during pregnancy and breastfeeding reduced the cumulative incidence of childhood eczema in the first two years of life (6). In the ProPact study, they randomly assigned pregnant mothers to daily intake of low fat fermented milk with the addition of 5×10^{10} *Lactobacillus rhamnosus* GG (LGG) and *Bifidobacterium animalis* subsp. *lactis* Bb-12 (Bb-12) plus *L. acidophilus* La-5 (La-5) or a sterile placebo milk, four weeks prior to delivery and for 3 months postpartum (6). In this issue (7), they report the results of a study investigating if maternal ingestion of this probiotic combination during pregnancy and breastfeeding impacts intestinal colonization in the mothers and their children. Additionally, they also examined if the intervention could impact gut microbial diversity in the children.

As assessed by q-PCR, the relative abundance of all administered probiotics was increased in maternal stool samples in the group receiving active treatment. However, only LGG was increased in their infants' stool at 10 days and at 3 months of age

compared with the placebo group. At later samplings, i.e. at 1 and 2 years of age, none of the administered probiotic strains was present in stool. It has been discussed if probiotic strains would be able to establish in the infant intestine if administration is initiated before the gut microbiota is established. The present study supports the notion that probiotics are transient colonizers also at this young age, however, in line with previous findings (8, 9). Probiotics is an umbrella term and the effects of probiotics are considered strain specific; this study further suggests that there are differences in the ability of probiotic strains to transfer from the mother to her child. Breast milk samples were not analyzed in this study, but others have shown that maternal ingestion of probiotic *L. reuteri* in pregnancy led to a slightly higher isolation frequency of *L. reuteri* in colostrum compared with a placebo group (8).

Reduced gut microbial diversity has now been associated with several inflammatory non-communicable diseases including allergic disease, although causality has not been proven (10). In the study by Dotterud and colleagues, the clinical benefit of the probiotic combination on eczema incidence does not appear to be linked to effects on gut microbial diversity at 3 months or at 2 years of age (7). The association between gut microbiota composition and diversity with eczema development in this study remains to be reported in detail, however. Gut microbial composition and diversity are affected by a number of environmental exposures (10), and profoundly so by caesarean delivery (11). As discussed by the authors, a possible confounder is that information on delivery mode was not available in this study setting, although assumed to be similar between the two study groups. An alternative explanation for the eczema preventive effect of this probiotic combination could be through influences on bioactive factors in breast milk

such as antibodies, cytokines and growth factors, with potential to modulate the infant's developing immune system (3).

There is much complexity in this area of research as the effect of a probiotic intervention is likely to be influenced by the complex interplay between genetics, epigenetics, immunity, environmental exposures and the global microbiota (10). Efforts to deepen our understanding of the mechanistic effects of probiotics and the interaction between the maternal and offspring microbiome and immunity are needed, requiring multidisciplinary approaches (4, 10).

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