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

Patrick Pithua, BVM, PhD; Sharif S. Aly, BVSc, MPVM, PhD; Deborah M. Haines, DVM, PhD; John D. Champagne, DVM, MPVM; John R. Middleton, DVM, PhD, DACVIM; Scott E. Poock, DVM, DABVP

Objective—To compare the efficacy of a lacteal-derived colostrum replacer (LDCR) for the prevention of failure of passive transfer of immunity (FPT) in calves with that of pooled maternal colostrum (MC).

Design—Randomized field trial.

Animals—568 heifer calves from 1 California dairy.

Procedures—Calves were randomly allocated to 1 of 2 treatment groups and fed 2 doses (200 g of IgG) of an LDCR or 3.8 L of pooled MC. From each calf, blood samples were collected before and approximately 24 hours after treatment. Serum IgG and total protein (TP) concentrations were quantified with standard methods, and the apparent efficiency of IgG absorption was calculated.

Results—At 24 hours after treatment, mean serum TP and IgG concentrations were significantly lower for calves fed pooled MC (TP, 4.77 g/dL; IgG, 7.50 g/L), compared with those for calves fed the LDCR (TP, 5.50 g/dL; IgG, 15.15 g/L). Calves fed the LDCR were 95% less likely to develop FPT (OR, 0.05; 95% confidence interval, 0.03 to 0.08) than were calves fed pooled MC. However, the mean IgG concentration in the pooled MC fed during the study (21.1 g/L) was substantially lower than that (64.3 g/L) determined for representative samples of pooled MC from other southwestern US dairies during a national survey.

Conclusions and Clinical Relevance—Results indicated that, on this particular dairy, calves fed an LDCR were at less risk of developing FPT than were calves fed pooled MC. The LDCR evaluated was a viable alternative for the prevention of FPT in calves. (J Am Vet Med Assoc 2013;243:277–282)
a plasma-derived colostrum replacer developed FPT, whereas only 28% (67/239) of calves fed MC developed FPT. Results of other studies,1,14 in which sufficient colostrum replacer was fed to provide each calf with 150 to 200 g of IgG, suggest that colostrum replacer is effective for the prevention of FPT, although the sample sizes in those studies was relatively small (ie, ≤ 22 calves/treatment group). Although approximately 57% of US dairies with ≥ 500 cows routinely feed pooled MC to calves,15 field trials conducted to compare the efficacy of colostrum replacers with that of pooled MC for the prevention of FPT in dairy calves are lacking. The objective of the study reported here was to compare the efficacy of an LDCR with that of pooled MC for the prevention of FPT in dairy calves on a large commercial dairy as determined by measurement of serum IgG and TP concentrations and calculation of the apparent efficiency of IgG absorption at approximately 24 hours after colostrum ingestion. The relative risk of FPT and the population attribution fraction of LDCR on FPT were also calculated.

Materials and Methods

Animals—All study protocols were reviewed and approved by the University of Missouri Animal Use and Care Committee. The study was conducted on a 3,600-cow dairy located in central California. This dairy was selected for the study on the basis of its large size, electronic records available through participation in the Dairy Herd Improvement Association’s milk testing program, and the owner’s interest and willingness to comply with the study protocol. On this dairy, calves were routinely fed 3.8 L of pooled MC within 12 hours after birth by means of a nipple bottle.

Newborn heifer calves were enrolled in the study between September and December 2010; bull calves were excluded from the study. Pregnant cows were moved to a group pen approximately 3 days before their expected calving date and were closely monitored until calving. Calves were separated from their dams within 6 hours after birth and prior to suckling their own dam or other cows in the pen. The calves were then randomly allocated to be fed either LDCR or pooled MC.

Sample size calculation—To calculate the number of calves that would need to be enrolled in the study, assumptions for the incidence rates of FPT in calves fed LDCR (10%) and pooled MC (19%) were made on the basis of results of another study,13 in which null calves were fed MC from their own dam or 1 dose of the same LDCR that was used in the study reported here. Other assumptions for the calculation included a type 1 error rate of 0.05 and ≥ 80% power, and the results indicated that 474 calves (237 calves/treatment group) would need to be enrolled in the study.

Study design—Calves were randomly allocated to receive 1 of 2 treatments (LDCR or pooled MC) in accordance with a treatment randomization list. Prior to study initiation, random permuted blocks were used to generate a treatment randomization list, which was then sealed with opaque sticky notes and provided to the herd personnel responsible for administering treatments to calves. As calves were born, the sticky notes were sequentially removed from the list to reveal the treatment assignment for each calf.

Calves in the treatment group were fed 2 packages of an LDCR10 that was mixed in accordance with the manufacturer’s instructions. Briefly, the powder in each package (1 dose; 100 g of IgG/dose) was dissolved in 1 L of warm water (approx 49°C), which yielded 1.4 L of a mixture that contained 71.4 g of IgG/L (ie, the treatment consisted of 200 g of IgG in a 2.8-L mixture of LDCR and water). Calves in the control group were fed approximately 3.8 L of pooled MC. Typically, colostrum was harvested from cows within 1 to 12 hours after calving. The colostrum from 5 to 10 cows was mixed together in a bulk storage tank and stored at 4°C until fed to the control calves, which was generally within 6 to 12 hours after collection. To each calf, the assigned treatment (LDCR or pooled MC) was administered as a single feeding within 6 hours after birth by means of a nipple bottle. Calves that failed to nurse the entire treatment volume were administered the remaining volume with an esophageal feeder.

Data and sample collection and processing—For each calf, dam identification, calf identification, date of birth, age at treatment, and treatment administered (LDCR or pooled MC) were recorded by a technician. Blood samples were collected through jugular venipuncture into 10-mL blood tubes3 that contained no preservative prior to and at approximately 24 hours after treatment for determination of serum TP and IgG concentrations. Additionally, for each calf in the control group, 20-mL samples of the pooled MC fed to that calf were collected for determination of IgG concentration.

Clotted blood samples were centrifuged1 at 1,000 × g for 15 minutes. A 5-mL aliquot of serum was obtained from each sample and stored at −20°C. Upon completion of the trial, the frozen serum and pooled MC samples were shipped on ice to a veterinary diagnostic laboratory4 for quantification of serum TP and IgG concentrations. Serum TP concentrations were measured with a temperature-compensating digital refractometer.5 The concentration of IgG in serum and pooled MC samples was quantified by a single radial immunodiffusion assay as described.16,17

Statistical analysis—Data were analyzed with standard statistical software,1 and values of P < 0.05 were considered significant. For each calf, the apparent efficiency of IgG absorption was defined as the percentage of IgG fed that was absorbed into the calf’s circulation and was calculated as described,18 with the assumption that plasma volume was equal to 9.9% of the calf’s birth weight. For each treatment group, descriptive statistics (mean ± SD and range) for birth weight, age at separation from dam, age at treatment, IgG concentration in treatment, amount of IgG fed, serum TP and IgG concentrations before and at 24 hours after treatment, and apparent efficiency of IgG absorption as well as the proportions of calves fed with an esophageal feeder and calves with FPT (serum IgG concentration, < 10 g/L) were calculated.

Histograms plots for continuous variables (ie, IgG concentration in treatment, amount of IgG fed, serum TP
and IgG concentrations prior to and after treatment, and apparent efficiency of IgG absorption) were generated and visually inspected to determine whether each variable was normally distributed. For skewed variables (eg, apparent efficiency of IgG absorption), a logarithmic transformation was applied to the data to normalize its distribution prior to analysis. For each continuous variable, the means for the treatment groups (LDCR or pooled MC) were compared with a t test. The association between the categorical outcome FPT and treatment group was evaluated with a Pearson $\chi^2$ test.

The effect of treatment group on the respective outcomes of serum TP concentration 24 hours after treatment, serum IgG concentration 24 hours after treatment, and apparent efficiency of IgG absorption was evaluated by generalized linear regression with the specification of an identity link function. Univariate logistic regression by generalized linear regression with the specification of a binomial family and logit link function was used to evaluate the effect of treatment group on the incidence of FPT and to calculate the population attribution fraction for LDCR on FPT.

To evaluate whether serum TP concentration 24 hours after treatment was associated with adequate passive transfer (ie, serum IgG concentration $\geq 10$ g/L), a linear regression model was used, in which serum IgG concentration 24 hours after treatment was the outcome variable and serum TP concentration 24 hours after treatment and treatment group were the independent variables. Results of the initial model suggested that there was a significant ($P < 0.001$) interaction between treatment group and serum IgG concentration. Consequently, a significantly higher proportion of calves in the control group (188/269 [70%]) had FPT (serum IgG concentration $< 10g/L$), compared with the proportion of calves in the treatment group (32/292 [11%]) with FPT. Thus, calves fed the LDCR were 95% less likely (OR, 0.05; 95% confidence interval, 0.03 to 0.8) to develop FPT than were calves fed pooled MC, and the population attribution fraction for LDCR was 72% (95% confidence interval, 63% to 79% [ie, for calves in the treatment group, 72% of the reduced risk for developing FPT was directly attributable to the LDCR]). However, the apparent efficacy of IgG absorption did not differ significantly between the treatment and control groups.

The regression equation for serum IgG concentration as a function of serum TP concentration was $(7.6 × \text{serum TP concentration}) − 27.3$. For calves fed LDCR ($R^2 = 0.60$; $P < 0.001$), and $(7.7 × \text{serum TP concentration}) − 28.5$ for calves fed pooled MC ($R^2 = 0.68$; $P < 0.001$; Figure 1). Therefore, at 24 hours after treatment, a serum TP concentration $\geq 4.9$ g/dL in calves fed the LDCR and $\geq 5$ g/dL in calves fed pooled MC was predictive of adequate passive transfer (serum IgG conc-

Table 1—Mean ± SD (range) of various descriptive variables for heifer calves prior to and at approximately 24 hours after the feeding of 2 doses of an LDCR (200 g of IgG in a 2.8-L mixture of LDCR and water; treatment group; $n = 295$) or 3.8 L of pooled MC (control group; $n = 292$) within 6 hours after birth on a large (8,600 lactating cows) California dairy between September and December 2010.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of calves</td>
<td>Mean ± SD (range)</td>
<td>Mean ± SD (range)</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>295 39.10 ± 5.40 (23.0–57.5)</td>
<td>269 39.43 ± 5.30 (22.0–54.5)</td>
</tr>
<tr>
<td>Age at separation from dam (h)</td>
<td>281 2.35 ± 2.42 (0.5–6.0)</td>
<td>263 2.34 ± 2.42 (0.5–5.5)</td>
</tr>
<tr>
<td>Age at treatment (h)</td>
<td>277 3.98 ± 2.31 (0.5–6.0)</td>
<td>256 4.12 ± 2.25 (0.5–6.0)</td>
</tr>
<tr>
<td>Serum IgG concentration prior to treatment (g/dL)</td>
<td>282 4.49 ± 1.38 (2.8–6.0)</td>
<td>275 4.45 ± 1.37 (2.3–6.5)</td>
</tr>
<tr>
<td>Serum TP concentration prior to treatment (g/L)</td>
<td>289 0.67 ± 1.24 (0.1–9.3)</td>
<td>268 0.70 ± 1.25 (0.1–7.8)</td>
</tr>
<tr>
<td>IgG concentration in colostrum (g/L)</td>
<td>295 71.40 ± 21.0 (3.0–70.3)*</td>
<td>211 21.08 ± 9.76 (8.8–55.4)*</td>
</tr>
<tr>
<td>Amount of IgG fed (g)</td>
<td>295 200.00 ± 9.76 (33.0–210.0)*</td>
<td>211 78.81 ± 38.90 (33.0–210.0)*</td>
</tr>
<tr>
<td>Serum TP concentration 24 h after treatment (g/dL)</td>
<td>262 5.50 ± 0.52 (3.3–7.3)</td>
<td>268 4.73 ± 0.35 (0.0–7.0)*</td>
</tr>
<tr>
<td>Serum IgG concentration 24 h after treatment (g/L)</td>
<td>292 15.15 ± 4.75 (0.6–37.2)</td>
<td>269 7.50 ± 5.01 (0.7–30.3)*</td>
</tr>
<tr>
<td>Apparent efficiency of IgG absorption 24 h after treatment (%)</td>
<td>290 26.98 ± 1.65 (0.8–63.6)</td>
<td>205 28.79 ± 2.10 (2.5–214.2)</td>
</tr>
</tbody>
</table>

Among variables, the number of calves varies from the number of calves enrolled in each treatment group because of missing data. The lack of an SD and range indicates that all values for that variable were equal to the mean.

*Within a variable, the value for the control group differs significantly ($P < 0.001$) from that for the treatment group as determined by a t test.

All calves were administered the entire volume of the assigned treatment; calves that did not nurse the entire volume from a nipple bottle were administered the remaining volume with an esophageal feeder.
centration ≥ 10 g/L. Serum TP concentration 24 hours after treatment explained approximately 60% and 68% of the variation in serum IgG concentration 24 hours after treatment for calves in the treatment and control groups, respectively.

Discussion

To our knowledge, the present study is the first field trial performed to compare the efficacy of a commercially available LDCR with that of pooled MC for the prevention of FPT in calves on a large commercial dairy that routinely administered pooled colostrum to calves within 6 hours after birth. We believe the internal validity of this study was very good because of the randomized experimental design used; however, the fact that significantly fewer calves administered LDCR developed FPT than did calves administered pooled MC should be interpreted with caution. Evaluation of calves born on 1 large dairy limited the generalizability of the results of this study to other dairies that may have different colostrum feeding practices or risks for FPT in calves.

Although the dairy of the present study was similar to approximately 57% of other large (≥ 500 lactating cows) US dairies in that it routinely fed pooled MC to newborn calves,19 it differed in that the mean IgG concentration (21.1 g/L) in the pooled MC was much lower than that (64.3 g/L) determined for pooled MC samples obtained from other southwestern US dairies during a national survey20 of colostrum quality. This finding suggested that the pooled MC from the dairy of the present study was of poor quality and may help explain the fact that the proportion of calves that were fed pooled MC and developed FPT (70%) was significantly higher, compared with that for calves of the present study that were fed the LDCR (11%) or calves that were fed pooled MC (23%) in a national survey.21 Furthermore, the low quality of the pooled MC fed to the control calves of the present study likely biased the results such that the efficacy of LDCR in comparison with pooled MC for the prevention of FPT in calves appeared much better than it would have had the control calves been fed pooled MC with an IgG concentration more typical of that for most large US dairies.

Regardless of the limitations of the present study, oral administration of LDCR to calves within 6 hours after birth was associated with increased serum TP and IgG concentrations 24 hours after ingestion, compared with those prior to administration, and a decreased incidence of FPT (11%), compared with that for calves fed pooled MC in the present (70%) as well as in a national survey22 (23%). The increases in serum TP and IgG concentrations were expected because the calves fed the LDCR ingested 200 g of IgG within 6 hours after birth, a period during which colostrum proteins are readily absorbed into the circulation from the intestinal tract, which in turn should decrease the incidence of FPT. In the present study, at 24 hours after treatment, the mean serum TP and IgG concentrations for calves in the treatment group (ie, fed LDCR) were significantly higher than those for calves in the control group (ie, fed pooled MC). This finding seems reasonable given that the amount of IgG fed to calves in the treatment group was approximately 2.5 times as great as that fed to calves in the control group.

The low IgG concentration in the pooled MC fed to control calves of the present study may have been the result of multiple factors, including the study dairy’s practice of pooling colostrum without consideration to its quality, overrepresentation of colostrum from primiparous cows, and the variable time from calving to colostrum collection. The theoretical basis for feeding pooled colostrum to calves is that the act of combining colostrum from multiple cows will mitigate the effect of a low IgG concentration in the colostrum from some cows. However, that theory may be flawed because the colostrum of cows that produce a large volume of colostrum often has a low IgG concentration, and a high volume of poor-quality colostrum from 1 cow may dilute the IgG concentration in the pooled colostrum.21 In the present study, 120 of 273 (44%) control calves were born to primiparous cows, and those cows contributed to the pooled MC that was fed. It is generally accepted that IgG concentration is lower in colostrum from primiparous cows than it is in colostrum from multiparous cows22,23 and is inversely associated with...
time after calving to colostrum collection. Although it is recommended that cows be milked within 6 hours after calving to ensure collection of high-quality colostrum, the time from calving to colostrum collection ranged from 1 to 12 hours for the cows of the present study and was dependent on the time of day the cows calved in relation to the scheduled milking times for that group of cows.

The amount of bacterial contamination in colostrum as measured by TPC is negatively correlated with serum IgG concentration after colostrum ingestion. Results of a study conducted to evaluate colostrum quality on US dairies indicated that samples of pooled MC had a significantly greater mean TPC (5.5 log₁₀ colony-forming units/mL) than did samples of colostrum obtained from individual cows (4.9 log₁₀ colony-forming units/mL). Unfortunately, in the present study, we did not perform TPCs on the samples of the pooled MC that was fed to the control calves; therefore, we could not ascertain whether bacterial contamination of the pooled MC was associated with the mean serum IgG concentration after colostrum ingestion for calves in the control group.

Results of the present study were inconsistent with results of other studies, in which the efficacy of plasma-derived colostrum replacer was compared with that of pooled MC for the prevention of FPT in calves. In 1 study, the mean ± SD plasma IgG concentration after treatment did not differ between calves fed pooled MC (13.78 ± 0.39 g/L) and calves fed a plasma-derived colostrum replacer (13.96 ± 0.39 g/L). In another study, the mean plasma IgG concentration at 24 hours after colostrum ingestion in calves fed pooled MC (10.7 g/L) was significantly higher, compared with that in calves fed a plasma-derived colostrum replacer (6.5 g/L). In both of those studies, the quality of each individual cow's colostrum was assessed with a colostrometer and only good-quality colostrum was pooled; therefore, the mean IgG concentration (50 g/L) in the pooled MC fed to the control calves of those studies was greater than that (21.1 g/L) in the pooled MC fed to the control calves of the present study. Also, in those studies, the amount of IgG administered to calves with the plasma-derived colostrum replacer was less than that administered to calves with the LDCR in the present study. Thus, substantial variation in the amount of IgG that was administered to calves is the most likely reason the results of the present study were inconsistent with the results of the other 2 studies.

The standard operating procedure for the dairy of the present study did not involve evaluating the quality of colostrum from each cow prior to pooling it with colostrum from other cows, a practice that is common on many large US dairies. In fact, results of a national survey of herd managers in the 17 major dairy states in the United States, including California, indicate that only 13% of dairies use some method to evaluate the IgG concentration in colostrum prior to feeding it to calves, despite the availability of several inexpensive and rapid on-farm methods for determination of colostrum IgG concentration. In the present study, adequate passive transfer (ie, serum IgG concentration ≥ 10 g/L) was achieved for the majority (263/295 [89%]) of calves that were fed 2 doses (approx 200 g of IgG) of the LDCR and only 82 of 273 (30%) calves that were fed poor-quality (approx 80.2 g of IgG) pooled MC. These results are similar to those of another study, in which 81% (17/21) and 95% (20/21) of calves that were administered 1 (100 g of IgG) or 2 (200 g of IgG) doses of the same LDCR that was used in the present study, respectively, achieved adequate passive transfer. Likewise, at 24 hours after treatment, the mean ± SD serum IgG concentration for calves fed 2 doses of the LDCR in that study (16.9 ± 6.2 g/L) was similar to that (15.15 ± 4.75 g/L) for calves in the treatment group of the present study. In contrast to the results of the present study, 19 of 21 (90%) calves fed 4 L of MC achieved adequate passive transfer in that study; however, the mean IgG concentration of the MC fed to those calves (118 g/L) was approximately 5.6 times as high as that (21.1 g/L) of the pooled MC fed to the control calves of the present study.

Results of the present study indicated that, in this particular dairy, feeding calves 200 g of IgG with an LDCR would reduce the risk of those calves subsequently developing FPT by approximately 72%. This finding was interesting because it suggested that approximately 28% of the risk for developing FPT in the calves on the study dairy was associated with factors other than those calves being administered an adequate amount of IgG with colostrum or a colostrum replacer. Other factors associated with FPT in calves include age at colostrum ingestion, volume of colostrum ingested, method of colostrum delivery, dam parity and breed, proximity of the calf to the dam during colostrum ingestion, and metabolic abnormalities of the calf. Evaluation of the effect of those factors on the development of FPT was beyond the scope of the present study; however, additional research to assess the effect of individual calf factors such as physiologic immaturity or acidosis on the development of FPT, despite timely delivery of an adequate amount of IgG, is warranted.

In the present study, serum TP concentrations of ≥ 4.9 g/dL and ≥ 5.0 g/dL were estimated as the cutoffs for the prediction of adequate passive transfer in dairy calves fed the LDCR or pooled MC, respectively. These cutoffs are similar to the mean serum TP concentration (5.0 g/dL) that was predictive of adequate passive transfer in calves of one study and the serum TP concentration range (3.0 to 5.2 g/dL) associated with a serum IgG concentration ≥ 10 g/L in calves in another study. However, the low R² obtained during regression analysis of the association between serum TP concentration and serum IgG concentration within each treatment group of the present study suggested that the use of serum TP concentration to predict adequate passive transfer in dairy calves may be unreliable.

Results of the present study indicated that feeding newborn dairy calves 2 doses (200 g of IgG) of an LDCR was more effective in the prevention of FPT than was the feeding 3.8 L of pooled MC. However, this study was performed on only 1 large dairy, and the pooled MC fed had an unusually low IgG concentration. These findings suggested that lowryes should measure IgG concentration in colostrum from individual cows prior to pooling and only good-quality colostrum should be
pooled, a practice that is not commonly performed on many large US dairies, but for which inexpensive and rapid on-farm methods are readily available. Regardless, adequate passive transfer was achieved in 89% (260/292) of calves fed 2 doses of the LDCR, which suggested that feeding an LDCR to newborn calves is a viable alternative for prevention of FPT when adequate amounts of high-quality MC are unavailable or herd managers want to avoid the transmission of colostrum-associated bovine pathogens, such as M avium subsp paratuberculosis or bovine leukemia virus, to herd replacements.

a. Land O’ Lakes Bovine IgG Colostrum Replacement, Land O’ Lakes Inc, Kelso, Wash, provided by Saskatoon Colostrum Co, Saskatoon, SK, Canada.

b. Becton, Dickinson & Co, Franklin Lakes, NJ.
d. Prairie Diagnostic Services Inc, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, SK, Canada.
e. Model No. 300027, SPER Scientific, Scottsdale, Ariz.
f. Stata Corp, College Station, Tex.

References


