Probiotic Supplementation in Very Low Birthweight Infants: Effects on Systemic Immunity and Intestinal Inflammation

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Objectives: To investigate serum immune/inflammatory profiles in preterm very low birthweight (BW) infants enrolled in a randomized trial of daily supplementation with a multi-strain probiotic. A central hypothesis is probiotics will promote T cell homeostasis via a T regulatory cell (Treg) response and suppress inflammatory Th1/Th17 cytokine profiles to promote intestinal microbiota diversity, reduce inflammation, and support barrier function.

Methods: After parental informed consent, preterm infants admitted to a neonatal ICU are randomized into 2 groups (+/- probiotics; 30/group by NNT) stratified by BW. The probiotic group receives daily Tri-Blend (Abbott; B. lactis [BB-12], B. infantis [BB-02], S. thermophilis [H-4]; 0.5 g, 10⁸ CFU/g) from early feeding to 34 weeks post-menstrual age. Data include: diagnoses, interventions, medications, feedings, growth trajectories, and length of stay; intestinal integrity protein biomarkers; fecal DNA analysis for intestinal microbiomics using amplicon-based 16S rRNA gene sequencing and shotgun metagenomics; and fecal metabolomics. This presentation focuses on results from bimonthly serum cytokine, chemokine, and growth factor profiles assayed using customized multiplex magnetic bead antibody panels (Luminex).

Results: Longitudinal serum immune/imunomodulatory profiles (up to 7 samples/subject) and clinical data are available for 17 subjects (as of 02/2022). We measured 18 inflammatory/imunomodulatory small proteins; all analytes varied within recognized ranges for human serum/plasma and, consequently, are interpretable for analysis of systemic pro-/anti-inflammatory polarization and for products released by circulating T cell and macrophage subsets. Data indicate chronic heightened inflammation in these preterm infants and evolving profiles of Th1, Th2, Th17, and Treg-dependent cytokines/chemokines.

Conclusions: This is the first study that comprehensively profiles circulating immune system/inflammatory biomarkers in young infants. We demonstrate novel findings on multiple, longitudinally sampled biomarkers and characterize chronic inflammation in this population. Small subject numbers to date preclude conclusions on immunomodulatory effects of probiotics.

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