Pain in the NEC: Choosing the Right “Biotic” for Preterm Neonates

Geoffrey A. Preidis, M.D., Ph.D.

Abstract

Controversy swirls around the neonatal intensive care unit when it comes to choosing the right probiotic, prebiotic, or synbiotic to prevent life-threatening morbidities (e.g., necrotizing enterocolitis) and death. The current body of evidence examining the use of microbiome-targeting therapies for preterm, low birth weight neonates is vast, yet controversial. Obstacles to routine administration of probiotics include the risk of invasive infection in a critically ill neonate, as well as our lack of knowledge regarding which gut microbial functions we should seek to alter through “biotic” manipulations. New data reveal a distinct pattern of microbiome maturation during the first four months of life in extremely preterm (<28 weeks gestation), extremely low birth weight (<1000 g) neonates. The most distinctive feature of this developmental process is the acquisition of microbial genes that synthesize secondary bile salts; this occurs with colonization by the bile salt hydrolase carrier *Clostridium perfringens*. We developed an *in vitro* assay sensitive enough to quantify bile salt hydrolase enzyme activity in very low abundance newborn stool samples. Our results indicate that delayed acquisition of bile salt hydrolase genes and impaired bile salt deconjugation activity predict poor neonatal outcomes. Bile salt hydrolase enzymes are carried by many commonly used probiotic strains and warrant further investigation as potentially protective to extremely preterm, extremely low birth weight neonates in the intensive care unit.