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Comparison of passive transfer of immunity in neonatal dairy calves fed colostrum or bovine serum-based colostrum replacement and colostrum supplement products

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Abstract

Objective—To compare serum total protein (sTP) and serum IgG (sIgG) concentrations in neonatal calves administered colostrum or a bovine serum-based colostrum replacement (CR) product followed by a bovine serum-based colostrum supplement (CS) product.

Design—Randomized controlled clinical trial.

Animals—18 Jersey and 269 Holstein neonatal heifer calves.

Procedures—141 calves were given 4 L of colostrum in 1 or 2 feedings (first or only feeding was provided \leq 2 hours after birth; when applicable, a second feeding was provided between 2 and 12 hours after birth). Other calves ($n = 146$) were fed 2 L of a CR product \leq 2 hours after birth and then 2 L of a CS product between 2 and 12 hours after birth. Concentrations of sTP and sIgG were measured 1 to 7 days after birth. Data from cohorts on individual farms and for all farms were analyzed.

Results—Mean sTP and sIgG concentrations differed significantly between feeding groups. In calves fed colostrum and calves fed CR and CS products, mean \pm SD sTP concentration was 5.58 ± 0.67 g/dL and 5.26 ± 0.54 g/dL, respectively, and mean sIgG concentration was $1,868 \pm 854$ mg/dL and $1,320 \pm 620$ mg/dL, respectively. The percentage of calves that had failure of passive transfer of immunity (ie, sIgG concentrations $< 1,000$ mg/dL) was not significantly different between groups.

Conclusions and Clinical Relevance—Results suggested that sequential feeding of bovine serum-based CR and CS products to neonatal calves is an alternative to feeding colostrum for achieving passive transfer of immunity.

Consumption of an adequate quantity of good-quality colostrum within the first 24-hour period after birth is important for the health and future productivity of dairy calves.¹⁻³ When the formation, ingestion, or absorption of colostrum-derived immunologic factors is inadequate, calves have FPT of immunity. Failure of passive transfer of immunity in calves causes substantial economic losses to stakeholders in the dairy industry because of increases in morbidity and mortality rates. The increased awareness of the importance of confirming successful passive transfer of immunity in neonatal calves has led to the development of several assays that provide quantitative or semiquantitative evidence for determining whether a calf has an adequate concentration of serum immunoglobulins.⁴ When quantified via an RID assay, passive transfer of immunity is generally considered adequate if sIgG

concentrations of neonatal calves are $\geq 1,000$ mg/dL.⁴ Serum total protein concentration is correlated with sIgG concentration; an sTP measurement ≥ 5.2 g/dL is considered to be indicative of adequate passive transfer of immunity in clinically normal hydrated calves.⁴⁻⁶ Despite the recognized importance of the ingestion of good-quality colostrums and the absorption of immunoglobulins after colostrum ingestion for providing passive transfer of immunity and improvement of productivity in neonatal dairy calves, FPT of immunity remains a serious risk factor for disease development and death.⁷⁻⁹

On some dairy farms, FPT of immunity is caused by a shortage in the supply of colostrum. Dairies that do not feed colostrum from primiparous cows or that have cows with health problems at calving, mastitis, or colostrum leaking from their teats before calving may have too few donors of good-quality colostrums. Colostrum shortages may also be observed on dairy farms that do not feed colostrum from cows that have positive test results for infection with *Mycobacterium paratuberculosis*, *Salmonella dublin*, *Mycoplasma bovis*, bovine leukosis virus, bovine viral diarrhea virus, or *Neospora caninum*. It is recognized that colostrum is a potential carrier for the transmission of *M paratuberculosis*. Therefore, the colostrum of cows with a positive test result for *M paratuberculosis* infection would not be used to feed calves at risk for FPT of immunity.^{10,12-16,a} Colostrum shortages are exacerbated because most dairy farms do not have protocols for pasteurizing colostrum before feeding and for eliminating colostrum from cows with a positive test result for *M paratuberculosis* infection.¹⁷ Furthermore, very few dairies have good-quality frozen colostrum reserved for use during a colostrum supply shortage.¹⁷

Several products have been marketed as a CS, complete CR, or both to provide adequate nutrition and immunoglobulin mass for neonatal calves born on farms with colostrum supply shortages. Although CS products have been used to increase the fed volume of colostrum or increase the quality of colostrum, IgG concentrations in these products are low. Furthermore, the immunoglobulins provided in these products are poorly absorbed after ingestion, and the products are considered inadequate when used as a colostrum substitute.¹⁸⁻²¹ A CR product that contains 125 g of bovine immunoglobulins concentrated from processed bovine serum is available for use in neonatal calves born on farms during a colostrum supply shortage²²⁻²⁴; investigators of a field study²² determined that immunoglobulin absorption after ingestion of the CR product was adequate for passive transfer of immunity. However, plasma IgG concentrations achieved following ingestion of this CR product did not mimic the plasma IgG concentrations achieved following ingestion of colostrum.²² A second feeding of the CR product or an increased immunoglobulin mass in the CR product enhanced the absorption of immunoglobulins.^{22,25} In both studies,^{22,25} no adverse effects were observed after feeding a CS product, a CR product, or colostrum, and in the earlier study,²² the number of veterinary treatments administered until calves were 60 days old was similarly low among all groups of calves regardless of the source of immunoglobulins. Mixed results have been reported²⁶⁻³⁰ following feeding of several other CR and CS products, compared with results following feeding of colostrum. When used alone, a serum-based CR product did not provide sufficient IgG mass for adequate passive transfer of immunity.²⁶ However, there was no significant difference in the number of treated calf illnesses between calves fed the serum-based CR product and those fed colostrum.²⁶ Increases in the mass of IgG in a serum-based CR product fed to neonatal calves resulted in a linear increase in sIgG and sTP concentrations despite decreased apparent efficiency of absorption.³⁰ In another study²⁹ of calves, 2 doses of a CR product that had 200 g of IgG were required to achieve sTP and sIgG concentrations that were similar to sTP and sIgG concentrations in calves fed 4 L of colostrum. The purpose of the

^aPoulsen KP, Hartmann FA, McGuirk SM. Bacteria in colostrum: impact on calf health (abstr). *J Vet Intern Med* 2002;16:339.

study reported here was to compare sTP and sIgG concentrations in calves fed once with colostrum or with a bovine serum-based CR product followed by a bovine serum-based CS product.

Materials and Methods

Animals

Two hundred eighty-seven neonatal heifer calves from 8 dairy farms were included in the study. Calves were born between June 15, 2002, and August 15, 2002.

Preparation of CR and CS products

Commercially available CR^b and CS^c products were used in this study. These products were manufactured according to previously described²²⁻²⁴ methods. One 500-g package (dose) of the CR product provided 125 g of IgG/dose. One 454-g package (dose) of the CS product provided 45 g of IgG/dose. Feeding instructions indicated that 1 package of the CR product or 1 package of the CS product was to be completely dissolved in 2 L of warm (40.6°C [105°F]) water before being fed.

Colostrum collection and storage

Colostrum used in this study was obtained from cows with a negative serum ELISA^d test for anti-*M paratuberculosis* antibody when tested at dry-off. Calves fed colostrum were fed either maternal colostrum or colostrum from another Johne's test negative cow that had calved in the previous 72 hours.

Feeding of colostrum or CR and CS products to calves

Every other neonatal calf born on each farm was fed 3 L (Jerseys) or 4 L (Holsteins) of colostrum during a single feeding or divided into 2 separate feedings. For calves that received colostrum in 2 separate feedings, the first feeding occurred ≤ 2 hours after birth and the second feeding occurred between 2 and 12 hours after birth. However, information was not collected for the number of calves that were fed colostrum during a single feeding versus 2 feedings. The remaining calves were fed 2 L of the CR product^b ≤ 2 hours after birth and 2 L of the CS product^c between 2 and 12 hours after birth (CR-CS products). Any colostrum, CR product, or CS product that was not suckled within 30 minutes was immediately administered via an esophageal feeder system.

Sample collection and analysis

A 10-mL blood sample was collected from each calf 1 to 7 days after birth from a jugular vein into evacuated tubes with no additive. Blood samples were allowed to clot and then centrifuged at 20°C for 10 minutes at 900 \times g. Serum was used to measure sTP concentration by use of a refractometer^{6,31} and sIgG concentration by use of an RID assay.^{32,e} Calves with sIgG concentrations $< 1,000$ mg/dL were considered to have FPT of immunity while calves with sIgG concentrations $\geq 1,000$ mg/dL had adequate passive transfer of immunity.

^bSecure, American Protein Corp, Ames, Iowa.

^cLifeline, American Protein Corp, Ames, Iowa.

^dHerdChek *Mycobacterium paratuberculosis* test kit, IDEXX Laboratories Inc, Westbrook, Me.

^eBovine IgG RID kit, VMRD Inc, Pullman, Wash.

Statistical analysis

Data for sTP and sIgG concentrations from cohort groups on individual farms were analyzed by use of a 2-way ANOVA with fixed effects (ie, treatment group and farm). The ANOVA assumptions of normality and constant variance across treatments were verified by visual inspection of residual plots. Mean \pm SD was calculated for sTP and sIgG concentrations for each farm and all farms. A Fisher exact test stratified by farm was used to determine whether the percentage of calves fed colostrum that had adequate passive transfer of immunity differed in each cohort by sIgG concentration. Serum IgG concentration data were used to categorize calves (a calf with an sIgG concentration $<$ 1,000 mg/dL was assigned a value of 0 [not passed]; a calf with an sIgG concentration \geq 1,000 mg/dL was assigned a value of 1 [passed]). A Fisher exact test was used to analyze combined data from all farms. A value of $P < 0.05$ was considered significant for all analyses.

Results

Farm and calf data and results of sample analysis were summarized (Table 1). Mean sTP ($P < 0.001$) and sIgG ($P = 0.001$) concentrations were significantly different among farms. No significant differences were detected between treatment group and farm for sTP and sIgG concentrations; in addition, these findings indicated that the relative outcome of the 2 treatments was approximately equal across all farms.

Calves fed colostrum had significantly higher sTP (5.59 ± 0.67 g/dL; $P < 0.001$) and sIgG ($1,868 \pm 853$ mg/dL; $P < 0.001$) concentrations, compared with sTP (5.27 ± 0.54 g/dL) and sIgG ($1,348 \pm 693$ mg/dL) concentrations in calves fed CR-CS (Table 1). No significant difference was detected among farms for the percentage of calves that had an adequate level of passive transfer of immunity as classified by sIgG concentrations \geq 1,000 mg/dL. When data from all farms were combined, there was no significant ($P = 0.09$) difference in the percentage of colostrum-fed calves that had an adequate level of passive transfer of immunity (81.6% [115/141 calves]), compared with this percentage (70.5% [103/146 calves]) in calves fed CR-CS products.

Discussion

Passive transfer of immunity through the ingestion of colostrum is a critical factor for the management of neonatal calf health. Ingestion and absorption of the immunologic substances in colostrum by neonatal calves reduce morbidity and mortality rates³³ and have a positive influence on the future productivity of dairy heifers.^{2,3} The FPT of immunity, which is typically defined as the failure to achieve an sIgG concentration \geq 1,000 mg/dL within the first week after birth, is associated with increases in risk of disease, antimicrobial use, and death and also reduced performance in benchmark production characteristics.^{1-3,34-36} Despite the importance of successful passive transfer of immunity, the absorption of an appropriate mass of antibodies and other immunologic and nutritional factors after colostrum ingestion is not consistently achieved when monitored at the herd level.^{35,37,38} Important contributing factors for FPT of immunity may be prolonged time spent with the dam,³⁸ marked variability in the immunoglobulin concentration in the ingested colostrum,^{39,40} a reluctance of farm personnel to feed a large volume of colostrum during a single feeding,¹⁷ or a shortage of available colostrum. It is believed that a calf must consume or be hand-fed 3 to 4 L of colostrum that has an IgG concentration \geq 50 g/L to provide an immunoglobulin mass sufficient to achieve an sIgG concentration \geq 1,000 mg/dL.³⁹ Investigators of a previous study³⁹ reported marked variability in the immunoglobulin concentration of colostrum in dairy cattle, with as many as 60% of colostrum samples having an immunoglobulin concentration $<$ 50 g/L. Although factors such as herd-level management, nutritional status, and environment may explain the variability in

immunoglobulin concentration of colostrum produced by dairy cows, lactation number, breed, time of colostrum collection, and previous episodes of suckling before colostrum collection may be more likely explanations of this phenomenon.^{21,41-43} Despite being aware of the inadequate immunoglobulin concentration of colostrum and knowing that calves have the highest apparent efficiency for absorption of immunoglobulins from ingested colostrum within the first 24-hour period after birth, dairy producers continue to be reluctant to feed 4 L of colostrum during a single feeding. A survey¹⁷ of dairy cattle health and management practices revealed that adequate volumes of colostrum are still not being fed to dairy calves; furthermore, 40% (4/10) of dairy calf managers reported feeding 4 L of colostrum during a single feeding. For various reasons that include an inadequate supply of clean, high-quality colostrum, FPT of immunity continues to be a problem for calves on many dairies. The emergence of CR and CS products that include a sufficient immunoglobulin mass to achieve an sIgG concentration $\geq 1,000$ mg/dL in calves following administration provides producers with alternatives to the feeding of colostrum.

The study reported here provided evidence that the feeding of a CR product followed by the feeding of a CS product from the same manufacturer can provide an adequate immunoglobulin mass for achieving an sIgG concentration $\geq 1,000$ mg/dL in neonatal calves; thus, these products appear to provide an alternative to feeding colostrum when the supply of colostrum is low or the quality of colostrum is inadequate. Investigators of other studies^{23,26,28,29} have also reported the effectiveness of selected CR products when administered in an amount that provides ≥ 150 g of immunoglobulins; however, for most CR products, > 1 package is required to provide ≥ 150 g of immunoglobulins.²⁹ Provision of an adequate immunoglobulin mass to neonatal calves may necessitate feeding a large volume of colostrum, but implementation of this management practice has failed to be consistently adopted by many dairy farm managers.¹⁷ The positive relationship between the quantity of the immunoglobulin mass fed and the improved efficiency of immunoglobulin absorption,²⁷ coupled with a decline in the efficiency of absorption of immunoglobulins with time after birth,⁴⁴ continues to fortify the argument for a single feeding of colostrum that provides ≥ 150 g of immunoglobulins as soon as possible after birth.

The combination of 2 feedings—1 with a CR product and another with a CS product—to provide an adequate immunoglobulin mass to neonatal calves can offer a low-cost alternative to administration of 2 feedings of a CR product. In a previous study,²⁶ calves from 7 of 12 dairies were fed the same CR and CS products, but the feeding with the CS product was administered 8 to 12 hours after the feeding of the CR product; this delay was slightly longer than the delay before feeding the CS product to calves in the study reported here. In addition, data from that study²⁶ for CR-CS-fed calves were grouped with data for calves only fed a CR product; a higher rate of FPT of immunity and lower sTP and sIgG concentrations were reported in that study, compared with the rate of FPT of immunity and sIgG and sTP concentrations in the calves of the study reported here. Similar to the present study, the feeding of a CR product to calves in that study²⁶ was frequently administered earlier than the feeding of colostrum for various reasons, including the convenience of the time of feeding, the ability to administer the colostrum, or the ability to feed the CR-CS products in two 2-L feedings rather than as a single 3- or 4-L feeding. Compliance with colostrum feeding protocols that are designed to achieve an adequate transfer of passive immunity in neonatal calves via 2 small-volume feedings may be the primary advantage of adopting the CR-CS products protocol used in the study reported here. In addition, the findings from the present and previous study²⁶ support the need for feeding ≥ 150 g of immunoglobulins to achieve the successful passive transfer of immunity in neonatal calves.

Another reason for development of FPT of immunity in calves, despite the timely administration of an adequate immunoglobulin mass and volume of colostrum, may be

bacterial contamination of the fed colostrum.^{10-12,26,a} Bacterial contamination of colostrum may be caused by mammary gland infection, poor hygiene during preparation of the udder for colostrum collection, poor sanitation of milking equipment, flawed protocols for colostrum storage, or contamination of colostrum administration equipment. Bacterial contamination of fed colostrum negatively impact the efficiency of the absorption of colostrum immunoglobulins and may be a source of infection of neonatal calves with organisms such as *M paratuberculosis*,^{14,16} *S dublin*,^{13,15} and bovine leukosis virus.^{10-12,a} For dairy herds that do not have a sustainable supply of colostrum or that have programs implemented to reduce the prevalence of infection with *M paratuberculosis*, *S dublin*, bovine leukosis virus, *N caninum*,⁴⁵ bovine viral diarrhea virus, or *M bovis* and mastitis caused by *Staphylococcus aureus* infection,⁴⁶ the feeding of a CR product or a combination of CR and CS products may reduce the rate of FPT of immunity and the prevalence of disease in neonatal calves.⁴⁷

Although the sequential feeding of CR and CS products provided an immunoglobulin mass necessary to achieve an adequate passive transfer of immunity in the calves of the study reported here, calves fed colostrum had significantly higher sTP and sIgG concentrations. The higher concentrations in colostrum-fed calves are similar to the results of other studies²²⁻²⁶ that assess the effects of CR products; the difference has been attributed to greater immunoglobulin mass and greater efficiency of absorption of immunoglobulins in colostrum or to an unknown effect of processing on the CR product. Investigators of another study²³ suggested that calves should ingest 150 to 200 g of immunoglobulins when fed CR or CS products. A total of 170 g of immunoglobulins was provided by the combination of the CR and CS products fed to calves in the study reported here; feeding this quantity of immunoglobulin in 2 feedings resulted in adequate passive transfer of immunity.

Similar to other studies,⁴⁻⁶ an sIgG concentration $\geq 1,000$ mg/dL was used to indicate adequate passive transfer of immunity in neonatal calves fed colostrum or CR-CS products in the present study. Although the relationships between FPT of immunity and calf morbidity and mortality rates have been reported,^{1-3,34,35} no assurance can be made for future good health in calves that have sIgG concentrations $\geq 1,000$ mg/dL for ≤ 7 days after birth. The study reported here attempted to show a relationship between the type of colostrum fed and benchmarks of calf health, but reliable farm data were not obtained. Thus, further investigation is necessary to determine the impact of feeding a combination of CR and CS products on calf health.

Throughout the present study, dairy farm managers commented on the ease of mixing and administering the CR and CS products and stated their preference for feeding a 2-L volume of the CR product, rather than feeding a 4-L volume of colostrum. Several dairy farm managers reported having a shortage in the supply of stored colostrums because of herd size, employee workload, and on-farm application of various disease-eradication programs. Dairy farm managers involved in the study reported here have having a preference for a CR product that was readily available and easy to prepare for use, such as the product used in the present study.

Analysis of the results of the present study revealed that feeding a combination of CR and CS products in 2 sequential feedings was an effective method for providing an immunoglobulin mass necessary to achieve adequate transfer of passive immunity in neonatal calves. Furthermore, this combination of products can be used under circumstances when there is a shortage of clean colostrum or when specific disease control measures preclude the use of colostrum in a herd. Further investigation is necessary to determine whether the health and future productivity of calves fed a combination of CR and CS products are comparable to findings in calves fed colostrum. Investigation of the roles of CR

and CS products in the prevention of diseases resulting from infection with *M paratuberculosis*, *S dublin*, *N caninum*, *M bovis*, bovine leukosis virus, or bovine viral diarrhea virus is warranted.

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Abbreviations

CR	Colostrum replacement
CS	Colostrum supplement
FPT	Failure of passive transfer
RID	Radial immunodiffusion
sIgG	Serum IgG
sTP	Serum total protein

Table 1

Comparisons of farm and calf data and sTP and sIgG concentrations in neonatal calves fed colostrum (n = 146) or a bovine serum-based CR product followed by a bovine serum-based CS product (141).

Variable	Farm									All farms	
	1	2	3	4	5	6	7	8	Total	Mean ± SD	
Breed	Holstein	Holstein	Holstein	Holstein	Holstein	Jersey	Holstein	Holstein	—	—	
No. of calves	31	16	81	45	23	18	45	28	287	—	
No. of calves fed colostrum [†]	16	7	43	21	13	9	21	11	141	—	
No. of calves fed CR-CS products	15	9	38	24	10	9	24	17	146	—	
sTP (g/dL) in calves fed colostrum*	6.0 ± 0.8	5.4 ± 0.5	5.4 ± 0.7	5.5 ± 0.5	5.6 ± 0.7	5.6 ± 0.6	5.5 ± 0.9	6.1 ± 1.0	—	5.6 ± 0.7	
sTP (g/dL) in calves fed CR-CS products*	5.5 ± 0.4	5.2 ± 0.3	5.2 ± 0.6	5.1 ± 0.5	5.5 ± 1.3	5.5 ± 0.3	5.2 ± 0.5	5.3 ± 0.4	—	5.3 ± 0.5	
sIgG (mg/dL) in calves fed colostrum*	1,414 ± 785	1,376 ± 534	1,892 ± 884	1,622 ± 806	2,014 ± 662	2,227 ± 985	1,657 ± 704	2,124 ± 1,027	—	1,868 ± 853	
sIgG (mg/dL) in calves fed CR-CS products*	1,475 ± 317	1,431 ± 571	1,258 ± 445	1,131 ± 855	1,730 ± 1,366	1,966 ± 819	1,288 ± 613	1,234 ± 458	—	1,348 ± 693	
No. of calves with sIgG concentrations ≥ 1,000 mg/dL	14	5	37	14	12	7	18	8	115	—	
No. of calves fed CR-CS products with sIgG concentrations ≥ 1,000 mg/dL	15	8	31	9	7	8	16	9	103	—	

For calves in the colostrum-fed group, 4 L of colostrum was fed in 1 or 2 divided feedings (first feeding was provided ≤ 2 hours after birth; when applicable, a second feeding was provided between 2 and 12 hours after birth); other calves received 2 L of a CR product and then 2 L of a CS product ≤ 2 hours and between 2 and 12 hours after birth, respectively.

* Values are reported as mean ± SD.

[†] Information was not collected for the number of calves that were fed colostrum during a single feeding versus 2 feedings.

— = Not determined.