Medical Xpress

Probiotics for premature babies provide microbiome boost

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Credit: University of East Anglia

Probiotics can improve the microbiome in premature babies, according to the results of a major new study from the Quadram Institute, the University of East Anglia and the Norfolk and Norwich University Hospital (NNUH).

New research published today shows how specific strains of probiotic Bifidobacterium and Lactobacillus bacteria given to preterm babies

along with breast milk helps shape their microbial populations and gut health to match those of babies born at full-term.

This helps them fight potential infections, derive the full benefits from digesting breast milk, and could help these vulnerable babies survive and get the healthiest start in life.

The gut microbiome is a complex community of trillions of bacteria and other microbes that resides in our digestive system. A healthy microbiome helps digest food and prevents disease-causing bacteria from colonizing, as well as providing other benefits to health that science is starting to understand.

We are colonized naturally by bacteria from our mothers at birth, but the one in nine babies that are born prematurely may not establish this healthy early microbiome.

Preterm babies are more likely to have been delivered by cesarean section, potentially missing out on picking up beneficial microbes from their mother, a problem confounded by lengthy spells in neonatal intensive care units.

Almost all preterms receive at least one course of antibiotics, with some having numerous courses. These may be vital to saving lives, but will also damage the susceptible "good" bacteria.

The altered microbial population in preterm babies has been linked to life-threatening infections and later problems including as asthma and eczema, so there is great interest in finding ways to help preterm babies establish a "normal" microbiome.

Probiotic supplementation with appropriate beneficial bacterial strains is one way of achieving this. A prior study by the Norwich team showed

that routine probiotic supplementation was associated with a halving in the rates of necrotising enterocolitis (NEC) and sepsis.

Some neonatal ICUs now routinely supplement preterm babies with probiotics, but currently the majority don't, in part because there hasn't been a large, long-term study into the benefits including how the microbiota may change.

To address this, Dr. Lindsay Hall's group from the Quadram Institute worked with Prof Paul Clarke from the NNUH and UEA to launch the Baby-Associated MicroBiota of the Intestine (BAMBI) Study. The study was funded by the Wellcome Trust and the Biotechnology and Biological Sciences Research Council, part of UKRI.

Prof Clarke, from UEA's Norwich Medical School and NNUH, said: "While the NNUH NICU has been giving probiotics routinely to protect very preterm babies since 2013, this study gives us a much better understanding of the mechanisms by which they benefit from us putting billions of live bacteria into their immature gut daily."

"We're thrilled to see the results published after many years' hard work. This study would not have been possible without the efforts of our neonatal unit's research and clinical nurses in collecting numerous study samples. We are especially indebted to all parents who allowed their babies to take part, and who continued to support the BAMBI study when their babies went home—we look forward to sharing the results with them."

Bifidobacterium and Lactobacillus are bacteria associated with a healthy term infant gut. The researchers carried out a prospective observational study, comparing 101 infants orally supplemented with specific strains of Bifidobacterium bifidum and Lactobacillus acidophilus in the NNUH Neonatal Intensive Care Unit (NICU) with 133 infants in other NICUs

that were not currently providing probiotic supplementation.

This multi-center approach involved working with colleagues at Imperial College London and the University of Cambridge to obtain samples from non-probiotic supplemented babies.

The babies were matched by age, sex, and delivery-method across the two groups. With the consent and cooperation of the parents, the researchers collected fecal samples from each of the babies over their first 100 days of life.

Publishing in the journal *Cell Reports Medicine*, the team showed clear differences in the microbiota profiles between the two groups.

The supplemented infants had microbiota dominated by Bifidobacterium, while the unsupplemented contained a range of bacteria including potentially disease-causing Staphylococcus, Escherichia, and Klebsiella. This varied profile is more typical of a preterm baby's gut, and the researchers suggest this shows that oral supplementation can effectively displace these bacteria.

What makes Bifidobacterium good at colonizing the infant gut is their ability to thrive on human breast milk. This contains sugars called human milk oligosaccharides (HMOs) that babies can't digest by themselves, but instead act as prebiotics, or nutrients for bacteria.

The researchers confirmed that the strain of Bifidobacterium used in this study contained genes enabling it to digest specific HMOs.

Analysis of the samples showed that there were lower levels of these HMOs excreted by the supplemented babies, but higher levels of their breakdown products, acetate and lactate. These compounds have beneficial effects by boosting the defense provided by cells lining the gut

and associated with the immune system.

They are also likely to be behind an observed drop in pH in the stool samples from the supplemented babies, which further boosts health by making the environment too acidic for some of the disease-causing bacteria to flourish.

Both groups of babies received breast milk, either from their mother or donors, but breast milk consumption itself was not sufficient to encourage high levels of Bifidobacterium, without probiotic supplementation.

To work successfully, supplementation needs to mimic the symbiotic relationship found in nature by using bacterial strains that can unlock the prebiotics in breast milk to establish a healthy population, and in doing so keep the baby healthy too.

Dr. Lindsay Hall from the Quadram Institute said: "This is one of the largest studies with preterm infants to date, and we were excited to find that matching the right probiotic Bifidobacterium—a strain that can digest breast milk—allowed it to persist in the gut and as a result significantly reduce potentially nasty bacteria that have been associated with serious infections. We hope that our findings will help direct future clinical trials and practice and help clinicians and healthcare professionals make a rational choice when it comes to diet-microbe combinations, and ultimately help these at-risk preterm babies."

"Microbiota supplementation with Bifidobacterium and Lactobacillus modifies the preterm infant gut microbiota and metabolome: an observational study' is published in the journal *Cell Reports Medicine* on August 25, 2020.

More information: Cristina Alcon-Giner et al. Microbiota

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Supplementation with Bifidobacterium and Lactobacillus Modifies the Preterm Infant Gut Microbiota and Metabolome: An Observational Study, *Cell Reports Medicine* (2020). DOI: 10.1016/j.xcrm.2020.100077

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