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Variation of Lactoferrin and Total Immunoglobulin G Concentrations in Colostrum from Canadian Holstein Dairy Cattle Classified as High, Average or Low Immune Responders

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Abstract: The objective of this study was to investigate phenotypic profiles of lactoferrin (LF) and total immunoglobulin G (IgG) in colostrum from Canadian Holsteins (n=87) previously classified as having High, Average or Low immune responses. A linear mixed model was used to account for parity, barn, somatic cell score, first milking volume and immune response group. Preliminary results show that High Immune Response (HIR) cows have significantly ($P<0.05$) greater concentrations of LF and total IgG in colostrum compared to Low Immune Response cows. These findings suggest that HIR cows produce colostrum of enhanced quality. Colostrum from these cows may mediate superior passive immunity in calves and also provide innovative ingredients for incorporation into functional foods and formulation of nutraceuticals to enhance human and animal health.
Keywords: immune response; colostrum quality; bioactive component

Introduction

Optimal dairy cattle health is important for safe and high quality milk production. Selection pressure for production traits with less attention to health status has been associated with disease (Appuhamy et al. (2009)). One potential solution to improve the health of dairy cattle is to identify and selectively breed cows capable of mounting robust antibody-mediated (AMIR) and cell-mediated (CMIR) immune responses (Mallard et al. (2011)). Cattle classified as High Immune Response (HIR) cows have approximately half the occurrence of diseases including mastitis, metritis, ketosis and retained placenta as Low Immune Response (LIR) cows (Thompson-Crispi et al. (2012a); Wagter et al. (2000)).

Bovine colostrum contains bioactive components such as lactoferrin (LF) and immunoglobulin G (IgG) that exert immunological activities against infectious agents, particularly mastitis-causing bacteria. In addition to bacterial defense, LF (Superti et al. (1997); Di Biase et al. (2003)) and total IgG (Butler et al. (1983)) have been shown to exert anti-viral activities. Moreover, LF has been shown to act as an anti-cancerous (Tung et al. (2013)) and anti-inflammatory (Drago-Serrano et al. (2012)) agent.

Since immunologically active components in colostrum exert anti-microbial activities against mastitis-causing pathogens and HIR cows have less mastitis, it is hypothesized that HIR cows produce colostrum of enhanced quality with increased concentrations of LF and total IgG. Heritabilities of LF (h^2=0.35) (Bastin et al. (2012)) and total IgG (h^2=0.10) (Mallard et al. (1983)) provide the potential to naturally improve the nutrition of colostrum in the future via implementing selective breeding programs. Breeding for HIR cows with increased concentrations of bioactive components in colostrum would lead to higher quality colostrum production to reduce infectious diseases in calves, as well as to provide a richer source of components for formulation of nutraceutical products.

Materials and Methods

Colostrum samples were collected from Canadian Holsteins at the University of Guelph research herd (n=74) and a commercial herd in Southwestern Ontario (n=13) on day 0 post-calving. Cows were ranked as having High, Average or Low immune responses using the patented HIR Technology (Thompson-Crispi et al. (2012b)). Enzyme-linked immunosorbent assay (Bethyl Laboratories, Inc., Montgomery, Texas, USA) was used to quantify LF concentrations and radial immunodiffusion (Triple J Farms, Bellingham, Washington, USA) was used to measure total IgG concentrations. Colostrum was defatted by centrifugation at 11,000xg for 15 minutes, similar to a study conducted by Wagter et al. (2000). Colostral LF and total IgG concentrations were analyzed independently using a linear mixed model (PROC Mixed, SAS Version 9.1.3). The model considered the effects of parity, first milking volume, barn, somatic cell score and immune response group. Data were log transformed if not normally distributed. P values ≤ 0.05 were considered significant.

Results and Discussion

Results indicate that High AMIR cows have significantly greater concentrations of LF (0.70 mg/mL) and total IgG (7645 ng/mL) in colostrum compared to Low AMIR cows (0.42 mg/mL and 5233 ng/mL, respectively). Concentrations of LF and total IgG in colostrum did not differ significantly among cows in different CMIR categories. The concentrations of LF and total IgG were significantly and positively (R=0.28) correlated. Parity was significantly associated with colostral LF and total IgG concentrations with cows in later parities having greater concentrations of LF and total IgG.

In simple terms, the immune system consists of two components, innate and adaptive immunity, with the latter further dividing into AMIR and CMIR arms. The antibody-mediated and cell-mediated arms eliminate extracellular and intracellular pathogens, respectively. Antibody-mediated effects are dependent on antibodies generated by B lymphocytes, whereas effector T lymphocytes are major constituents of cell-mediated defenses. Since antibodies are immunoglobulins with specificities to identified antigens, it is not surprising that HIR cows with enhanced AMIR produce colostrum with increased concentrations of total IgG.

Colostrum LF and total IgG concentrations were positively correlated and significant. This suggests that cows with high LF concentrations have high concentrations of total IgG in colostrum. A study by Butler (1973) found that IgG_2 forms complexes with LF, suggesting that the two proteins are functionally related. It is commonly known that immunoglobulins mark pathogens for cellular and molecular recruitment to destroy infectious agents. A cationic peptide motif of LF called lactoferricin has recently been shown to directly bind pathogens via anionic residues on pathogen membranes and cationic binding sites on lipopolysaccharide (Drago-Serrano et al. (2012)). Lactoferricin is amphipathic and may insert into pathogen membranes, promoting destabilization (Groenink et al. (1999)). Therefore, it could be hypothesized that IgG2 acts as a specific vehicle in delivering LF to pathogens for neutralization and destruction due to the bactericidal activities of lactoferricin.

Enhanced colostrum quality can be defined as having greater than 5,000 mg of IgG per dL and has been associated with enhanced calf health (Weaver et al. (2000)). In this study, at least 70% of High AMIR cows (76%) and High CMIR cows (71%) contained more than 5,000 mg of IgG per dL in colostrum. Fewer Low AMIR (52%) and Low CMIR (67%) met this minimum. As a result, selectively breeding for HIR cattle that produce high quality colostrum containing greater concentrations of total IgG may help prevent failure of passive transfer in calves. Increased concentrations of LF in colostrum from High AMIR cows may also prove to prevent infection in newborn calves. Banking colostrum from High AMIR cows as well as higher parity cows may serve as an important herd management strategy.

Cancer, osteoporosis, obesity, diabetes as well as cardiovascular, musculoskeletal and infectious diseases in the Canadian human population are prevalent and of financial significance (Health Canada, (1998)). Optimistically, consumers have become interested in the health-promoting and potential disease prevention benefits of functional foods and nutraceutical products. Breeding for HIR cattle with increased concentrations of LF and IgG in colostrum may serve as an efficient source of ingredients for natural health product preparation.

Conclusion

Total IgG and LF concentrations were measured to determine if HIR cows had higher quality colostrum compared to LIR cows. Preliminary results show that colostrum from High AMIR responders has greater quantities of total IgG and LF. Measuring LF and total IgG in milk collected day 5 post-calving and calculating heritabilities of these components is currently underway. Ultimately, breeding for HIR cows may lead to the production of higher quality colostrum, which may provide a natural genetic solution to improve the health of humans and subsequent generations of dairy cattle.

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