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A randomized controlled trial on preweaning morbidity, growth and mortality in Holstein heifers fed a lacteal-derived colostrum replacer or pooled maternal colostrum

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Abstract

Background: The objective of this randomized controlled trial was to determine the effect of feeding a commercial lacteal-derived colostrum replacer (CR) or pooled maternal colostrum (MC) on preweaning morbidity, growth and mortality in Holstein heifer calves. A total of 568 calves were randomly assigned to be fed either 3.8 L of pooled MC or two doses (200 g IgG) of a CR. Calves were monitored daily for preweaning morbidity until weaning at 60 d old. Birth and weaning weights were measured to estimate growth rates.

Results: Calves fed CR were significantly less likely to be affected with a diarrhea event (OR = 0.58; 95% CI, 0.38 to 0.88; P value = 0.011) and had a higher rate of daily weight gain (0.051 kg/day; 95% CI, 0.03 to 0.08; P value <0.001) compared to calves fed pooled MC. Use of lacteal-derived colostrum replacer was not significantly associated with respiratory disease (OR = 1.01; 95% CI 0.67 to 1.51; P value = 0.974), omphalitis (OR = 0.93; 95% CI 0.06 to 14.86; P value = 0.956), or mortality (HR = 0.71; 95% CI 0.27 to 1.92; P value = 0.505) in the study calves.

Conclusions: The lacteal-derived CR fed at the study dose was a viable colostrum alternative in the event of poor quality pooled MC for the prevention of preweaning diarrhea and resulted in higher growth rates in comparison to calves fed pooled MC in the study herd.

Keywords: Lacteal-derived colostrum replacer, Pooled maternal colostrum, Calf morbidity, Daily weight gain

Background

Bovine maternal colostrum (MC) contains immune factors that provide a critical first line of defense against a variety of infectious pathogens to which calves become exposed after birth [1]. There is consensus in the literature that at least 3.8 L of good-quality MC (IgG >50 g/L and Total Plate Counts, TPC <100,000 cfu/mL) should be administered to prevent failure of passive transfer (FPT) of immunity, a condition characterized by serum IgG < 10 g/L ≥ 24 h post colostrum ingestion in calves [2-4]. Failure of passive transfer of immunity is a well-

recognized risk factor for increased preweaning calf morbidity and mortality [5-8]. The condition has also been associated with milk yield losses and decreased longevity in lactating adult cows [5,6].

Adequate intake of MC is critical for preventing FPT and its negative consequences on calf health and future production performance. Several studies have confirmed the presence of bovine specific pathogens (e.g. *Escherichia coli*, *Salmonella* sp., *Mycoplasma* sp., bovine leukemia virus, and *Mycobacterium avium* subsp. *paratuberculosis*) in MC suggesting that feeding raw MC is an early means by which newborn calves can become exposed to such pathogens [9-15]. In addition, negative correlations have been reported between bacterial contamination levels in colostrum and post-feeding serum IgG concentrations [3,16]. Hence, feeding colostrum of inferior quality (IgG < 50 g/L and TPC > 100,000 cfu/mL) can exacerbate the risk

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of FPT in calves and compromise preweaning performance [3].

Colostrum replacers derived from either spray-dried bovine plasma or spray-dried cow colostrum are formulated to provide ≥ 100 g of IgG to calves when ingested at the replacer dose [17]. Specific heat treatment must be utilized along with spray-dry processing of the plasma or colostrum to effectively destroy all pathogens present in MC [18]. Therefore, CR products have the potential to limit calf exposure to bovine pathogens that may be shed or contaminate MC and are indicated for calves when quality or quantity (or both attributes) of raw MC may be compromised.

Previous IgG absorption studies on various CR products yielded conflicting results [19-22]. In addition, studies that report a positive association between bovine lacteal or serum based CR products and adequate transfer of immunity in calves rarely include an assessment of preweaning morbidity and performance [19-21]. In one Minnesota study, 93% of calves fed a plasma-derived CR product (125 g of IgG) after birth experienced FPT compared with 28% of calves fed MC [19]. Even so, preweaning morbidity and mortality risks did not differ between groups in this study [22]. Several studies reported that feeding a higher IgG mass (≥ 200 g of IgG) delivered using CR products resulted in greater IgG absorption and lower FPT risks [19,20,23]. However, these studies did not evaluate post-administration performance in terms of preweaning morbidity and mortality risks, feed intake, and weight gain for calves fed larger masses of IgG in the CR products evaluated.

We recently completed a study comparing IgG and serum total protein (TP) in calves fed pooled MC or lacteal-derived CR [24]. In that study, serum TP and IgG concentrations at approximately 24 hours post-colostral intake were significantly lower for calves fed pooled MC (TP = 4.77 g/dL, SD = 0.55; IgG = 7.50 g/L, SD = 5.0) compared to calves fed CR (TP = 5.50 g/dL, SD = 0.52; IgG = 15.15 g/L, SD = 4.75). Colostrum IgG concentration and mass fed were significantly higher in the CR (71.4 g/L; 200 g, respectively) compared with MC group (21.08 g/L, SD = 9.77; 79.79 g, SD = 36.96, respectively). The apparent efficiency of IgG absorption (AEA) was similar for calves fed MC (28.79%, SD = 2.098) or CR (26.98%, SD = 1.65). A significantly higher proportion of calves fed MC (188/269 [70%]) suffered from FPT (serum IgG < 10 g/L) compared with calves fed CR (32/292[11%]) ($P < 0.001$). However, producers are often interested not only in passive transfer of immunity in calves, but also in preweaning health and growth rates. The objective of this randomized trial was to determine the effect of feeding a higher dose of a commercial lacteal-derived CR or pooled MC on preweaning morbidity, daily weight gain and mortality in Holstein heifer calves.

Results

Descriptive data

In total, 568 newborn calves were enrolled in the study. Of these, 273 (48%) were fed pooled MC while 295 (52%) were fed lacteal derived-CR. Calves did not significantly differ in birth weight, precolostral serum IgG or total protein between trial groups (P value > 0.05). In addition, calves fed MC or CR did not differ in time to separation from dam (2.35 hours (SD = 2.42) and 2.34 (SD = 2.42), respectively) and time to feeding colostrum (3.99 hours (SD = 2.31) and 4.12 hours (SD = 2.25), respectively).

Preweaning health and mortality events and the mean birth and weaning weights are summarized in Table 1. The proportion of calves with diarrhea, and those treated with antibiotics were significantly higher for calves fed pooled MC compared with calves fed lacteal-derived CR. However, the proportions of calves with respiratory disease, omphalitis or those that died in the preweaning period were similar between groups (CR vs. pooled MC, Table 1). The preweaning mean daily weight gain was significantly higher ($P < 0.0001$, Table 1) in calves fed lacteal-derived CR compared with calves fed pooled MC.

Multivariable models

Heifer calves fed lacteal-derived CR were significantly less likely to experience a preweaning event of diarrhea ($OR = 0.58$; 95% CI = 0.38 to 0.88) (Table 2). Similarly, calves fed lacteal-derived CR were less likely to be treated with antibiotics during the preweaning period ($OR = 0.66$; 95% CI = 0.47 to 0.93), compared with calves fed pooled MC. While calves fed 200 g IgG in lacteal-derived CR (vs. pooled MC) at birth experienced significantly higher preweaning mean daily weight gain by 0.051 kg/d (95% CI = 0.026 to 0.075; P value < 0.001), the risk of respiratory disease and omphalitis was not dependent on the type of colostrum fed (Table 2). In addition, the Hazard Rate Ratio (HRR) estimated from the Cox proportional hazard model showed that there was no significant effect of type of colostrum fed on the hazard for mortality (HRR = 0.71; 95% CI = 0.27 to 1.92; $P = 0.505$).

Based on findings from this study, we estimate that routine feeding of 200 g of IgG (formulated as the current lacteal-derived CR powder) instead of pooled-MC could eliminate approximately one-fifth of the cases of diarrhea (Population Attributable Fraction, PAF = 0.21; 95% CI = 0.03 to 0.35) and approximately one-tenth of the number of antibiotic-treated calves (PAF = 0.12; 95% CI 0.02 to 0.22) in this population (Table 3).

Discussion

As reported elsewhere [24], a significantly higher proportion of calves fed pooled-MC (70%) suffered from

Table 1 Comparison of preweaning morbidity, growth and mortality in a randomized trial of the effect of feeding a lacteal-derived colostrum replacer (CR) or pooled maternal colostrum (MC) in calves

	Treatment group								P value
	Lacteal-derived CR				Pooled MC				
	Estimate	n	95% Confidence interval		Estimate	n	95% Confidence interval		
			Lower	Upper			Lower	Upper	
Number of calves enrolled	295				273				
Preweaning health events									
Diarrhea (%)	15.9	47	11.8	20.1	24.5	67	19.4	29.6	0.011
Respiratory disease (%)	21.4	63	16.7	26.0	21.2	58	16.4	26.1	0.974
Omphalitis (%)	0.3	1	0.0	1.0	0.4	1	0.0	1.1	0.956
Treatment with antibiotics (%)	33.6	99	28.2	38.9	43.2	118	37.3	49.1	0.018
No health events or treatments (%)	63.4	187	57.9	68.9	54.2	148	48.3	60.1	0.026
Preweaning mortality/100 calves, 60-day follow-up period	2.4	7	0.6	4.1	3.3	9	1.2	5.4	0.506
Mean birth weight (kg)	39.1	293	38.5	39.7	39.4	269	38.8	40.1	0.452
Weaning weight (kg)	58.9	275	57.9	59.8	57.0	248	56.0	57.9	0.006
Mean daily weight gain (kg/day)	0.405	274	0.388	0.422	0.355	247	0.337	0.372	<0.001

FPT (serum IgG < 10 g/L) in comparison to calves fed lacteal-derived CR (11%). Failure of passive transfer of immunity is a well-recognized predictor for increased preweaning calf morbidity [5-8]. It is therefore not surprising that calves fed raw pooled MC in this study were more likely to be treated with antibiotics or experience preweaning event of diarrhea compared with calves fed lacteal-derived CR in the study herd.

Bovine specific pathogens (*Salmonella* sp., *Escherichia coli*, *Mycoplasma* sp.) are frequently shed in colostrum of infected fresh cows either during an epidemic or intermittently during the peripartum period [3]. It is possible that the higher proportion of diarrhea in preweaned calves fed pooled MC (vs. lacteal-derived CR)

was a consequence of direct ingestion of such pathogens in pooled MC. However, this theory could not be further investigated given that culture of the pooled MC samples for specific pathogens (example *Salmonella* sp., *Escherichia coli*, *Mycoplasma* sp.) was not performed in the current study.

Our results indicate that only 21% of diarrhea cases and 12% of antibiotic-treated calves would be eliminated in this population if the pooled MC feeding program was replaced by 200 g IgG/ calf delivered in a lacteal-derived CR product. This should not be surprising given that in replacement heifer rearing, improved preweaning health is a function of several factors including reducing calf exposure to risk factors (infectious agents inclusive).

Table 2 Final model estimates for preweaning morbidity and mortality events in a randomized trial of the effect of feeding a lacteal-derived colostrum replacer (CR) compared to pooled maternal colostrum (MC) in calves

Outcome	Type of colostrum	Number of calves		β coefficient (SE)	P value	OR* (95% CI)
		At risk	Events			
Diarrhea	Lacteal-derived CR	295	47	-0.540 (0.212)	0.011	0.58 (0.38 to 0.88)
	Pooled MC	273	67	Reference	-	
Respiratory disease	Lacteal-derived CR	295	63	0.007 (0.205)	0.974	1.01 (0.67 to 1.51)
	Pooled MC	273	58	Reference	-	
Omphalitis	Lacteal-derived CR	295	1	-0.078 (1.417)	0.956	0.93 (0.06 to 14.86)
	Pooled MC	273	1	Reference	-	
Treatment with antibiotics	Lacteal-derived CR	295	99	-0.410 (0.174)	0.018	0.66 (0.47 to 0.93)
	Pooled MC	273	118	Reference	-	
Healthy calves**	Lacteal-derived CR	295	187	0.380 (0.171)	0.027	1.46 (1.05 to 2.05)
	Pooled MC	273	148	Reference	-	

* OR is the ratio of the odds of outcome in calves fed lacteal-derived CR to the odds of outcome in calves fed pooled maternal colostrum.

** Calves raised from birth to weaning without morbidity or treatment with antibiotics.

Table 3 Population Attributable Fraction (PAF) for feeding raw pooled maternal colostrum compared to a lacteal-derived colostrum replacer at birth to Holstein heifer calves on a California dairy on preweaning diarrhea and treatment with antibiotics in a randomized trial

Item	PAF		P value
	Estimate (%)	95% Confidence interval	
Diarrhea	21	3.3 to 35	0.021
Treated with antibiotics	12	1.5 to 22	0.026

This can be accomplished through proper housing, ventilation, and general hygiene; increasing levels of specific and non-specific immunity through providing good quality colostrum, balanced nutrition, stress minimization; and boosting specific resistance through preventive vaccinations of either the dams or newborn calves against specific pathogens [22,25,26]. Calves in the present study were housed in raised individual wooden hutches up to 60 d of age and maintained on preweaning diets of milk replacer, calf starter grain, and fresh water ad libitum. While a number of calf management practices were in place to reduce calf exposure to risk factors for disease in the current herd, it is possible that some yet unidentified factor (unrelated to pooled MC) may have contributed to the additional risk of diarrhea (e.g. compromised sanitation) leading to increased antimicrobial use on this specific farm.

The overall finding that calves fed raw pooled MC (vs. lacteal-derived CR) were more likely to be treated with antibiotics or experience preweaning diarrhea differed from a previous report [22]. Swan et al. reported no difference in post-feeding morbidity risk observed between calves fed a plasma-derived CR compared with calves fed individual maternal colostrum (i.e. non-pooled colostrum) [22]. In contrast, another study found significantly lower morbidity risk for calves fed MC (46.9%) compared with calves fed a lacteal-derived CR (67.3%) [27]. Although not statistically significant, Priestley et al. reported that a greater proportion of calves fed a lacteal-derived CR experienced diarrhea (44.9%) compared to calves fed MC (28.6%) [27,28]. Although some studies have found no link between FPT and the risk of treatment for diarrhea in beef calves, a possible reason for the difference in findings could be the higher proportion of FPT in calves fed MC in the current study, and in calves fed a lacteal-derived CR (vs. MC) in the Priestley et al. study [27-29]. The difference in FPT is likely to be due to better quality MC fed to calves in the aforementioned studies compared to the current study [22,27]. In a recent survey, 41% of individual colostrum samples met industry recommended colostrum quality benchmarks

(IgG >50 g/L and TPC <100,000 cfu/mL) compared with only 26% of pooled colostrum samples [30,31]. The mean IgG mass in the pooled MC fed to the calves in this study was approximately 21 g/L compared with approximately 69.7 g/L of IgG reported for non-pooled colostrum in the recent survey of colostrum quality [24,30].

While there were no differences in the proportion of preweaning respiratory disease, omphalitis or death in calves fed lacteal-derived CR compared to those fed pooled MC, mean daily weight gain was significantly higher in the former. This reflected perhaps a general benefit accruing from the improved preweaning health outcomes associated with feeding lacteal-derived CR rather than a direct role in enhancing daily weight gain in the study calves [2]. Such a link between reduced morbidity and increased weight gain was also reported in a Florida study, although unlike in the current study, the Florida study reported reduced morbidity in calves fed MC compared to those fed a lacteal-derived CR [27,28].

In the current study, type of colostrum fed (CR versus MC) had no effect on mortality risk between birth and weaning in the study calves. These results are consistent with results from an earlier study in which feeding a plasma-derived CR (vs MC) had no effect on preweaning mortality [22]; however they differed from the Florida study which found a significantly lower proportion of mortality in calves fed MC compared to calves fed a lacteal-derived CR [27]. These contradictions may reflect the fact that in concert with passive transfer of immunity, calf survival in the preweaning period is a function of several herd factors including housing and nutrition.

Although a major strength of this study included its randomized assignment of treatment, the results presented here must be interpreted cautiously. It is possible that the ability to correctly assign a disease diagnosis (i.e. diarrhea, respiratory disease, omphalitis) varied among the study personnel involved in the care of the calves during the follow-up period. This potential bias, if present, was likely to be non-differential because the study personnel were blinded to treatment group assignment (lacteal-derived CR vs. pooled MC). Moreover, a veterinarian (SA) cross-validated each recorded diagnosis and treatment with the herd veterinarian's drug protocols. The extent to which this study's results can be extrapolated to a wider population of dairy herds is limited by the use of a single herd to evaluate the current study objectives. While approximately 57% of large dairy operations in the US routinely feed pooled MC [31], the current herd was not representative of this wider population with respect to FPT risk profiles and quality of pooled MC fed. Recent findings [32] suggest that approximately 23% of calves in US operations that fed pooled MC experienced FPT compared with 70% of calves fed the pooled MC in this study. In addition, the mean IgG mass in the pooled MC fed to the calves in this study

was 3-fold lower than similar estimates of IgG concentration in nationally representative samples of pooled MC [30]. The lower quality of the pooled MC fed to calves in this study compared to comparable US herds likely biased the morbidity outcomes in a direction suggestive of a better efficacy for the lacteal-derived-CR for improving preweaning health in calves. Hence, it is possible that the benefits of feeding lacteal-derived CR (vs. pooled MC) on preweaning health may not be similar in dairy herds managed under a different husbandry system.

The findings reported here indicate that producers should adopt colostrum management strategies that improve colostrum quality. To achieve this, producers can begin by pooling only colostrum with acceptable immunoglobulin concentration (>50 g/liter IgG). This can be achieved by testing individual cow colostrum samples prior to pooling and by properly identifying dams so that first milking colostrum is pooled separate from colostrum harvested from subsequent milkings. Alternatively, pooling colostrum can be replaced by feeding a colostrum replacement product with a known immunoglobulin concentration. Other recommendations identified from previous research should also be followed such as observing proper sanitation and hygiene during harvesting, processing, and storage of colostrum, feeding colostrum replacement products or heat-treated colostrum [2,3,33].

Conclusions

In this study, calves fed CR had a significantly higher rate of daily weight gain and were less likely to be affected with diarrhea compared to calves fed MC. Type of colostrum fed was not predictive of the preweaning risks for pneumonia and mortality in this particular herd. Although a major strength of this study included its randomized design, the extent to which the current findings can be extrapolated to a wider population of dairy herds may be limited by the use of a single herd.

Methods

This study was approved by the Institutional Animal Use and Care Committee at the University of California, Davis and the University of Missouri –Columbia (Protocol # 6439).

Herd selection criteria

This study was conducted in a 3,600 milking Holstein dairy in California that routinely fed 3.8 L of raw pooled MC to newborn calves. The study herd was selected based on its large size, maintenance of electronic records through participation in the California Dairy Herd Information Association routine milk testing and willingness of the owner to comply with the study requirements. Monthly bulk tank milk cultures conducted over the

12 months prior to the study were negative for *Mycoplasma* species by culture on Hayflick medium and enrichment broth.

Feeding protocols and experimental design

A total of 568 newborn calves were enrolled in the study between September and December, 2010 while the follow up period ended in March 2011. Pregnant dams were moved to a group calving pen approximately 3 d prior to the expected calving date and monitored until calving. Heifer calves born between 6 AM and midnight were separated from their dams immediately after birth. Cows calving otherwise were monitored by the dairy's night shift staff and newborn calves were removed immediately after birth to the holding pen until fed the assigned colostrum type by study personnel the following morning. Once in the holding pen, each calf had its navel dipped in an iodine-based antibacterial solution, its ear tagged and its dam ID recorded on farm paper records.

Calves were randomized to one of two treatment groups and fed either 3.8 L of raw pooled MC (control group, $n = 273$) or two doses of a lacteal-derived CR (Land O Lakes Colostrum Replacement, Lake O Lakes Animal Milk Products) (treatment group, $n = 295$). The CR was reconstituted based on the manufacturer's instructions as follows. Each package (100 g IgG/dose) of the lacteal-derived CR powder was dissolved in 1 L of warm water (approx. 49°C) yielding a mixture of 1.4 L containing 71.4 g/L of IgG. Maternal colostrum was harvested after morning milking sessions within 1 to 12 h of calving, pooled and refrigerated at 4°C until feeding within 6–12 h of collection. Both the lacteal-derived CR and pooled MC were administered as a single oral dose (CR ~2.8 L and MC ~3.8 L) within 6 h of birth. All calves were fed using a bottle nipple. However, when a calf failed to ingest some or all of the colostrum quantity, an esophageal tube feeder was used to deliver the complete dose in lieu of the bottle.

Following feeding, each calf was housed in an individual raised wooden hutch until weaning at approximately 60 d of age. During the preweaning period, calves were fed daily diets consisting of 2 L of pasteurized hospital pen milk, clean water and a starter grain mix.

Enrollment and preweaning health monitoring

Before feeding the assigned colostrum type, calves were bled for serum IgG and TP concentration estimation. Calves were also weighed (kg) at birth and weaning which occurred at approximately 60 days of age. Other data recorded included dam identification, colostrum type fed (lacteal-derived CR or pooled MC), birth date, time from birth to separation from dam (h), time from birth to colostrum feeding (h), quantity of colostrum fed

(L) and whether or not an esophageal tube feeder was used to administer the colostrum.

Calf morbidity from birth to weaning were monitored and recorded daily by trained study personnel including study authors (SA and JC) while blinded to the type of colostrum fed (lacteal-derived CR or pooled MC) at enrollment. For uniformity in morbidity recordings the following working definitions were applied based on a modification of the University of Wisconsin Calf Health Scoring Chart (http://www.vetmed.wisc.edu/dms/fapm/fapmtools/8calf/calf_health_scoring_chart.pdf): (I) diarrhea was indicated in calves that voided abnormal feces with watery consistency and foul smell (score 2 or 3) with or without dehydration or elevated body temperature ($\geq 40^{\circ}\text{C}$), (II) respiratory disease was reported for calves that exhibited increased respiratory rate, nasal discharges, or cough (score 1, 2 or 3 except no attempt was made to induce a cough) with or without an elevated body temperature ($\geq 40^{\circ}\text{C}$), (III) omphalitis (navel infections) was associated with presence of overt umbilical inflammatory signs, including heat, swelling, purulent discharges, or evidence of pain on palpation of the umbilical area. Furthermore, a calf's joints were physically examined for heat if a joint or umbilicus appeared enlarged. Treatments including antibiotics administered by the dairy's staff to the study calves were recorded on a daily basis. No specific treatment protocols were developed for this study. Instead, dairy staff relied on protocols implemented by the herd veterinarian. All morbidity events and treatments recorded were validated by a veterinarian (SA).

Statistical analysis

An estimate for daily weight gain (DWG) for each calf was calculated using the following formula: $\text{DWG} = (\text{WWT} - \text{BWT}) / T$; where DWG = Daily weight gain (kg), WWT = weaning weight (kg), BWT = birth weight (kg), T = age of the calf at weaning (d). Mean \pm standard error of the mean (SEM) for birth weights, weaning weights, and daily weight gains were calculated. The proportion of calves with an event of diarrhea, respiratory disease, omphalitis, and treated with antibiotics during the preweaning period were calculated for each group (lacteal-derived CR vs. pooled MC). Similarly, the proportion of healthy calves defined as the proportion of calves that did not experience a morbidity event and were not treated with antibiotics from birth to weaning was compared between the study groups. The distribution of the preceding variables between groups (lacteal-derived CR vs. pooled MC) was tested using *t*-tests for continuous variables (birth weight, weaning weights and daily weight gain) and Pearson χ^2 -test for categorical variables (diarrhea, respiratory disease, omphalitis, and preweaning treatments with antibiotics, healthy calves, and death).

The association between type of colostrum fed (lacteal-derived CR vs. pooled MC) and diarrhea, respiratory disease, omphalitis, treatment with antibiotics, or producing a healthy calf from birth to weaning were investigated by fitting 5 separate logistic regression models to the data for each outcome. Birth weight and the method by which colostrum was fed (tube vs. bottle feeding) were presented to each model as additional independent variables in a manual forward stepwise selection procedure. Variables that significantly improved model fit based on the Akaike Information Criterion (AIC) values and likelihood ratio test $P < 0.05$ were retained or else excluded from the final models. Population attribution fractions for lacteal-derived CR as a predictor of diarrhea, and treatment with antibiotics in the study calves were estimated separately. Population attributable fractions were estimated using the approach of Greenland and Drescher [34].

Next, to quantify the effect of feeding a lacteal-derived CR (vs. pooled MC) on preweaning time (d) to death, a Cox proportional hazards regression model was fitted to the preweaning mortality data to compare the hazard rate (HR) for mortality in calves fed CR to the HR in calves fed MC using the HRR [35]. Graphical evaluation of the Cox proportional hazard assumption for the treatment group (pooled MC vs. lacteal-derived CR) variable revealed no evidence of violation of the proportional hazards assumption [36].

Finally, a simple least-squares regression model was fitted to the data to evaluate the effect of treatment (lacteal-derived CR (vs. pooled MC) on daily weight gain. Data was analyzed using standard software (Stata[®] Corp., College Station, TX, USA). A 5% level of significance was indicative of statistical significance.

Competing interest

Dr. Haines is affiliated with The Saskatoon Colostrum Co. Ltd., the manufacturer of the product kindly donated for the purpose of this study. Her participation did not influence or bias the performance or presentation of the research described in this manuscript in any way.

Authors' contributions

SSA, conducted the study, supervised the experiments, performed statistical analysis, and wrote the manuscript. PP conceived the study design, obtained funding for the study, and was actively involved in interpreting the data and writing the manuscript. JDC was actively involved in assisting with supervision of the experiment and data collection. DMH assisted with data interpretation. All authors reviewed and approved the final manuscript.

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