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Effect of feeding whole as compared to cell-free colostrum on calf immune status: Vaccination response

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ABSTRACT

Vaccination contributes to improved herd health and production. Boosting immune development at a young age may have long-term effects by enhancing vaccine immune response and efficacy. In the bovine, colostrum is the sole source of maternal immunity, having a substantial effect on health status in the neonate. To date, colostral antibody concentration is used to evaluate colostrum quality. However, colostrum also contains proteins and cells, which may affect immune development and future responses to vaccines. To determine the effect of maternal colostral cells on immune development, 37 female Holstein and Jersey dairy calves were bottle-fed 4 quarts total of whole colostrum (WC) or cell-free colostrum (CFC) at birth. Calves were vaccinated with 2 series of multivalent vaccines. Series A consisted of vaccines given between 1 and 4 mo of life. Series B consisted of vaccines given between 5 and 10 mo of life. Calf peripheral blood samples were obtained before each vaccination series and monthly for 3 mo after each vaccination series. Cellular blood parameters were determined by flow cytometry. Quantitative real-time PCR was used to determine cytokine gene expression in peripheral blood mononuclear cells before vaccination series B and once a month for 2 mo after vaccination series B. Calves fed CFC had fewer numbers of B cells in mo 2 after vaccination series A when compared with WC-fed calves. Calves fed CFC had decreased gene expression levels of IL-2 in mo 1 and numbers of $CD4^+CD62L^+CD45RO^-$ and $CD4^+CD62L^+CD45RO^+$ T cells in mo 0 and 1 after vaccination series B as compared with WC-fed calves. Our findings indicate a greater response to vaccines up to 6 to 10 mo post-WC feeding when compared with CFC. These data suggest that adoptive transfer of maternal colostral cells at birth has a long-term effect on development of the neonatal immune system.

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INTRODUCTION

The bovine neonate is born with deficiencies in the amount and functioning capacity of nonspecific and specific immune cells. This results in a decreased ability to combat infections associated with scours and respiratory diseases. The dairy calf does not obtain immune cells via cross-placental transfer during gestation and relies solely on colostrum for maternal immunity. Colostrum serves as an immunologic link between mother and offspring, containing cells, proteins, and soluble molecules that may affect neonatal immune development. Previous work indicates that colostral cells traffic through the intestine into neonatal circulation (Schnorr and Pearson, 1984; Williams, 1993; Liebler-Tenorio et al., 2002). In dairy calves, ingestion of colostral immune cells increases levels of $CD4^+$ T cells in the blood within the first month of life (Langel et al., 2015).

Conferring successful vaccine protection in cattle is important in preventing new or recurring infections. Ingestion of colostral immune cells can enhance antigen-specific responses in calves. For instance, calves born from vaccinated dams have enhanced leukocyte proliferative responses to the vaccinate antigen in vitro. However, this increase is absent in calves fed either frozen or cell-free colostrum (**CFC**) (Donovan et al., 2007). This effect could be attributed to maternal colostral memory cells, which may enter the mammary gland during colostrogenesis (Saif et al., 1983; Bandrick et al., 2008). Previous studies show that leukocytes from calves fed whole colostrum (**WC**) have enhanced expression of activation markers and major histocompatibility complex II (Reber et al., 2008a,b; Langel et al., 2015). Together, these studies suggest that calves fed WC have a greater ability to activate immune cells, leading to enhanced responses to antigen exposure.

The objective of our research was to continue following dairy calves from a previous study (Langel et al., 2015) and determine the effect of maternal colostral

cells fed at birth on subsequent immune responses to vaccinations. We hypothesized that feeding WC containing intact, viable cells at birth would enhance cellular parameters after vaccination when compared with feeding of CFC in which cells were lysed.

MATERIALS AND METHODS

Feeding Colostrum with Intact Compared to Lysed Cells

Dairy heifers and cows from the Virginia Tech Dairy Center were equipped with a birth monitoring system (FoAlert, Acworth, GA). All animal handling and sampling protocols were in accordance with the Virginia Tech's Institutional Animal Care and Use Committee. The FoAlert birth monitoring system was used for immediate notification of parturition. In brief, a veterinarian sutured a transmitter to the outside of the vulva on each cow at ≥2 wk before calving. During parturition, physical separation of the vulva triggered the transmitter, resulting in an audible alarm and phone calls to preprogrammed numbers on an automated dialer. This system ensured that staff arrived before parturition and prevented suckling of the dam by the calf.

Following parturition, the calf was cleaned by the cow but not permitted to suckle. The calf was then removed, weighed, and administered 1 dose of TSV-2 nasal vaccine (Zoetis, Madison, NJ). The dam was moved into a chute where colostrum was aseptically collected from all quarters with a portable milking unit. If clumps or blood were observed in colostrum, mastitis was assumed and the calf was not enrolled. Colostrum was tested with a Brix refractometer (NASCO, Fort Atkinson, WI) to assess total colostral protein and samples were saved for subsequent standard bacteriological analyses (NMC, 2004). Only calves fed quality colostrum with a Brix score of 23 or higher (Deelen et al., 2014) were enrolled in this study.

Calves were fed quality WC or CFC from their respective dams, according to the following protocols. Following collection and testing, 1.9 L of WC was used to fill two 2-quart bottles. One bottle was fed to the calf within 3 h of birth. The second bottle was refrigerated (4°C) and, immediately before the second feeding at 5 to 8 h after birth, slowly warmed to 37°C. Refrigeration had no significant effect on cell viability in WC (data not shown). A total of 14 Holstein and 4 Jersey calves in the WC group and 15 Holstein and 4 Jerseys calves in the CFC group were enlisted in the study.

To lyse immune cells for the CFC treatment, 4 perfluoroalkoxy (**PFA**) bags (Welch Fluorcarbon, Inc., Dover, NH) were filled each with 1 L (1.06 quarts) of colostrum. Each PFA bag was placed in a styrofoam box and covered with liquid nitrogen. Precautions were taken to ensure that liquid nitrogen did not come into direct contact with colostrum. The PFA bag was turned approximately every 3 min until colostrum was completely frozen. Following complete freezing of colostrum, the first 2 L of colostrum were slowly warmed to 37°C and fed to the calf within 3 h of birth. The second 2 L of colostrum were thawed at 37°C, transferred to a bottle, refrigerated (4°C), and, immediately before the second feeding at 5 to 8 h after birth, slowly warmed to 37°C.

An esophageal tube feeder was used only in cases when calves did not suckle from the bottle. In this study, the low number of animals requiring esophageal feeing (2 calves fed WC and 3 calves fed CFC) did not warrant statistical analyses and was unlikely to affect results. Animals fed by esophageal tube feeder received colostrum in the same volume and at the same time points as bottle-fed calves. Concentrations of plasma IgG1, IgG2, IgM, and IgA were analyzed from blood samples collected before colostrum ingestion and on d 1 of life. Treatment did not affect concentrations (μg/mL) of IgG1, IgG2, IgM, and IgA antibodies (Langel et al., 2015). All calves entered the Virginia Tech dairy herd and routine farm management protocols were applied.

Vaccinations

Animals were given 2 series of vaccinations according to protocols put forth by the Virginia Tech Dairy Center and the herd veterinarian (Table 1). Vaccination series A was administered between 1 and 4 mo of age and included a label dose of a multivalent killed vaccine Ultrachoice 7 (Zoetis) and a multivalent modified live vaccine Vira Shield (Novartis, Basel, Switzerland). Vaccination series B was administered between 5 and 9 mo of age and included a second dose of Ultrachoice 7 and Vira Shield. A dose of modified live RB-51 vaccine (Professional Biological Company, Denver, CO) was also given between mo 5 and 9. Mean (± SD) age of calves was 2.167 (± 0.515) and 2.263 (± 0.452) mo at vaccination series A and 6.313 (± 0.947) and 5.6 (± 0.633) mo at vaccination series B for WC and CFC, respectively. Due to a managing error on farm, 6 animals were double vaccinated during series B and therefore removed from subsequent analysis. The final number of animals analyzed in vaccination series B included 16 animals fed WC and 15 fed CFC.

Blood Collection for Isolation of Peripheral Blood Mononuclear Cells

Each calf was bled before each vaccination series and once a month for 3 mo subsequent to their respective