The effect of bovine colostrum products on intestinal dysfunction and inflammation in a preterm pig model of necrotizing enterocolitis

Necrotizing enterocolitis (NEC), primarily seen in preterm infants, is associated with high morbidity and mortality. The pathogenesis is not fully understood but risk factors include prematurity, enteral feeding (especially with milk formula), and the intestinal microbiota. Mother’s milk, rich in bioactive factors, has a protective effect against NEC, but not all preterm infants are able to receive mother’s milk. The overall aim of this thesis was to investigate if bovine colostrum (BC), also rich in bioactive factors, could serve as an alternative to mother’s milk. A preterm pig model of NEC was used to investigate the effect of BC products on intestinal structure, digestive and absorptive functions, microbiota, plasma and tissue proteins and tissue gene expression levels of inflammatory markers. In Study I, the aim was to investigate if BC could correct intestinal dysfunction and reduce inflammation induced by total parenteral nutrition (TPN) combined with an abrupt transition to milk formula, which has shown to initiate detrimental intestinal responses. A group of preterm pigs fed milk formula followed by BC was compared with groups of preterm pigs fed either milk formula or BC alone after the TPN period. This study showed that BC feeding restores intestinal dysfunction and reduces a proinflammatory response induced by short term (6 hours) formula feeding to preterm TPN-fed pigs. A prerequisite for the use of BC in clinical settings is that a standardized product is readily available, and in Study II it was investigated if pasteurized and/or spray dried BC had similar beneficial effects on intestinal dysfunction and inflammation as fresh BC. Preterm pigs were given TPN for two days followed by 6 hours of formula feeding before given either formula, BC, spray dried BC, or pasteurized and spray dried BC. The study showed that even though spray drying and pasteurization affected BC proteins, pasteurized and/or spray dried BC decreased the severity of NEC in pigs compared with milk formula, while a tendency towards lower NEC severity was observed in pigs fed raw BC compared with milk formula. All three BC products maintained trophic and anti-inflammatory effects on the immature pig intestine. A simple and standardized system was required to investigate the effects of milk formula versus BC on intestinal epithelial cells. In Study III, the IPEC-J2 cell line was evaluated as an in vitro model for the premature pig intestine. It was investigated if diet-induced effects could be observed on the expression of 48 epithelial- and immune response-related genes in IPEC-J2 cells stimulated with milk formula, BC or growth medium. Distal small intestinal samples from preterm pigs fed milk formula or colostrum were included for comparison. This study showed that careful considerations must be made prior to gene expression analysis of diet-induced responses in IPEC-J2 cells as a system for the premature intestine, since no dietinduced effects in the IPEC-J2 cells were detected. C. perfringens is a pathogen associated with NEC in preterm infants and pigs, and in Study IV, the association between NEC and the abundance of C. perfringens and total bacteria in intestinal samples from preterm pigs was investigated using quantitative polymerase chain reaction. Furthermore, host-pathogen interactions were investigated in IPEC-J2 cells by analyzing the expression of 48 epithelial- and immune response-related genes after stimulation with C. perfringens. An association between the abundance of total bacteria and C. perfringens and NEC was observed, and an in vitro study in IPEC-J2 cells showed that increased numbers of C. perfringens were associated with changes in gene expression response. To increase the effect of BC against C. perfringens, Study V aimed to investigate if BC with increased activity toward C. perfringens could be produced. Western blot confirmed that anti-C. perfringens hyperimmune BC could be produced by immunization of pregnant cows with a clostridial specific vaccine. In conclusion, BC products have a beneficial effect on the intestinal environment in preterm pigs based on improvements in intestinal structure, digestive and absorptive functions, the microbiota, and by reduced level of inflammatory markers. BC products, modified to meet the nutritional requirements of preterm infants, may serve as valuable alternatives to mother’s milk during the first critical days after birth. However, well-designed studies in preterm infants are required to investigate if BC is a safe and effective alternative for these vulnerable infants when mother’s milk is not available.

General information
State: Published
Organisations: National Veterinary Institute, Section for Immunology and Vaccinology
Contributors: Støy, A. C. F.
Number of pages: 150
Publication date: 2012

Publication information
Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
ISBN (Print): 978-87-992685-5-9
Original language: English
Electronic versions: Ann_Cathrine_F_Støy_Final_B5_thesis_2013.pdf
Research output: Research › Ph.D. thesis – Annual report year: 2013