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Routine Supplement of Prebiotics and Probiotics to Newborn Infants Is Not Recommended

Touraj Shafai

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clinical grounds before hospital discharge. The first 2 infants had pulmonary stenosis not requiring immediate intervention and were followed up as outpatients. The infant with hypoplastic left heart syndrome was transferred to our NICU by 5 hours of life secondary to cyanosis that did not improve with supplemental oxygen. In addition to these 3 infants who were identified as true-positives, another 768 failed initial screening but passed screening at discharge and, therefore, were false-positives. On the basis of our data, the positive predictive value for a POS failure at 4 hours of age was only 0.4%. Although we agree that early detection of CCHD is a laudable goal, a screening test that identifies 1 true-positive of >250 failed screening tests runs the risk of being exceptionally costly. Routine hospital care identified the same number of infants at no additional cost.

It is possible that there is utility for POS in hospitals where early discharge is the norm, although for the 3 infants identified early in our study, outcomes would have been similar. It is also possible that our results are not generalizable, given our uniquely large delivery population and highly experienced health care providers. Our concerns are that POS has yet to be shown to be cost-effective, will lead to a burdensome number of excess echocardiograms that may not be readily available in many communities, and will fail to detect an as-yet-unknown number of infants. Before implementing large-scale screening, these issues must be addressed.

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To the Editor.—

Kuitunen and co-workers[1] reported that they have ascertained that prebiotics and probiotics may be safely administered to pregnant and nursing mothers and their newborn infants. However, it seems that the authors made several false assumptions, and then they proceeded to prove the long-term safety of prebiotic and probiotic supplements in newborn infants. These false assumptions include reduction in the incidence of infections, allergy, and autoimmune disorders. In addition, the study was basically flawed, because they did not separate the breastfed and formula-fed infants. Breast milk provides many benefits to infants, including reduction in the rate of allergies, infection, and autoimmune disorders, which the authors claimed to be the result of supplementation of prebiotics and probiotics. The authors reported that 70% of the infants in both groups were breastfed, and they pointed to a reduction in infection rates in infants who were receiving supplements versus those in the placebo group. The authors reported a slight decrease in the group receiving supplements (90%) versus those in the placebo group (97%). However, the authors did not report whether they were examining all respiratory infections (upper and lower) or the rate of hospitalization from lower respiratory infections. A meta-analysis of several reports on the rate of hospitalizations from lower respiratory infections demonstrated a significant reduction of 72% in exclusively breastfed infants as compared with formula-fed infants.[2]

Similarly, the reduction in the rate of otitis media in the supplemented group was not significant (15% vs 19% in the placebo group). Several meta-analyses that compared the rate of otitis media in exclusively breastfed versus formula-fed infants revealed significant reduction in otitis media of 50% in breastfed infants.[2]

Gastroenteritis occurred at approximately the same rate in both groups at 13% vs 14%. Recent studies have demonstrated significant reduction of 64% in exclusively breastfed infants from gastroenteritis from any cause. It seems that the infants in the study had a significantly higher rate of infection, even for the infants who were breastfed; therefore, one would naturally assume that supplementation with prebiotics and probiotics actually negated the immunity that breastfeeding provided to the infants.

The prebiotic bifidus factor in human breast milk is species specific, and other oligosaccharides may not have the same efficacy. Similarly, the probiotic in breastfed infants' intestinal tract is bifidobacter, and other probiotics may not provide the same function.

Rubaltelli et al[3] reported that the bifidobacter colony count in the stools of breastfed infants was higher than the stools of oligosaccharide-supplemented formula-fed infants.

Finally, the World Health Organization and United Nations Children's Fund (UNICEF) recommend exclusive breastfeeding for all newborns with no supplementation. The type of research that Kuitunen and co-workers have reported seems to pose serious moral and ethical concerns.

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In Reply.—

Dr Shafai considers our study on probiotics and prebiotics (synbiotic) in breastfed infants unethical. The world-wide allergy epidemic forms a great socioeconomic burden for societies and families, and exclusive breastfeeding (alone) has failed to solve the problem. The evidence of breastfeeding in the prevention of allergies is controversial and may depend of heredity.[1,2] We performed the randomized, placebo-controlled study on probiotics and prebiotics because these agents had been reported to be promising in the prevention of allergic diseases in high-risk infants. The study protocol was judged as sound and accepted by the ethics committee of the Helsinki University Central Hospital.

We considered studying the safety of probiotics and prebiotics essential, because their use during pregnancy and the neonatal period is increasing. In the referred trial, we primarily aimed to study the safety of synbiotics in neonates and infants. Previously, probiotics were reported to be safe in a pediatric population.[3]

We agree with Dr Shafai that prebiotic oligosaccharides in human breast milk are species specific, and other oligosaccharides may not have the same efficacy. Galactooligosaccharides are specific for human milk and have promoted the growth and activity of bifidobacteria.[4,5] Our daily dose of 0.8 g of galactooligosaccharides was relatively small and equal to the amount of galactooligosaccharides in 100 mL of breast milk. We encouraged mothers to breastfeed. The mean duration of exclusive breastfeeding was 2.5 months, and of any breastfeeding 8.4 months, with no significant difference between those in the synbiotic and placebo groups. We used probiotic strains of human and bovine origin. *Lactobacillus rhamnosus* GG (ATCC 53103) was isolated from adult human (feces) and has been used since 1990 in fresh dairy products, juices, and cheese; *L rhamnosus* LC705 (DSM 7061) was isolated from milk and has been used since 1995 in cheeses in Finland; *Propionibacterium freudenreichii* sp. *shermanii* PJS (DSM 7067) was isolated from cheese and has been used since 1979 in cheeses in Finland; and *Bifidobacterium breve* 99 (DSM 13692) was isolated from breastfed infants' feces. The isolated products were purified and contained <0.03 ppm of β-lactoglobulin.

Our conclusions of the effects of the synbiotic were drawn from a randomized, double-blind, placebo-controlled trial. Although breastfeeding was equally common in the synbiotic and placebo groups, we considered breastfeeding to be a possible confounding factor and adjusted the occurrence of infections and antibiotic use to breastfeeding. Therefore, we feel that the assumptions may be trustworthy in a population of healthy term atopy-prone infants.

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Treatment of Pyelonephritis and Risk of Renal Scarring

To the Editor.—

In a secondary analysis of data from 2 randomized trials, Hewitt et al[1] reached the conclusion that early treatment of acute pyelonephritis in infants and young children has no significant effect on the incidence of subsequent renal scarring. This conclusion was based, in part, on data from a clinical trial[2] that enrolled children who had a first episode of febrile urinary tract infection (UTI) and met entry criteria for a "clinical diagnosis of acute pyelonephritis." Importantly, one third of the subjects in this trial proved not to have evidence of acute pyelonephritis when a technetium-99m-dimercaptosuccinic acid (DMSA) scan was obtained soon after enrollment.

Hewitt et al restricted their subgroup analysis to subjects who had a positive acute scan results and, as it turns out, extraordinarily high levels of systemic inflammation; mean erythrocyte sedimentation rate and C-reactive protein values exceeded values reported for the entire trial cohort.[2] Although Hewitt et al found no correlation between the duration of fever before treatment and the risk of subsequent renal scarring, this observation must necessarily apply only to the select population they studied: febrile children with UTI in whom acute pyelonephritis is known (by DMSA scan) to have already developed. Instead, Hewitt et al attempted to apply the result of their subgroup analysis to various

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