Short communication: Variation in serum immunoglobulin G concentrations from birth to 112 days of age in Holstein calves fed a commercial colostrum replacer or maternal colostrum

A. J. Lopez,¹ C. M. Jones,¹ A. J. Geiger,² and A. J. Heinrichs^{1*}

¹Department of Animal Science, The Pennsylvania State University, University Park 16802

²Zinpro Corporation, Eden Prairie, MN 55344

ABSTRACT

Serum IgG concentrations in dairy calves change throughout their first weeks of life, peaking at 24 h and then steadily decreasing until calves begin to produce endogenous IgG. The objective of this study was to observe serum IgG dynamics from birth until 16 wk of life in calves fed either maternal colostrum (MC) or colostrum replacer (CR). A total of 44 Holstein calves were randomly assigned to 1 of the 4 colostrum treatments and followed throughout the study. Treatments consisted of feeding high-quality MC, low-quality MC supplemented with CR, or 1 of 2 distinct levels of IgG concentration from CR. Overall, the interaction between type of colostrum fed and sampling time was significant. Individual differences for this effect were found at d 1, 7, 14, 21, 28, and 98, while the other time points were not different.

Key words: serum IgG, colostrum, immunoglobulin G

Short Communication

Colostrum is composed of various components including proteins, fats, growth factors, and immunoglobulins (Davis and Drackely, 1998). Immunoglobulins are proteins that help develop a calf's immune system through passive transfer of immunity (Elizondo-Salazar and Heinrichs, 2009). Feeding management depends on the quality and quantity of colostrum fed, feeding time (Stott and Fellah, 1983), and bacteria level (Gelsinger et al., 2015). These 4 factors determine the amount of immunoglobulins a calf can absorb, which helps them fight against diseases during their first weeks of life (Butler, 1969). In summary, the basic recommendation is to feed a calf 4 L of maternal colostrum (MC) containing at least 50 g/L of IgG during the first 2 h of life (McGuirk and Collins, 2004). By approximately 3

wk of age, calves start to produce their own antibodies and begin to develop their active immune systems (Devery et al., 1979; Kertz et al., 2017). The delay in endogenous antibody production until wk 3 makes colostrum a crucial source of protection until a calf is able to mount an immune response (Banks and McGuire, 1989). In this period, calves experience a stage in which they stop using their passively acquired immunoglobulins and start actively producing antibodies. However, the amount and rate of increase of antibody production depends on the amount of IgG absorbed and consumed at birth (Husband and Lascelles, 1975; Machado Neto et al., 1997; Aldridge et al., 1998). Husband and Lascelles (1975) showed that calves that were provided insufficient immunoglobulins at birth started producing antibodies faster than calves that had successful passive transfer. The earlier antibody production and higher peak IgG levels of colostrum-deprived calves can be attributed to inhibition of endogenous production by colostrum immunoglobulins. This negative effect was earlier demonstrated by Logan et al. (1974). Pauletti et al. (2003) also concluded that calves with lower initial serum IgG concentrations start their endogenous antibody production earlier than calves fed higher amounts of IgG due to a compensatory synthesis. This suggests that colostrum, in addition to conferring passive immunity, also has immunomodulatory properties that might inhibit calves from producing active immune responses to antigens (Menanteau-Horta et al., 1985). In summary, variation in serum IgG starts with a peak at 24 h after colostrum ingestion, followed by a gradual decrease to a minimum point. This decrease is accredited to the biological decay of proteins. Later in life, a calf starts to synthesize its own immunoglobulins in response to antigenic influences from its environment. During this “immunity gap,” created as passively acquired IgG reaches its lowest concentration and before the onset of endogenous production, calves could be more susceptible to diseases (Husband et al., 1972). With the suggestion that colostrum-deprived calves start to produce their own immunoglobulins faster than

Received February 19, 2020.

Accepted April 15, 2020.

*Corresponding author: ajh@psu.edu

calves provided a sufficient amount of colostrum, the objective of this study was to compare the IgG concentrations and changes of calves fed MC or colostrum replacer (**CR**) at birth until 112 d of life. Moreover, because each treatment provided a distinct amount of IgG, we expected to see differences in IgG dynamics and the onset of endogenous IgG production.

This study used 44 calves (33 females and 11 males) that were randomly assigned to be fed 1 of 4 colostrum treatments. Calves enrolled in the study were animals available from The Pennsylvania State University farm and were similar in numbers to other previous studies that measured similar variables (Elizondo-Salazar and Heinrichs, 2009; Gelsinger et al., 2015). All calves were removed from the calving pen immediately after birth to prevent any colostrum suckling from the dam. Afterward, calves were moved to a naturally ventilated calf barn, weighed, navel dipped, placed in an individual pen, stratified by sex, and randomly assigned to treatments. Treatments consisted of (1) high-quality MC from first milking (MC; 106 g of IgG/L; 401 g total of IgG fed; positive control), (2) MC from second and third milking (30 g of IgG/L) supplemented with 40 g of IgG from a CR (**LMC-CR**; final concentration = 41 g of IgG/L; 154 g total of IgG fed), (3) whey-based CR containing 110 g of IgG (**CR-110**), or (4) whey-based CR providing 150 g of IgG (**CR-150**). Calves assigned to CR-110 or CR-150 were fed the same CR product in different doses (Premolac PLUS Bovine IgG, Zinpro Corporation, Eden Prairie, MN). First milking colostrum (MC) and second and third milking colostrum (LMC-CR) were obtained from cows from The Pennsylvania State University in 2018. All colostrum was stored in 1.89-L plastic containers and frozen immediately at -20°C until adequate volume for the study was available. Before the study began, 2 different colostrum batches were made. After thawing, all containers of high-quality colostrum from first milking (≥ 75 mg/mL of IgG) were mixed using a milk pasteurizer (PLV model, 2c Duecinox, Guastalla, Italy) for mixing only. Once the batch was uniformly mixed, colostrum was stored in new individual 1.89-L plastic bottles and immediately frozen at -20°C until feeding. This same process was done to make the low-quality colostrum batch from milkings 2 and 3, using colostrum with a concentration of ≤ 40 g of IgG/L. All colostrum treatments were fed to calves within 1.5 h after birth in a single feeding.

Calves assigned to MC and LMC-CR were fed 3.79 L. The CR product was derived from dried bovine colostrum and was high in IgG (40.64%) and other whey proteins content, as a result of casein and fat removal during manufacturing. Calves fed CR-150 were fed a

complete dose of the product (375 g of powder) reconstituted in 1 L of water. Calves fed CR-110 were fed a reduced dose (270.7 g of powder) of the same CR used for calves fed CR-150. All calves were fed via esophageal feeder (Handi Grip 4-Qt. Feeder, Nasco, Fort Atkinson, WI).

Jugular blood samples were taken at 0 h before colostrum feeding and on d 1, 7, 14, 21, 28, 35, 42, 49, 63, 70, 84, 98, and 112. Samples taken at 0 h were used only to verify that the calf did not suckle colostrum from its dam; these were not included in the statistical analysis. All samples were collected in 10-mL serum blood collection tubes (Vacutainer, Becton, Dickinson and Co., Franklin Lakes, NJ), refrigerated overnight, centrifuged at $1,500 \times g$ for 15 min at 4°C to separate the serum, and stored at -20°C until further IgG analysis. Serum IgG analysis was done by radial immunodiffusion (#728411; Triple J Farms, Bellingham, WA). Samples that required dilution were diluted at 1:10 or 1:5 proportions with 0.85% saline solution, and final readings were determined following manufacturer instructions. After colostrum feeding, all calves were fed 6 L of pasteurized saleable milk in 2 feedings/day through 6 wk of age, 3 L once/day for 1 wk, and fully weaned at wk 7. From d 3 until wk 7, starter grain and water were offered ad libitum. Afterward, these calves were assigned to a different study in the same barn where they were fed diets containing different forage inclusions from d 49 to 112.

Changes in IgG concentrations from d 1 to 112 of life were analyzed using the mixed procedure of SAS (Version 9.4, SAS Institute, Cary, NC). The model included fixed effects of colostrum quality, calf sex, time, and all interactions of these effects. Calf within colostrum quality was included as a random effect. Time was evaluated as a repeated effect, using calf within quality as the subject and the spatial power covariance structure to account for uneven spacing of the measurements. Comparisons of least squares means were completed using the slice and PDIFF options, and Tukey adjustments were applied to *P*-values for multiple comparisons. Nadir values for serum IgG and the corresponding age also were analyzed using mixed procedure in SAS. No time effects were included in this model, and contrast statements were used to compare treatment means.

No differences were detected between male and female calves. As expected, both colostrum treatments and time of sampling affected serum IgG concentration, and an interaction between treatment and time was observed, as well ($P < 0.001$). Mean IgG concentration changes from d 1 through 112 are shown in Figure 1. Treatment differences were found on d 1, 7, 14, 21, 28,

Figure 1. Serum IgG concentration dynamics (mean $\pm$ SE) from d 1 to 112 for calves fed maternal colostrum (MC; 401 g of IgG), supplemented low-quality colostrum (LMC-CR; 154 g of IgG), or colostrum replacer providing 150 or 110 g of IgG (CR-150 and CR-110, respectively). Differences were detected due to colostrum treatment, time, and their interaction ($P < 0.01$). Letters a–c indicate differences between treatments at a given time.

and 98 ($P < 0.01$, $P < 0.01$, $P < 0.01$, $P < 0.01$, $P < 0.01$, and $P = 0.03$, respectively), while no differences were detected at d 35, 42, 49, 63, 70, 84, and 112 ($P > 0.05$). The IgG concentrations of the MC treatment were higher than the rest of the treatments at time 7, 21, and 28 ($P < 0.01$), and higher than CR treatments, but not LMC-CR, at d 1 ($P = 0.09$) and 14 ($P = 0.12$). Both CR treatments were similar at all time points ($P > 0.05$).

Calves fed the highest amount of IgG, MC treatment (401 g of IgG fed), had the highest IgG concentration at d 1 (26.46 mg/mL), while calves fed the least amount of IgG, CR-110 treatment, had the lowest IgG concentration at d 1 (12.27 mg/mL; $P < 0.01$). This was expected because total IgG fed and serum IgG concentration are positively correlated (Zaremba et al., 1993). As mentioned by Butler (1983), all calves had an expected IgG peak at d 1. Afterward, they experienced a gradual decline until reaching their lowest point, when concentrations stabilized before they began to increase. This linear decrease can be attributed to normal biological degradation (Husband et al., 1972). Once endogenous antibody production began, IgG gradually increased until d 98, followed by a slight decrease until d 112.

These IgG changes are similar to the ones reported by Klinkon et al. (2008), who also found a slight decrease from d 98 to 112, but did not report an explanation. The increase in IgG concentration in calves fed CR-150 did not end at d 98, but continued to increase through d 112.

The lowest IgG concentrations for calves fed CR-150 (7.90 ± 0.77 mg/mL) and CR-110 (6.63 ± 0.89 mg/mL) occurred at 22.0 ± 5.3 and 21 ± 6.1 d (least squares mean $\pm$ SE), respectively, which aligns with results reported by Klinkon et al. (2008) and Devery et al. (1979). Hammon et al. (2000) reported an IgG concentration decrease until 21 d in studies with calves fed MC. Calves fed MC achieved their lowest IgG concentration (9.80 ± 0.71 mg/mL) in the current study at 46.1 ± 5.2 d, which is later than results reported by Klinkon et al. (2008) and Erhard et al. (1999). The lowest IgG concentration point (9.48 ± 0.90 mg/mL) for calves fed LMC-CR in the current study was at 30.2 ± 6.2 d. These results agree with data from Erhard et al. (1999), who reported that IgG was lowest at d 28 and then gradually increased until the end of study at d 77; calves in that study were also fed pooled MC. Calves fed CR reached a lower ($P < 0.01$) nadir sooner ($P <$

0.01) than those fed MC. No differences in the IgG value or age at nadir were detected between CR-110 and CR-150. Calves fed MC tended to reach nadir later than calves fed LMC-CR ($P = 0.06$). Differences in the concentrations between this study and others indicate that individual calves have different IgG synthesis capabilities (Klinkon et al., 2008). Calves fed LMC-CR, CR-150, and CR-110 exceeded their initial (d 1) IgG levels at 84, 70, and 63 d, respectively.

In general, from the IgG changes shown in Figure 1, it can be inferred that calves with the lowest IgG ingestion at birth (CR-110 and CR-150) either started to produce antibodies, specifically IgG, earlier (d 21) or produced them at a faster rate than calves fed a greater amount of IgG. Calves fed MC who received a significantly greater amount of IgG (401 g compared with 110 and 150 g) experienced an extended IgG catabolism through d 46. As a result, their endogenous IgG production was either delayed or slow enough that it could not be observed in light of the high concentration of passively acquired IgG. The linear rate of decrease from the initial level at 24 h to nadir was 0.44 mg/mL per day for all treatments. These responses concur with Husband and Lascelles (1975) and Pauletti et al. (2003), who stated that colostrum-deprived calves, or in this case calves with lower IgG initial levels, experience earlier endogenous IgG production. Furthermore, Pauletti et al. (2003) reported a higher peak IgG level in colostrum-deprived calves compared with colostrum-fed calves, who had a slow IgG increase after their lowest IgG concentration at 16 d of life. Whether calves fed a large mass of IgG experienced a delay in the start of endogenous IgG production or a reduced rate of IgG production, these calves maintained a higher serum IgG concentration for a longer period after birth compared with calves fed a lower mass of IgG. Research to further examine changes in IgG in young calves could implement labeled IgG to differentiate between exogenous and endogenous sources of IgG in the calf's bloodstream.

Failure of passive transfer rates were 0, 0, 0, and 9.09% for calves fed MC, LMC-CR, CR-150, and CR-110, respectively. One calf out of the 11 assigned to LMC-CR had a failure of passive transfer with a serum IgG concentration of 4.61 mg/mL at 24 h. Although all colostrum treatments resulted in acceptable successful passive transfer rates, it is interesting to note that calves fed CR-110 and CR-150 had serum IgG concentrations <10 mg/mL for a greater portion of their first month of life than calves fed MC or LMC-CR. Most colostrum research has focused on the effects of IgG at 24 h of age, and it is well established that passive transfer status can have long-term effects on calf health

and performance. It is less clear if differences in IgG over time have additional direct effects on calves.

In conclusion, we observed classic variation in IgG concentrations from d 1 until 112 with decreasing IgG levels until active immunity began at levels of 7 to 9 mg/mL of IgG, depending on the amount of IgG calves consumed at birth. It could be that calves fed less IgG in colostrum demonstrated earlier IgG production than calves fed higher amounts of IgG due to the earlier increase in IgG production. However, direct or specific tracking of exogenous against endogenous IgG was not determined in the current experiment.

ACKNOWLEDGMENTS

The authors thank the employees of the Penn State Dairy Farm who helped with calvings and calf care. We also acknowledge Zinpro Corporation (Eden Prairie, MN) for provision of the CR used in the study and partial funding of the study. This research was a component of NC-2042; Management Systems to Improve the Economic and Environmental Sustainability of Dairy Enterprises. The authors have not stated any conflicts of interest.

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