Increased Intestinal Inflammation and Digestive Dysfunction in Preterm Pigs with Severe Necrotizing Enterocolitis

The risk factors for necrotizing enterocolitis (NEC) are well known, but the factors involved in the different NEC presentations remain unclear. We hypothesized that digestive dysfunction and intestinal inflammation are mainly affected by severe NEC lesions. In 48 preterm pigs, the association between the macroscopic NEC score (range 1-6) and the expression of 48 genes related to inflammation, morphological, and digestive parameters in the distal small intestine was investigated. Only severe NEC cases (score of 5-6) were associated with the upregulation of genes involved in inflammation (CCL2, CCL3, CD14, CD163, CXCL8, HP, IL1B, IL1RN, IL6, IL10, NFKBIA, PTGS2 and TNFAIP3) compared to pigs that appeared healthy (score of 1-2) or showed mild NEC (score of 3-4). Pigs with a score of 5-6 had higher intestinal tissue IL-1β levels and a lower mucosal mass, villus height, and aminopeptidase N activity compared to pigs with a score of 1-4, and lower crypts and activities of lactase, dipeptidylpeptidase IV, and aminopeptidase A than pigs with a score of 1-2. The expression of a range of inflammation-related genes was increased only in pigs with severe NEC, concomitant with morphological changes and decreased hydrolase activity. A severe inflammatory response and digestive dysfunction are associated mainly with severe NEC. Still, it remains difficult to separate the initial causes of NEC and the later intestinal consequences of NEC in both infants and experimental models.