Transition from parenteral to enteral nutrition induces immediate diet-dependent gut histological and immunological responses in preterm neonates

Necrotizing enterocolitis (NEC) in preterm infants develops very rapidly from a mild intolerance to enteral feeding into intestinal mucosal hemorrhage, inflammation, and necrosis. We hypothesized that immediate feeding-induced gut responses precede later clinical NEC symptoms in preterm pigs. Fifty-six preterm pigs were fed total parenteral nutrition (TPN) for 48 h followed by enteral feeding for 0, 8, 17, or 34 h with either colostrum (Colos, n = 20) or formula (Form, n = 31). Macroscopic NEC lesions were detected in Form pigs throughout the enteral feeding period (20/31, 65%), whereas most Colos pigs remained protected (1/20, 5%). Just 8 h of formula feeding induced histopathological lesions, as evidenced by capillary stasis and necrosis, epithelial degeneration, edema, and mucosal hemorrhage. These immediate formula-induced changes were paralleled by decreased digestive enzyme activities (lactase and dipeptidylpeptidase IV), increased nutrient fermentation, and altered expression of innate immune defense genes such as interleukins (IL-1α, IL-6, IL-18), nitric oxide synthetase, tight junction proteins (claudins), Toll-like receptors (TLR-4), and TNF-α. In contrast, the first hours of colostrum feeding induced no histopathological lesions, increased maltase activity, and induced changes in gene expressions related to tissue development. Total bacterial density was high after 2 days of parenteral feeding and was not significantly affected by diet (colostrum, formula) or length of enteral feeding (8–34 h), except that a few bacterial groups (Clostridium, Enterococcus, Streptococcus species) increased with time. We conclude that a switch from parenteral to enteral nutrition rapidly induces diet-dependent histopathological, functional, and proinflammatory insults to the immature intestine. Great care is required when introducing enteral feeds to TPN-fed preterm infants, particularly when using formula, because early feeding-induced insults may predispose to NEC lesions that are difficult to revert by later dietary or medical interventions.