J. Dairy Sci. 101:1344–1354
https://doi.org/10.3168/jds.2017-13032

Efficacy of colostrum replacer versus maternal colostrum on immunological status, health, and growth of preweaned dairy calves

A. Lago,*[1] M. Socha,† A. Geiger,† D. Cook,‡ N. Silva-del-Río,§ C. Blanc,# R. Quesnell,* and C. Leonardi*
*DairyExperts Inc., Tulare, CA 93274
†Zinpro Corporation, Eden Prairie, MN 55344
‡Milk Products Inc., Chilton, WI 53014
§Veterinary Medicine Teaching and Research Center, Tulare, CA 93274
#GTV Dairies, Tipton, CA 93272

ABSTRACT

Commercially available colostrum replacers (CR) are commonly used when maternal colostrum (MC) is unavailable, for managerial convenience, to ensure quality consistency at first feeding, or in disease control and eradication programs. The objective of this study was to determine the efficacy of feeding First Day Formula (Accelerated Genetics, Baraboo, WI) CR versus pooled MC on immunological status, growth, and health of preweaned dairy calves. A total of 1,220 Jersey and Jersey × Holstein calves born on a California Central Valley dairy farm were assigned after birth to receive either CR or MC following a systematic allocation procedure. Calves assigned to MC were tube fed 2.8 L of MC, and calves assigned to CR were tube fed a total of 500 g of CR (150 g of immunoglobulin G; IgG) mixed into 1.9 L of water at 1 h ± 5 min after the calf was born. A subset of calves was selected for passive transfer (n = 592) and growth (n = 268) analyses. Although both coliform count and total bacteria count were low for MC and CR fed to calves during the study, the predicted probability of calves receiving contaminated liquid feed (coliform count >10,000 cfu/mL) at first feeding was reduced for calves fed CR (1.5%) compared with calves fed MC (6.1%). The mean blood concentration of IgG was lower for calves fed CR than for calves fed MC (19.6 vs. 23.4 mg/mL). However, the apparent efficiency of absorption of IgG did not differ between treatments (34.4 and 35.9% for CR and MC, respectively). Total proteins were lower in calves fed CR compared with MC at 24 h (5.16 vs. 5.84 g/dL, respectively). Calves fed CR were 1.5 kg lighter at weaning and gained 0.03 kg less per day (0.30 vs. 0.33 kg/d, respectively) than calves fed MC before weaning. Height at weaning did not differ between the 2 treatment groups. Calves fed CR tended to have a higher predicted probability of not being treated for diarrhea than calves fed MC (0.142 vs. 0.110, respectively). However, when the disease was present, CR had a higher number of treatment days compared with MC (11.6 vs. 10.8 d, respectively). The hazard ratio of dying did not differ between MC and CR; however, CR calves had a numerically higher risk (hazard ratio = 1.347) of dying compared with calves that received MC. In conclusion, IgG absorption and serum concentration of calves were adequate when calves were fed either CR or MC. The CR-fed calves had a lower probability of receiving contaminated liquid feed and performed similar in terms of health compared with calves receiving high-quality MC, although they were slightly lighter at weaning. Therefore, the CR evaluated in this study is a valid alternative to high-quality (>50 mg of IgG/mL) MC.
Key words: calf, colostrum, colostrum replacer, passive transfer

INTRODUCTION

Maternal colostrum (**MC**) is an important source of nutrients and immune factors for the newborn calf. Additionally, the importance of achieving successful passive transfer to the young calf cannot be denied (Davis and Drackley, 1998). To achieve successful passive transfer of immunity (>10 mg of IgG/mL of serum; Godden, 2008), it has been suggested that a calf needs to receive at least 150 to 200 g of IgG within 2 h of birth (Chigerwe et al., 2008). This normally can be achieved by feeding 3 to 4 L of high-quality MC (>50 mg of IgG/mL; McGuirk and Collins, 2004). Current industry recommendations for high-quality MC specify that it should (1) contain >50 mg of IgG/mL, (2) have a total bacteria count (**TBC**) <100,000 cfu/mL, and

Received April 15, 2017.
Accepted September 25, 2017.
[1]Corresponding author: alfonso.lago@dairyexperts.com

(3) have a coliform count (**CC**) <10,000 cfu/mL (McGuirk and Collins, 2004). In a nationwide study of 67 farms in 12 states, almost 43% of samples collected had a TBC >100,000 cfu/mL, and 16.9% of the samples had a TBC >1 million cfu/mL (Morrill et al., 2012). Only 39.4% of the samples collected met industry recommendations for both IgG concentration and TBC.

When colostrum quality is poor or unavailable, colostrum replacers (**CR**) may be an alternative. Although some studies have reported that feeding one package of some commercial CR products was successful (Quigley et al., 2001; Jones et al., 2004; Foster et al., 2006; Pithua et al., 2013; Priestley et al., 2013), other products failed to achieve mean concentrations of 10 mg/mL of IgG in serum of calves fed CR (Mee et al., 1996; Quigley et al., 2001; Foster et al., 2006; Smith and Foster, 2007; Swan et al., 2007; Godden et al., 2009; Fidler et al., 2011; Priestley et al., 2013). Researchers have reported that the risk of *Mycobacterium avium* ssp. *paratuberculosis* infections was reduced by almost 50% when using a plasma-derived CR compared with using MC (Pithua et al., 2009). Previous studies have not reported a difference in bacteria counts of CR compared with MC when fed to calves. The objective of this study was to determine the effect of feeding a commercially available CR versus pooled MC on immunological status, growth, and health of preweaned dairy calves.

MATERIALS AND METHODS

Dairy Farm and Calf-Raising Facility

The study was conducted on a commercial freestall dairy farm in California with about 9,000 Jersey, Jersey × Holstein cross, and Holstein lactating cows from July to August 2014. Cows in maternity pens were continuously monitored (every 10 min) for calving by research technicians from DairyExperts (Tulare, CA). No later than 10 min after parturition, calves were separated from dams and kept in a group until being transported to another location where calves were raised in California-style wooden hutches. After the initial feeding, calves were fed by farm personnel with 1.9 L of waste milk enriched with a milk balancer (26% CP, 15% fat) to 15% solids twice a day until weaning and offered calf starter after 3 d of age. Weaning occurred at 46 ± 3 d of age, and calves were fed milk once a day for 1 wk until they were moved out of the hutch. Water was offered by farm personnel to calves starting at 3 d of age. Experimental procedures during the first 1 to 2 h of life were performed at the dairy, and additional procedures occurred at the calf-raising facility.

Study Design

A randomized field study was designed to determine the efficacy of feeding First Day Formula (Accelerated Genetics, Baraboo, WI) CR versus pooled MC. Newborn female Jersey and Jersey × Holstein calves and male Jersey × Holstein calves were enrolled in the study by research technicians. Newborn male Jersey calves and male and female Holstein calves were excluded from enrollment. Calves were born from multiparous and primiparous dams. Following birth, calves were systematically assigned following birth order to MC (2.8 L of colostrum; n = 609) or CR (500 g of CR containing 150 g of colostrum-derived IgG mixed into 1.9 L of water; n = 606). All treatments were given via an esophageal feeder at 1 h ± 5 min after birth. Both MC warming and CR preparation as well as feeding were done by research technicians.

MC Management

Colostrum fed to MC calves was harvested twice a day from individual cows at the milking parlor, pooled, and poured into 2.8-L bottles by farm personnel. Bottles were then transported to the maternity area and stored in a refrigerator within 1 h after collection by the same farm personnel. When a calf was born, colostrum was removed from the refrigerator by research technicians and warmed up by immersing bottles in hot water not exceeding 60°C. The temperature of colostrum was checked about 10 min before feeding. Temperature of colostrum was targeted at about 41°C.

CR Preparation

Fifteen minutes before feeding CR, a 3.8-L container of bottled water (DS Waters of America, Atlanta, GA) was immersed in a bucket with hot tap water. Ten minutes before feeding, the temperature of the water in the container was measured with a thermometer to ensure it reached a target temperature of 41°C. The bucket used to mix the replacer was filled with 1.9 L of water. One package of CR powder was added while the mix was stirred using a whisk for 40 to 60 s to ensure complete dispersal. Afterward, the mix was poured into an esophageal feeder container. Tasks related to CR preparation were done by research technicians.

Sample Collection and Laboratory Analyses

MC and CR. Volumes of 40 mL of MC and CR were collected by research technicians into 60-mL plastic

tubes from the esophageal feeder before feeding every sixth calf born between 0100 and 0700 h and between 0900 and 1500 h. Samples were stored at −20°C until analysis. The TBC and CC of MC and CR samples was analyzed at the DairyExperts Laboratory (Tulare, CA) by personnel blinded to the treatment administered to calves. Briefly, after colostrum samples were thawed and thoroughly mixed, serial 10-fold dilutions of the colostrum were made up to the dilution 10^4. One milliliter of the 10^2, 10^3, and 10^4 dilutions was placed on a Petri dish plate, and plate count agar was poured on for determination of TBC. Then, 1 mL of the 10^2, 10^3, and 10^4 dilutions was pipetted onto MacConkey agar for CC. After 24 h of incubation for MacConkey agar and 48 h of incubation for plate count agar, colony-forming units were countered and total counts were calculated by multiplication of the dilution factor. Frozen MC samples were shipped to the California Animal Health Food Safety Lab at University of California, Davis, for IgG analysis with radial immunodiffusion (**RID**) using a commercially available kit (Triple J Farms, Bellingham, WA). Immediately before feeding, research technicians performed Brix refractometry readings with a digital refractometer (model r2min, Reichert, Depew, NY), placing 50 μL on the refractometer well. After each reading the refractometer was rinsed with distilled water and dry cleaned with wipes.

In addition, IgG concentration was measured in 3 randomly selected packages of CR used in the study at the California Animal Health Food Safety Lab for IgG analysis with RID using a commercially available kit (Triple J Farms). Results indicated that the amount of IgG provided by 2 of the packages was 154 g and that the amount provided by the third package was 157 g.

Blood. Every sixth calf born between 0100 and 0700 h and between 0900 and 1500 h enrolled was bled before first feeding by research technicians (n = 96). An 8-mL venous blood sample was collected via the jugular vein into a 10-mL Vacutainer serum collection tube (cat. no. 366430, Becton Dickinson, Franklin Lakes, NJ). Blood samples were centrifuged to separate the serum from the clot, and IgG concentration was determined by RID at the California Animal Health Food Safety Lab.

Blood samples from calves born between 0100 and 0700 and between 0900 and 1500 h were collected by research technicians blinded to the treatment administered to calves twice per day (0600 and 1400 h) at 22 to 28 h after feeding (n = 593). Total proteins (**TP**) were determined using a digital refractometer (model DD-2, Misco, Solon, OH), and serum IgG by RID was determined at the California Animal Health Food Safety Lab in all samples. All calves that were bled at birth were bled at 22 to 28 h.

Measurements and Records Collection

Weight and Height. After birth, all calves born between 0100 and 0700 and between 0900 and 1500 h were weighed by research technicians before first feeding using a digital floor scale (model PS1000, Brecknell, Fairmont, MN). At weaning, 2 to 3 times per week, withers height and weight were measured by research technicians blinded to the treatment administered to calves on every other calf weighed at birth using the same scale. These measurements occurred 1 to 3 d before calves were moved out of the hutches. Growth measures are calculated based on a subset of calves (n = 269).

Treatment Records. Calves were evaluated by farm personnel blinded to the treatment administered to calves twice daily after feeding for the following signs: depression, decreased appetite, abnormal fecal consistency, increased respiratory rate, cough, nasal and ocular discharges, and other abnormal appearances. When deemed necessary, the joints were evaluated for heat, swelling, and abnormal gait, and navels were assessed for swelling or discharge. A calf displaying one or more of these signs was further examined by taking rectal temperature measurements and by evaluating hydration status. Treatments were administered and recorded on calf hutches by farm personnel. Standardized treatment protocols were developed and monitored by the herd veterinarian. Study technicians blinded to the treatment administered to calves collected those records for all calves enrolled in the study that fitted the inclusion criteria (n = 1,215), including calf treatment date and treatment provided. Calf disease and presence of fever were derived from the treatments administered.

Mortality Records. The calf ID and date for calves that died or were culled before calves were moved out of the hutches were recorded by research technicians blinded to the treatment administered to calves (n = 1,215).

Definitions

Failure of Passive Transfer. Calves with serum IgG <10 mg/mL in blood samples collected between 22 and 28 h after birth, as gathered from a subset of calves, were considered to have failure of passive transfer (**FPT**).

IgG Absorption. Apparent efficiency of absorption (**AEA**) was calculated for the subset of calves weighed at birth. It was calculated as grams of IgG absorbed into circulation (difference in serum IgG concentration between birth and 22 to 28 h), multiplied by plasma volume (calculated as 9% of birth BW), divided by

grams of IgG intake (150 g of IgG for the CR group or MC IgG concentration), multiplied by volume of colostrum intake for the MC group (Quigley and Drewry, 1998):

$$\text{AEA IgG (g)} = \{[\text{serum IgG (g/L) 24 h} - \text{serum IgG (g/L) birth}] \times \text{birth weight (kg)} \times 0.09\}/\text{IgG intake (g)}.$$

Average Daily Height and Weight Gain. Average daily height and weight gain was estimated as the difference of the height and weight before calves were moved out of the hutch minus the height and weight at enrollment, respectively, and divided by the duration of the period.

Treatment Days. Count of treatment days was obtained by summing all the days during which an animal was treated for a disease where the diseases reported were diarrhea, respiratory disease, and fever. Total treatment days consisted of days when a calf had either diarrhea or respiratory disease.

Time to Illness. Time to illness was calculated from birth to the first treatment day of the disease (diarrhea, respiratory disease, or fever) or death. The day animals were moved out of the hutch was termed the surviving time (d) for animals that did not contract disease or died.

A Priori Sample Size Estimation

It was estimated that a total of 1,200 calves (600 calves per treatment group) should provide in excess of 95% confidence and 80% power to detect a reduction in mortality from 5 to 2%. The number of calves needed per treatment group to detect a reduction in FPT from 25 to 15% was 300, and the number needed to detect an increase in AEA from 30 to 35% was 41, assuming an SD of 8.

Data Assembly

Five calves were removed from the original data set because they failed the breed inclusion criteria (4 calves in the CR group and 1 calf in the MC group were Holstein breed). Therefore, a total of 1,215 calves were included in the analysis (606 for CR and 609 for MC).

The number of weight and height observations at weaning differed between both treatment groups (110 calves for CR and 159 for MC). Every other calf born between 0100 and 0700 h and between 0900 and 1500 h was weighed and measured. Because every other calf born was assigned to receive either CR or MC following a systematic allocation procedure, most of the calves selected from 1 day time interval belonged to the same treatment group. The end result was that more calves assigned to the MC group were selected for growth metrics before being moved out of the hutches.

Statistical Analysis

Data were analyzed using SAS/STAT software (version 9.2, SAS Institute Inc., Cary, NC). Significance was declared at $P < 0.05$, and a tendency was declared at $0.05 \leq P < 0.10$. Overall, summary statistics were produced using means or frequency procedures.

The TBC data were $\log_{10}$ transformed to meet the assumptions of normality and homeostacity. The CC after log transformation was still skewed, and therefore no parametric analysis could be performed. It was redefined as an ordinal variable in 3 levels (<100 cfu/mL, 100 $\geq$ cfu/mL < 10,000, and $\geq$10,000 cfu/mL), and it was analyzed using the Glimmix procedure available in SAS/STAT software. Multinomial distribution with the cumulative logit link was implemented, including the fixed effect of treatment in the model.

Calf blood and growth metrics parameters were analyzed using the Mixed procedure of SAS. The model included the fixed effect of treatment, a repeated statement with the group = treatment option, and a selection among the following covariates: weight at birth (kg), twinning (0, 1), calving ease (1, 2, 3, and 4), time from birth to feed (min), time from feed to bleed (min), breed (Jersey, Jersey × Holstein), and age at weaning (d). Covariates were included in the model in a forward stepwise selection method whenever the variable effect had $P < 0.15$ or if it had a confounding treatment effect (difference between crude and adjusted estimates of >10%).

The effect of treatment on survival time (time to treatment or death) was modeled using the Cox proportional hazards regression using the Phreg procedure of SAS. Animals that survived or showed no disease for the entire length of the follow-up period were right-censored. Count of treatment days was analyzed using the Genmode procedure of SAS with a zero-inflated negative binomial distribution as it provided the best fit based on the Akaike information criterion. Covariates were included in the model as previously described, and results are reported unadjusted and adjusted; adjusted models had an important reduction in sample size. Reported differences in *P*-values for similar point estimates obtained with unadjusted and adjusted models are mainly differences in power. Differences in estimated probability of no event (zero treatment days), count of treatment days, when it occurred, and their

95% confidence interval were produced at the covariates mean using estimate statements when covariates were included.

Count of treatment days was modeled using a zero-inflated negative binomial, where the zero count was modeled as a separate event than when the count was greater than zero. Therefore, the following parameters were estimated for each group: the probability of having no treatment days (no event) and the mean count of treatment days when the event occurred (treatment days >0). The expected count of treatment days from the mixture of the 2 models was obtained by multiplying the expected counts from the negative binomial model by the probability of getting a nonzero from the zero-inflation model.

RESULTS AND DISCUSSION

To the best of the authors' knowledge, this is the clinical trial with the largest sample size comparing the effect of feeding CR versus MC. All 1,215 calves were used for evaluation of mortality, 1,214 for diarrhea treatment, 1,208 for respiratory disease treatment, 1,211 for fever, 594 for serum TP at 24 h, 592 for serum IgG at 24 h, 96 for calculating AEA of IgG at 24 h, 268 for wean weight, 267 for average daily weight, and 269 for wean height. Descriptive statistics of the calves and colostrum presented by treatment are reported in Table 1. Average weight at birth (kg), time from birth to feed (min), time from feed to bleed (min), and age moved out of hutches (d) were similar between treatments. Most enrolled calves were female Jersey (69.5%) and had a calving ease score equal to 1 (92.8%).

IgG Intake, CC, and TBC

The MC contained an average of 63.6 ± 17.7 mg/mL of IgG. All but 1 of the samples (measuring 1.96 mg/mL) ranged from 22.7 to 96.9 mg/mL, with 80% of the samples ≥50 g/L of IgG. Thus, on average, calves fed MC consumed 178 ± 50 g of IgG, whereas calves fed CR consumed 150 g of IgG. The average Brix value of MC was 20.3 ± 2.9%. The amount of IgG provided to calves by MC is a function of the volume administered and the concentration of IgG. The difference in the amount of IgG provided by both treatments is not as large as if 3.8 L of MC was fed, which is recommended for the Holstein breed. Additionally, although the calves used in this trial were Jersey and Jersey × Holstein, the amount of MC fed as a percentage of BW (approximately 10%) was similar to what is recommended for the Holstein breed.

The cumulative predicted probability of the various levels for CC is reported in Table 2. The cumulative predictive probability for CC to be above a certain value differed between CR and MC ($P = 0.010$) as well as for TBC ($P = 0.027$). The predicted probability of having CC >10,000 cfu/mL was 0.015 for CR and 0.061 for MC, whereas the predicted probability of having CC ≥100 cfu/mL was 0.093 for CR and 0.307 for MC.

Table 1. Descriptive statistics of calves and colostrum presented by treatment[1]

	CR				MC			
Item	n	Mean	SD	Minimum, maximum	n	Mean	SD	Minimum, maximum
Weight at birth, kg	309	29.0	5.4	15.7, 48.3	302	29.5	5.4	15.2, 53.4
Time from birth to feeding, min	606	60.1	1.1	55, 70	609	60.2	1.2	53, 75
Time from feeding to bleeding, h	307	24.8	1.7	21.9, 28.4	299	24.8	1.7	21.9, 28.3
Age moved out of hutches, d	606	53.2	0.8	51, 55	609	53.2	0.8	51, 55
Colostrum IgG, mg/mL	—	—	—	—	53	63.6	17.7	1.96, 96.9[2]
Colostrum Brix, %	—	—	—	—	606	20.3	2.9	10.5, 27.4
	n	%			n	%		
Sex and breed								
Female Jersey	428	70.6			416	68.3		
Female crossbred	80	13.2			82	13.5		
Male crossbred	98	16.2			111	18.2		
Calving ease								
1	567	93.6			561	92.1		
2	10	1.6			10	1.7		
3	8	1.3			8	1.3		
4	21	3.5			30	4.9		
Twin	28	4.6			27	4.4		

[1]CR = colostrum replacer; MC = maternal colostrum.

[2]One sample measured 1.96 mg/mL, whereas the remaining ranged from 22.7 to 96.9 mg/mL.

Table 2. Predicted probability of coliform count (CC) ≥10,000 cfu/mL and >100 cfu/mL and estimated mean of total bacteria count (TBC) for colostrum replacer (CR; n = 53) and maternal colostrum (MC; n = 53)

	CR			MC			
Item[1]	n	Probability	95% CI	n	Probability	95% CI	Treatment effect *P*-value
CC							
≥10,000 cfu/mL	0	0.015	0.004–0.053	4	0.061	0.022–0.157	0.010
>100 cfu/mL	5	0.093	0.039–0.206	12	0.307	0.196–0.445	
TBC ≥100,000 cfu/mL	0	0.0	—	0	0.113	—	0.027
	n	Mean	95% CI	n	Mean	95% CI	Treatment effect *P*-value
TBC,[2] cfu/mL	53	897	578–1,392	53	2,476	996–6,156	0.052

[1]A total of 53 samples were collected for each treatment group.

[2]Data were analyzed on a $\log_{10}$ and then back transformed.

The predicted probability of having TBC >100,000 cfu/mL was 0 for CR and 0.113 for MC. Therefore, MC had higher predictive probability to have higher CC and TBC. Note that no CR samples had CC >10,000 cfu/mL or TBC >100,000 cfu/mL. When a cell has very few observations (<5), the model may become unstable; therefore, caution should be used in interpreting these cumulative predictive probabilities. The mean TBC was 1,579 cfu/mL higher in MC compared with CR ($P = 0.052$). Furthermore, as suggested by the 95% confidence interval in Table 2, the variability in TBC for MC was higher than that for CR. The higher variability in MC was confirmed by the estimated variance of $\log_{10}$ TBC, as it was 4.3 times the estimate for CR (0.503 for CR and 2.16 for MC; data not shown).

The MC in this study was of high quality. When compared with a nationwide evaluation of colostrum quality on 67 farms in 12 states, reported IgG concentrations were ≥50 g/L in 71.6% of the samples (vs. 80.0% in this study), and TBC <100,000 cfu/mL in 54.8% of the samples ranged from 67.0% for fresh samples to 23.0% for refrigerated samples (vs. 88.7% in this study using refrigerated colostrum; Morrill et al., 2012). Despite the lower CC and TBC of MC in this study compared with the MC in the Morrill et al. (2012) study, the probability of calves receiving contaminated liquid feed at first feeding was reduced for calves fed CR compared with calves fed MC. Bacterial contamination of colostrum has been shown to interfere with colostral IgG absorption. In a study including 49 calves, serum IgG was greater for calves fed heat-treated colostrum (22.3 g/L) than for those fed fresh colostrum (18.1 g/L; Johnson et al., 2007). In another trial, Godden et al. (2012) reported a negative correlation between serum IgG and total CC of heat-treated and fresh colostrum. Additionally, when calves received colostrum exceeding a CC of 10,000 cfu/mL, AEA was reduced from 31 to 23% (Lago et al., 2012).

Blood Parameters

The AEA of IgG, serum IgG, and TP at 24 h is reported in Table 3. The AEA did not differ between treatments and was 34.4 ± 1.3% for CR and 35.9 ± 1.9% for MC ($P = 0.522$). Only 1 calf in each treatment group (CR and MC) had FPT (IgG <10 mg/dL). The mean blood concentration of IgG was 19.6 ± 0.17 mg/mL for calves fed CR and 23.4 ± 0.23 mg/mL for calves fed MC, representing a higher blood IgG concentration at 24 h for MC calves ($P < 0.0001$). Similarly, TP was 0.68 g/dL lower (5.16 ± 0.02 for CR and 5.84 ± 0.04 for MC) in calves fed CR compared with MC at 24 h ($P < 0.0001$).

Results evaluating the efficacy of commercial CR to prevent FPT in calves have produced very mixed, and often unacceptable, results. Although studies have reported that feeding commercial CR products was successful (Quigley et al., 2001; Jones et al., 2004; Foster et al., 2006; Pithua et al., 2013; Priestley et al., 2013), other products failed to achieve average concentrations of 10 mg/mL of IgG in serum of calves fed CR (Mee et al., 1996; Quigley et al., 2001; Foster et al., 2006; Smith and Foster, 2007; Swan et al., 2007; Godden et al., 2009; Fidler et al., 2011; Priestley et al., 2013), which is most likely a function of IgG dose provided, source of IgG, and other additives. This is the first study finding the same levels of FTP when feeding a single package of a CR designed to provide 150 g of IgG compared with feeding MC with an IgG concentration representative of the US dairy industry. The extremely high percentage of calves achieving adequate passive transfer in this study may be attributable not only to the quality of the CR and MC fed but also to the compliance achieved on the volume administered, timing of feeding (all calves were fed at 1 h ± 5 min after birth), and hygienic procedures for liquid feed preparation and administration.

Table 3. Effect of colostrum replacer (CR) and maternal colostrum (MC) on calf blood parameters and growth metrics

Item	CR				MC				Treatment effect *P*-value	Model covariates[1]
	n	Mean	SEM	Minimum, maximum	n	Mean	SEM	Minimum, maximum		
Blood at 24 h										
AEA,[2] %	50	34.4	1.3	33.3, 70.9	46	35.9	1.9	32.6, 76.9	0.522	W
IgG, mg/mL	300	19.6	0.17	1.96, 27.4	292	23.4	0.23	1.96, 27.4	<0.0001	W, AW, TBF
Total protein, g/dL	299	5.16	0.02	5.2, 6.6	294	5.84	0.04	5.8, 8.1	<0.0001	W, TBF
Calf growth										
Wean weight, kg	110	47.1	0.52	30.0, 67.5	158	48.6	0.43	33.4, 77.3	0.036	B, TBF, TFB
ADG, kg	110	0.33	0.01	0.08, 0.66	157	0.36	0.008	0.08, 0.67	0.028	AW, TBF, TFB
Wean height, cm	110	76.63	0.28	67.5, 83.8	159	77.11	0.23	66.0, 87.6	0.159	B, C, AW, TBF, TFB

[1]W = weight at birth (kg); AW = age at weaning (d); TBF = time from birth to feed (min); B = breed (Jersey, Jersey × Holstein); TFB = time from feed to bleed (min); C = calving ease (1, 2, 3, and 4).
[2]AEA = apparent efficiency of absorption.

The mean blood concentration of IgG was slightly lower for calves fed CR compared with those fed MC. Similarly, TP were lower in calves fed CR compared with MC at 24 h. However, the AEA of IgG was high for both treatments and did not differ between CR and MC. The slightly higher mean blood concentration of IgG for calves fed MC may have been attributable to a higher IgG intake (178 ± 50 vs. 150 g of IgG, respectively). The AEA of IgG for CR reported in this study is among the highest reported for CR and comparable with colostrum-derived CR (Godden et al., 2009; Place et al., 2010; Pithua et al., 2013; Priestley et al., 2013). Data supporting decreased TP or IgG concentration in serum of CR-fed calves compared with MC-fed calves is lacking. Recent data have suggested that 10 mg/mL of IgG (successful passive transfer) in Jersey calves is achieved at a lower refractometer reading compared with Holstein calves (Morrill et al., 2013, 2015). The decrease in refractometer reading required for Jerseys to achieve 10 mg/mL of IgG in serum compared with Holsteins may be attributable to differences in colostrum composition (i.e., increased protein in Jersey milk). This hypothesis requires further investigation, but a similar mechanism could be at play and explain why calves fed CR achieve successful passive transfer at a lower TP than calves fed MC (i.e., less protein in CR compared with MC). Further, these data may call into question whether traditional refractometer cut-points are appropriate to assess successful passive transfer in CR-fed calves.

Calf Growth

Weight and height at weaning and ADG are reported in Table 3. Calves fed CR weighed 1.5 kg less at weaning ($P = 0.036$) and gained 0.03 kg/d less ($P = 0.028$) during the study period than those fed MC. Height at weaning did not differ between the 2 treatment groups ($P = 0.159$). Similar to our findings, a study conducted in a commercial dairy enrolling 49 calves per treatment found that calves fed MC were heavier than those fed a plasma-derived CR (4.0 kg) and numerically weighed more (1.7 kg) than those fed a colostrum-derived CR (Priestley et al., 2013). Conversely, when poor-quality pooled MC was fed, calves weighed more at weaning when fed a colostrum-derived CR (Aly et al., 2013).

In our study ADG was declared significant; however, the small magnitude of this difference may lack biological or economic significance. If existent, the difference in ADG (and weaning weight) might be attributable to a different nutrient content, growth and immunological factors of MC (Foley and Otterby, 1978; Yvon et al., 1993; Hammon et al., 2000), or higher IgG intake. Some previous studies reported that serum IgG is posi-

tively associated with ADG (Robison et al., 1988; Mee et al., 1996); however, others did not find associations between serum IgG and growth during the first 6 mo of age (Furman-Fratczak et al., 2011).

Treatments

Hazard ratios for calves being treated for diarrhea or respiratory disease or having fever (rectal temperature ≥39.4°C) are reported in Table 4. The hazard ratio for being treated for diarrhea or respiratory disease was not different between treatment groups in unadjusted or adjusted models. Calves who received CR had a 13.5% (hazard ratio MC = 1.135; 95% CI = 0.998–1.292; $P = 0.054$) increase in the hazard ratio to have a fever compared with calves that received MC. For calves assigned to CR and MC, respectively, the proportion of calves being treated for diarrhea (calculated as 1 − predicted probability of not having events) was 85.8 versus 89.0; the proportion for respiratory disease was 55.2 versus 58.6, and the proportion for fever was 80.5 versus 78.8 (Table 5).

Calves fed CR tended to have a lower predicted probability of being treated (Table 5). The predicted probability of being treated for diarrhea was greater for MC calves ($P = 0.091$), but the predicted number of days treated for diarrhea was lower for MC calves ($P = 0.011$). The predicted probability of being treated for respiratory disease and the number of days treated for respiratory disease did not differ between treatments. The overall predicted probability of being treated for either diarrhea or respiratory disease was lower for CR calves ($P = 0.070$), but the sum of diarrhea and respiratory disease was lower for MC calves ($P = 0.048$). The predicted probability of having no fever did not differ between treatment groups ($P = 0.495$). Calves receiving CR had 0.66 more days of fever compared with calves receiving MC ($P = 0.036$) in the adjusted model. The predicted probability of having no fever did not differ between treatment groups.

The lower incidence of diarrhea could be attributable to a lower probability of exposure to disease, as bacteria counts in the CR solution were lower than for MC before feeding. Godden et al. (2012) found that a reduction in bacteria load due to heat treatment was associated with a reduced risk for diarrhea and overall illness as a function of improved serum IgG concentrations. However, when disease was present, CR calves had a higher count of treatment days compared with MC. The authors are not presently aware of similar studies reporting disease duration or treatment days. However, other studies have reported an association between serum IgG and incidence of disease. Aly et al. (2013) found a lower incidence of diarrhea when feeding

Table 4. Effect of colostrum replacer (CR) on calf hazard ratio (HR) to being treated for diarrhea, respiratory disease, or fever

Item	Unadjusted HR[1]			Treatment effect	Adjusted HR[2]			Treatment effect	Model
	n	HR	95% CI	*P*-value	n	HR	95% CI	*P*-value	covariates[3]
Diarrhea	1,214	0.975	0.865–1.100	0.684	1,214	0.974	0.864–1.099	0.674	T
Respiratory disease	1,208	0.931	0.799–1.086	0.364	609	0.876	0.705–1.088	0.230	W
Fever	1,211	1.135	0.998–1.292	0.054	1,211	1.128	0.991–1.283	0.068	T, TBF

[1]Unadjusted HR of CR versus maternal colostrum.
[2]Adjusted HR of CR versus maternal colostrum.
[3]T = twin (0, 1); W = weight at birth (kg); TBF = time from birth to feed (min).

Table 5. Effect of colostrum replacer (CR) and maternal colostrum (MC) on calf predicted probability of not being treated (no events) and estimated count (events) of preweaning treatment days for diarrhea (D), respiratory disease (RD), and fever (F)

Item	CR		MC		Treatment effect *P*-value	Model covariates[1]
	Estimate[2]	95% CI	Estimate	95% CI		
Unadjusted[3]						
D						
No events	0.142	0.116–0.172	0.110	0.087–0.137	0.091	—
Events	11.6	11.2–12.0	10.8	10.5–11.2	0.011	—
RD						
No events	0.448	0.406–0.491	0.414	0.373–0.457	0.266	—
Events	3.78	3.52–4.06	3.72	3.47–3.99	0.761	—
Total (D or RD)						
No events	0.137	0.111–0.167	0.103	0.082–0.130	0.070	—
Events	13.8	13.3–14.3	13.1	12.7–13.6	0.048	—
F						
No events	0.195	0.161–0.233	0.212	0.178–0.252	0.495	—
Events	5.25	4.93–5.60	4.92	4.60–5.25	0.154	—
Adjusted[4]						
D						
No events	0.138	0.103–0.182	0.099	0.070–0.139	0.188	W
Events	11.4	10.9–12.0	10.6	10.1–11.2	0.072	W, AW
RD						
No events	0.458	0.399–0.518	0.406	0.347–0.468	0.279	W
Events	3.79	3.42–4.20	3.66	3.31–4.05	0.563	W, TBF
Total (D or RD)						
No events	0.127	0.093–0.170	0.086	0.059–0.124	0.149	W
Events	13.6	13.0–14.3	12.9	12.9–13.5	0.164	W, AW
F						
No events	0.211	0.164–0.267	0.200	0.152–0.259	0.826	W, TBF
Events	5.35	4.89–5.85	4.69	4.26–5.15	0.036	AW, TBF, C

[1]W = weight at birth (kg); AW = age at weaning (d); TBF = time from birth to feed (min); C = calving ease (1, 2, 3, and 4).

[2]Estimate is the predicted probability of a calf not being treated (no events) or the estimated count of treatment days for treated calves during the preweaning period (events) from negative binomial distribution.

[3]Unadjusted model, n = 1,215 calves.

[4]Adjusted model, n = 611 calves.

a CR; however, Priestley et al. (2013) reported that feeding CR resulted in higher morbidity. Serum IgG levels were inversely related to the incidence of disease in both studies. Serum IgG levels were much higher in CR-fed calves than in MC-fed calves in the study by Aly et al. (2013), and the opposite was observed in the Priestley et al. (2013) study. Conversely, Swan et al. (2007) reported that although a trend was present, the proportion of calves treated for illness was not statistically different for calves fed MC (51.9%) versus CR (59.6%) even though FPT was much higher in CR calves than in MC calves.

Mortality

There were no significant differences in mortality between CR and MC calves. Calves who received CR had numerically higher (hazard ratio MC = 1.347, 95% CI =0.907–2.002; $P = 0.140$) risk of dying compared with calves that received MC. The survival distribution function for both treatments is reported in Figure 1. In the adjusted model, where weight at birth was the

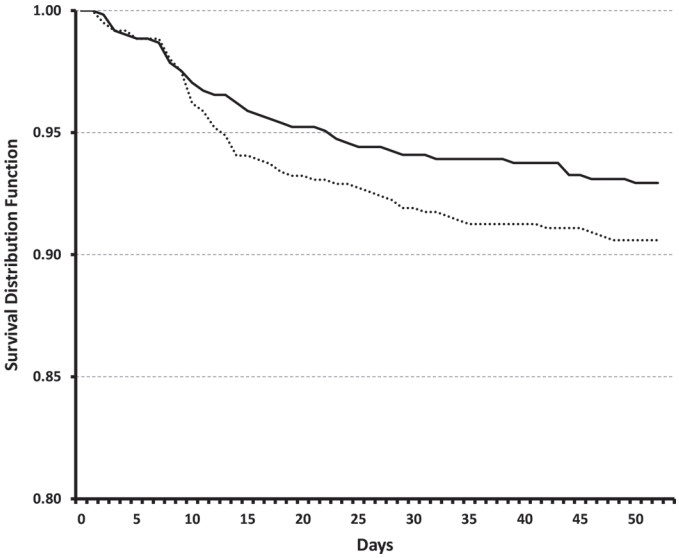

Figure 1. Unadjusted survival distribution functions presented by treatment (dotted line = colostrum replacer, CR; solid line = maternal colostrum, MC). Hazard ratio of MC = 1.347; 95% CI = 0.907–2.002; $P = 0.140$. Unadjusted and adjusted death risk were 9.4% (95% CI = 7.3–12.0) and 8.9% (95% CI = 5.8–12.4) for CR and 7.1% (95% CI = 5.3–9.4) and 5.3% (95% CI = 3.3–8.5) for MC, respectively.

only variable that met the inclusion criteria, the hazard ratio increased to 1.619.

The mortality observed in the present study (7.06% for MC and 9.40% for CR) was within the range of previous reports. Priestley et al. (2013) reported that 8.2% of MC calves and 24.5% of CR calves died before weaning time. However, in the aforementioned study, MC calves averaged 190 g of IgG intake, whereas CR calves were fed only 100 g of IgG, resulting in a high prevalence of FPT. Swan et al. (2007) reported similar mortality for MC (10.0%) and CR (12.4%) even though FPT was much higher in CR calves than in MC calves. Two other studies evaluated the effect of CR on mortality and found no treatment effect (Pithua et al., 2010; Aly et al., 2013).

Strengths and Limitations

The major strengths of this study include (1) the large sample size comparing the effect of feeding CR versus MC, which translates in statistical power to find differences between groups and diminish the risk of spurious findings; (2) the fact that MC fed in this study was high quality, which validates the use of the CR in situations other than when MC is not available or low quality; and (3) compliance with experimental procedures due to the implementation of the study by research technicians. Study limitations include the fact that the study was conducted in only 1 herd, which limits the interpretation of the study results to all herds. Also, calves from the Holstein breed were not included in this study, which limits the comparison of the CR and MC feeding rates recommended for Holstein calves.

CONCLUSIONS

Absorption of IgG and serum concentration of calves were adequate when fed either CR or MC, although calves fed CR had a decrease in serum IgG and TP concentration, had decreased ADG, and were slightly lighter at weaning. Only 1 of the analyzed calves in each treatment group (CR and MC) had FPT. The probability that a calf received contaminated liquid feed at first feeding was reduced for calves fed CR compared with calves fed MC. Finally, CR-fed calves performed similarly in terms of health to calves receiving high-quality MC. Use of CR may result in less exposure to bacterial contamination in early life while resulting in acceptable calf performance. Therefore, the CR evaluated in this study appears to be a valid alternative to MC. Future work is needed to assess long-term effects of early-life CR feeding.

ACKNOWLEDGMENTS

Financial support for this research was provided by Accelerated Genetics (Baraboo, WI), Milk Products Inc. (Chilton, WI), and Zinpro Corporation (Eden Prairie, MN).

REFERENCES

Aly, S. S., P. Pithua, J. D. Champagne, and D. M. Haines. 2013. A randomized controlled trial on preweaning morbidity, growth and mortality in Holstein heifers fed a lacteal-derived colostrum replacer or pooled maternal colostrum. BMC Vet. Res. 9:168.

Chigerwe, M., J. W. Tyler, L. G. Schultz, J. R. Middleton, B. J. Steevens, and J. N. Spain. 2008. Effect of colostrum administration by use of oroesophageal intubation on serum IgG concentrations in Holstein bull calves. Am. J. Vet. Res. 69:1158–1163.

Davis, C. L., and J. K. Drackley. 1998. The Development, Nutrition and Management of the Young Calf. Iowa State University Press, Ames.

Fidler, A. P., M. L. Alley, and G. W. Smith. 2011. Short communication: Serum immunoglobulin G and total protein concentrations in dairy calves fed a colostrum-replacement product. J. Dairy Sci. 94:3609–3612.

Foley, J. A., and D. E. Otterby. 1978. Availability, storage, treatment, composition and feeding value of surplus colostrum: A review. J. Dairy Sci. 61:1033–1060.

Foster, D. M., G. W. Smith, T. R. Sanner, and G. V. Busso. 2006. Serum IgG and total protein concentrations in dairy calves fed two colostrum replacement products. J. Am. Vet. Med. Assoc. 229:1282–1285.

Furman-Fratczak, K., A. Rzasa, and T. Stefaniak. 2011. The influence of colostral immunoglobulin concentration in heifer calves' serum on their health and growth. J. Dairy Sci. 94:5536–5543.

Godden, S. 2008. Colostrum management for dairy calves. Vet. Clin. North Am. Food Anim. Pract. 24:19–39.

Godden, S. M., D. M. Haines, and D. Hagman. 2009. Improving passive transfer of immunoglobulins in calves. I: Dose effect of feeding a commercial colostrum replacer. J. Dairy Sci. 92:1750–1757.

Godden, S. M., D. J. Smolenski, M. Donahue, J. M. Oakes, R. Bey, S. Wells, S. Sreevantsan, J. Stabel, and J. Fetrow. 2012. Heat-treated colostrum and reduced morbidity in preweaned dairy calves: Results of a randomized trial and examination of mechanisms of effectiveness. J. Dairy Sci. 95:4029–4040.

Hammon, H. M, I. A. Zanker, and J. W. Blum. 2000. Delayed colostrum feeding affects IGF-1 and insulin plasma concentrations in neonatal calves. J. Dairy Sci. 83:85–92.

Johnson, J. L., S. M. Godden, T. Molitor, T. Ames, and D. Hagman. 2007. Effects of feeding heat-treated colostrum on passive transfer of immune and nutritional parameters in neonatal dairy calves. J. Dairy Sci. 90:5189–5198.

Jones, C. M., R. E. James, J. D. Quigley III, and M. L. McGilliard. 2004. Influence of pooled colostrum or colostrum replacement on IgG and evaluation of animal plasma in milk replacer. J. Dairy Sci. 87:1806–1814.

Lago, A., J. D. Quigley, J. Polo, and J. Campbell. 2012. The association between colostrum bacteria counts and immunoglobulin absorption, calf growth and mortality. J. Dairy Sci. 95(E-Suppl. 2):395. (Abstr.)

McGuirk, S. M., and M. Collins. 2004. Managing the production, storage, and delivery of colostrum. Vet. Clin. North Am. Food Anim. Pract. 20:593–603.

Mee, J. F., K. J. O'Farrell, P. Reitsma, and R. Mehra. 1996. Effect of a whey protein concentrate used as a colostrum substitute or supplement on calf immunity, weight gain, and health. J. Dairy Sci. 79:886–894.

Morrill, K. M., E. Conrad, A. Lago, J. Campbell, J. Quigley, and H. Tyler. 2012. Nationwide evaluation of quality and composition

of colostrum on dairy farms in the United States. J. Dairy Sci. 95:3997–4005.

Morrill, K. M., J. Polo, A. Lago, J. Campbell, J. Quigley, and H. Tyler. 2013. Estimate of serum immunoglobulin G concentration using refractometry with or without caprylic acid fractionation. J. Dairy Sci. 96:4535–4541.

Morrill, K. M., K. E. Robertson, M. M. Spring, A. L. Robinson, and H. D. Tyler. 2015. Validating a refractometer to evaluate IgG concentration in Jersey colostrum and the impact of multiple freeze-thaw cycles on evaluating colostrum quality. J. Dairy Sci. 98:595–601.

Pithua, P., S. S. Aly, D. M. Haines, J. D. Champagne, J. R. Middleton, and S. E. Poock. 2013. Efficacy of feeding a lacteal-derived colostrum replacer or pooled maternal colostrum with a low IgG concentration for prevention of failure of passive transfer in dairy calves. J. Am. Vet. Med. Assoc. 243:277–282.

Pithua, P., S. M. Godden, J. Fetrow, and S. J. Wells. 2010. Effect of a plasma-derived colostrum replacement feeding program on adult performance and longevity in Holstein cows. J. Am. Vet. Med. Assoc. 236:1230–1237.

Pithua, P., S. M. Godden, S. J. Wells, and M. J. Oakes. 2009. Efficacy of feeding plasma-derived commercial colostrum replacer for the prevention of transmission of *Mycobacterium avium* subsp *paratuberculosis* in Holstein calves. J. Am. Vet. Med. Assoc. 234:1167–1176.

Place, N., A. Bents, K. Leslie, B. Nelson, D. Haines, and S. Godden. 2010. Relationship between serum total protein and serum IgG in Holstein calves fed either a lacteal- or plasma-derived colostrum replacer. Page 193 in Proc. Ann. Conf. AABP, Albuquerque, NM. Am. Assoc. Bovine Pract., Auburn, AL.

Priestley, D., J. H. Bittar, L. Ibarbia, C. A. Risco, and K. N. Galvão. 2013. Effect of feeding maternal colostrum or plasma-derived or colostrum-derived colostrum replacer on passive transfer of immunity, health, and performance of preweaning heifer calves. J. Dairy Sci. 96:3247–3256.

Quigley, J. D., III, and J. J. Drewry. 1998. Nutrient and immunity transfer from cow to calf pre- and postcalving. J. Dairy Sci. 81:2779–2790.

Quigley, J. D., III, R. E. Strohbehn, C. J. Kost, and M. M. O'Brien. 2001. Formulation of colostrum supplements, colostrum replacers and acquisition of passive immunity in neonatal calves. J. Dairy Sci. 84:2059–2065.

Robison, J. D., G. H. Stott, and S. K. DeNise. 1988. Effects of passive immunity on growth and survival in the dairy heifer. J. Dairy Sci. 71:1283–1287.

Smith, G. W., and D. M. Foster. 2007. Short communication: Absorption of protein and immunoglobulin G in calves fed a colostrum replacer. J. Dairy Sci. 90:2905–2908.

Swan, H., S. Godden, R. Bey, S. Wells, J. Fetrow, and H. Chester-Jones. 2007. Passive transfer of immunoglobulin G and preweaning health in Holstein calves fed a commercial colostrum replacer. J. Dairy Sci. 90:3857–3866.

Yvon, M., D. Levieux, M. C. Valluy, J. P. Pelissier, and P. P. Mirand. 1993. Colostrum protein digestion in newborn lambs. J. Nutr. 123:586–596.