Effects of Pasteurized β-Lactam Antibiotic Milk on Growth and Gastrointestinal Development in Calves: Postprint

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Abstract

This experiment was conducted to investigate the effects of feeding pasteurized β-lactam antibiotic milk on growth and gastrointestinal development in calves. Eighteen healthy 3-day-old Holstein bull calves with similar body weight were randomly divided into 2 groups: the control group was fed β-lactam antibiotic milk, and the experimental group was fed pasteurized β-lactam antibiotic milk. The pasteurization conditions for the experimental milk were heating at 63-65°C for 30 min. Calves were weaned at 60 days of age, and the experimental period was 180 d. The results showed that: 1) Compared with β-lactam antibiotic milk, pasteurized β-lactam antibiotic milk had extremely significantly decreased counts of total bacteria, Escherichia coli, and Salmonella ($P<0.01$); 2) Compared with the control group, calves in the experimental group had significantly increased average daily gain (ADG) during 3-60 days of age ($P<0.05$), and significantly decreased fecal scores and diarrhea rates during 3-10 days and 3-60 days of age ($P<0.05$); 3) There were no significant differences in papilla height, papilla width, and mucosal thickness of ruminal dorsal and ventral sacs between the experimental and control groups at 60, 90, and 180 days of age ($P>0.05$). Compared with the control group, calves in the experimental group had significantly increased duodenal villus height and villus height/crypt depth ratio at 60 days of age ($P<0.05$), significantly decreased duodenal crypt depth at 90 days of age ($P<0.05$), significantly increased jejunal villus width at 90 days of age ($P<0.05$), significantly decreased jejunal crypt depth at 60, 90, and 180 days of age ($P<0.05$), and significantly increased jejunal villus height/crypt depth ratio at 90 and 180 days of age ($P<0.05$), while there were no significant differences in ileal histomorphology at any measured time points ($P>0.05$). Therefore, feeding pasteurized β-lactam antibiotic milk improved the growth and development of calves during the suckling period and, to a certain extent,

promoted gastrointestinal development, mainly reflected in the promotion of small intestinal morphological development.

Full Text

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Abstract

This study investigated the effects of feeding pasteurized β-lactam antibiotic milk on growth and gastrointestinal development in calves. Eighteen healthy 3-day-old Holstein male calves with similar body weight were randomly divided into two groups: a control group fed β-lactam antibiotic milk and an experimental group fed pasteurized β-lactam antibiotic milk. The pasteurization conditions were 63-65 °C for 30 minutes. Calves were weaned at 60 days of age, and the experimental period lasted 180 days. The results showed that: (1) compared with β-lactam antibiotic milk, pasteurized β-lactam antibiotic milk had significantly lower counts of total bacteria, *Escherichia coli*, and *Salmonella* ($P<0.01$); (2) compared with the control group, the experimental group exhibited significantly higher average daily gain during 3-60 days of age ($P<0.05$), and significantly lower fecal scores and diarrhea rates during both 3-10 days and 3-60 days of age ($P<0.05$); (3) no significant differences were observed between groups in papilla height, papilla width, or mucosal thickness of the dorsal and ventral rumen sacs at 60, 90, or 180 days of age ($P>0.05$); however, compared with the control group, the experimental group showed significantly increased duodenal villous height and villous height/crypt depth at 60 days of age ($P<0.05$), significantly decreased duodenal crypt depth at 90 days of age ($P<0.05$), significantly increased jejunal villous width at 90 days of age ($P<0.05$), significantly decreased jejunal crypt depth at 60, 90, and 180 days of age ($P<0.05$), and significantly increased jejunal villous height/crypt depth at 90 and 180 days of age ($P<0.05$), while no significant differences were found in ileal histomorphology at any time point ($P>0.05$). These findings demonstrate that feeding pasteurized β-lactam antibiotic milk improves growth performance during the nursing period and promotes gastrointestinal development in calves, primarily by enhancing small intestinal morphological development.

Keywords: calves; antibiotic milk; pasteurization; growth; gastrointestinal development

β-lactam antibiotics such as penicillin are the most commonly used drugs for disease treatment in dairy production. During the treatment period and withdrawal period, milk from treated cows contains these antibiotics. Milk containing antibiotics and high somatic cell counts is collectively referred to as "antimilk" (also called waste milk abroad). In Germany, annual waste milk production accounts for 1%–4% of total milk output, which is sufficient to feed all calves on dairy farms. As a zero-cost feed resource, producers often feed antimilk to calves to reduce rearing costs. According to a 2016 survey of over 300 dairy farms in Heilongjiang Province conducted by our research group, approximately 95% of farms use antimilk to feed calves, with 66% of these farms performing no treatment on the antimilk before feeding. However, milk quality plays a crucial role in calf growth and health, necessitating research on the effects of antimilk on calf development.

Pasteurization is defined as "a broad category of heat treatment processes that inactivate alkaline phosphatase activity naturally present in raw milk while retaining lactoperoxidase activity." Its purpose is to kill pathogenic bacteria in milk while maximizing nutrient preservation and maintaining pure flavor. Liu et al. investigated the effects of feeding pasteurized colostrum on calf growth performance and gastrointestinal development, finding that pasteurized colostrum significantly reduced the ratio of forestomach weight to live weight and improved average daily gain while reducing diarrhea rates. Currently, few studies have reported on the application of pasteurized antimilk in young ruminants, particularly regarding its effects on calf growth and gastrointestinal development. Therefore, this study aimed to investigate the effects of feeding pasteurized β-lactam antibiotic milk on calf growth and small intestinal development, providing a theoretical basis for the scientific and effective utilization of antimilk in Chinese dairy farms.

1.1 Experimental Animals and Design

Eighteen healthy 3-day-old Holstein male calves with a body weight of (42.82$±$0.35) kg were randomly divided into a control group and an experimental group, with 9 calves per group. The control group was fed β-lactam antibiotic milk, while the experimental group was fed pasteurized β-lactam antibiotic milk. Both types of milk were fed at 37–39 °C. Calves were weaned at 60 days of age, and the experimental period lasted 180 days.

1.2 Experimental Diet

The milk fed to calves was obtained from lactating cows during the treatment and withdrawal periods after administration of the β-lactam antibiotic ceftiofur sodium. The pasteurization conditions for the experimental antimilk were heating at 63–65 °C for 30 minutes. The experimental diet consisted of starter pellets and high-quality Chinese wildrye, with formulations optimized using CPM software. The composition and nutrient levels of the experimental diet are shown in .

1.3 Feeding Management

Calves were fed 4 kg of colostrum per head within 0.5 h after birth. During the experimental period, feeding amounts for both antibiotic milk and pasteurized antibiotic milk were as follows: 5 kg/d divided into 3 feedings at 3–7 days of age; 5.5 kg/d divided into 3 feedings at 8–20 days; 4 kg/d divided into 2 feedings at 21–40 days; 3 kg/d divided into 2 feedings at 41–50 days; and 1 kg/d as a single feeding at 51–60 days. Calves in both groups were offered high-quality Chinese wildrye and starter pellets beginning at 8 days of age, with an initial amount of 0.3 kg/d per head increasing to 1.0 kg/d at weaning. Fresh water was available ad libitum. Calf pens were cleaned daily and disinfected regularly to maintain sanitary conditions.

1.4.1 Milk Sample Analysis

Milk samples were collected once every 10 days, with three collections per day (morning, noon, and evening) pooled at a ratio of 4:3:3. For milk composition analysis, 50 mL of the pooled sample was placed in a tube containing 5% potassium dichromate as a preservative and stored at 4 °C. For microbial analysis, another 50 mL of pooled sample was placed in a sterile bottle and stored at 4 °C for determination of total bacteria, *E. coli*, and *Salmonella* counts within 2 h of collection.

Milk composition was determined using a Foss Milkoscan 133B analyzer (Foss Electric, Denmark). Somatic cell count was measured using a Foss® Bentley Somacount CC-5000 (Foss Electric, Denmark). Antibiotic residues were quantified by liquid chromatography-tandem mass spectrometry (LC-MS/MS, Agilent Technologies, USA). For microbial counts, milk samples were serially diluted 1:10 to 10^{-7}, with 1 mL from each dilution added to sterile culture media. Total bacterial count was determined using plate count agar (PCA) incubated at 37 °C with 5% CO_2 for 48 h. *E. coli* was cultured on violet red bile agar (VRBA) under the same conditions for 24 h, and *Salmonella* was cultured on SS agar for 24 h, followed by colony counting.

1.4.2 Growth Performance

Body weight and body measurements were recorded before morning feeding at 30, 60, 90, and 180 days of age. Average daily gain was calculated for each period.

1.4.3 Fecal Scoring and Diarrhea Rate

Before 60 days of age, fecal consistency was scored daily for each calf using the following system: 1 = normal, firm but not hard, retaining shape when dropped; 2 = soft, piled but not retaining shape; 3 = runny, spreads easily; 4 = watery, liquid-solid separation. Scores $ $3 were considered diarrhea. The diarrhea rate was calculated using the formula: Diarrhea rate (%) = Σ[(number of diarrheic calves × diarrhea days)/(total calves in group × recording days)] × 100.

1.4.4 Gastrointestinal Development

At 60, 90, and 180 days of age, three calves from each group were slaughtered after overnight fasting by exsanguination from the carotid artery. The abdominal cavity was opened along the midline, and the gastrointestinal tract was removed intact onto a tray. Tissue samples (1.5 cm × 1.5 cm) were collected from the dorsal and ventral rumen sacs. Additionally, 2–3 cm segments were taken from the proximal duodenum (5 cm from the pylorus), anterior/middle/posterior jejunum, and mid-ileum. Samples were rinsed with physiological saline, blotted dry, and fixed in 10% neutral formalin for histological examination.

Fixed rumen and intestinal tissues were stained with hematoxylin-eosin (HE) for morphological observation. Five sections per tissue per calf were examined and photographed using an ML-50 microscopic image acquisition system. Ten intact fields were selected per section (complete rumen papillae with straight orientation, intact intestinal villi). Papilla height and width were measured at the longest and widest points using a 40× ocular micrometer. Intestinal villous height, villous width, and crypt depth were measured similarly, and villous height/crypt depth (V/C) ratio was calculated.

1.5 Statistical Analysis

Data were analyzed using the GLM procedure in SAS 9.2 software. Results are expressed as means ± standard error. Differences were considered significant at $P<0.05$ and extremely significant at $P<0.01$.

2 Results

2.1 Composition of β-Lactam Antibiotic Milk and Pasteurized β-Lactam Antibiotic Milk

As shown in , pasteurized β-lactam antibiotic milk had significantly lower counts of total bacteria, *E. coli*, and *Salmonella* compared with β-lactam antibiotic milk ($P<0.01$). However, no significant differences were observed in lactose percentage, milk protein percentage, milk fat percentage, total solids percentage, urea nitrogen content, or somatic cell count ($P>0.05$).

2.2 Effects of Pasteurized β-Lactam Antibiotic Milk on Calf Growth

As shown in , average daily gain during 3–60 days of age was significantly higher in the experimental group than in the control group ($P<0.05$). Although no significant differences were found in body weight at 30, 60, 90, or 180 days of age, or in average daily gain during 61–180 days or 3–180 days of age ($P>0.05$), values were consistently higher in the experimental group.

As shown in , body height at 60 days of age and heart girth at 90 and 180 days of age were significantly greater in the experimental group compared with the control group ($P<0.05$). No significant differences were observed in body oblique length, body straight length, cannon bone circumference, leg circumference, or chest depth at any time point (P>0.05).

2.3 Effects of Pasteurized β-Lactam Antibiotic Milk on Fecal Score and Diarrhea Rate

As shown in , fecal scores and diarrhea rates during 3–10 days and 3–60 days of age were significantly lower in the experimental group than in the control group (P<0.05). No significant differences were observed during 11–30 days or 31–60 days of age (P>0.05), although the experimental group showed reductions of 6.57% and 5.76%, respectively. Fecal scores and diarrhea probability decreased with age in both groups.

2.4 Effects of Pasteurized β-Lactam Antibiotic Milk on Rumen and Small Intestinal Morphological Development

As shown in , no significant differences were found in papilla height, papilla width, or mucosal thickness of the dorsal and ventral rumen sacs between groups at 60, 90, or 180 days of age (P>0.05). In the duodenum, villous height and V/C ratio at 60 days of age were significantly higher in the experimental group (P<0.05), while crypt depth at 90 days of age was significantly lower (P<0.05). No significant differences were observed in duodenal villous width, mucosal thickness, or muscularis thickness at any time point (P>0.05).

In the jejunum, villous width at 90 days of age and V/C ratio at 90 and 180 days of age were significantly higher in the experimental group (P<0.05), while crypt depth was significantly lower at 60, 90, and 180 days of age (P<0.05). No significant differences were found in jejunal villous height, mucosal thickness, or muscularis thickness at any time point (P>0.05). No significant differences were observed in any ileal parameters between groups at 60, 90, or 180 days of age (P>0.05).

3 Discussion

3.1 Composition Comparison Between β-Lactam Antibiotic Milk and Pasteurized β-Lactam Antibiotic Milk

β-lactam antibiotics are the first-choice treatment for clinical and subclinical mastitis and endometritis in dairy cows due to their broad spectrum, low cost, convenience, and low toxicity. In this study, no significant difference in antibiotic content was observed between the two milk types, indicating that pasteurization did not affect antibiotic residues, consistent with the findings of Jorgensen et al. The milk fat and protein percentages in pasteurized β-lactam antibiotic milk met international standards. Although some milk components such as protein are partially lost during pasteurization, no significant differences were observed between the two milk types in this study, aligning with the results of Zang et al. Lactose is relatively stable during pasteurization, with minimal content variation, which matches our findings. Zhu et al. reported that milk fat and lactose are negatively correlated with somatic cell count; however, this relationship was not observed in our study. Somatic cell count is an important indicator of dairy cow health. When the udder is infected by bacteria or mechanically injured by milking equipment, white blood cells are secreted in large quantities to combat infection and repair tissue, resulting in elevated somatic cell counts in milk. Therefore, udder inflammation leads to rapid increases in somatic cell count and changes in milk composition. In this study, no significant difference in somatic cell count was found between β-lactam antibiotic milk and pasteurized β-lactam antibiotic milk, with both exceeding 1×10^{6} cells/mL, consistent with the pathological status of lactating cows and indicating that pasteurization does not affect somatic cell count.

Most cases of clinical and subclinical mastitis are caused by bacterial infection. Bacteria can adhere to epithelial cells in the infected mammary gland, triggering local immune responses characterized by redness, inflammation, and decreased milk production. Total bacterial count is an indicator of microbial contamination and milk quality, with higher counts reflecting poorer cow health and milk quality. In this study, pasteurization significantly reduced total bacteria, *E. coli*, and *Salmonella* counts, consistent with the findings of Li et al. Jorgensen et al. also reported that pasteurization significantly reduces *E. coli* and *Salmonella* populations. Our results clearly demonstrate that pasteurization effectively kills pathogenic bacteria, reducing disease transmission risk to calves and improving milk quality.

3.2 Effects of Pasteurized β-Lactam Antibiotic Milk on Calf Growth

Body weight is a key indicator of calf growth status. Aust et al. reported that feeding waste milk did not affect calf growth. Other studies have shown that calves fed pasteurized waste milk had higher body weights before and after weaning compared with those fed unpasteurized waste milk. In this study, average daily gain during 3-60 days of age was significantly higher in the experimental group, similar to the findings of Song et al., indicating that feeding pasteurized β-lactam antibiotic milk can promote calf growth to some extent. This may be because pasteurization substantially reduces total bacteria and harmful microorganisms, decreasing potential disease incidence and maintaining calves in a healthy growth state. No significant differences were observed in body weight at each time point or in average daily gain during 60-180 days and 3-180 days of age, suggesting that pasteurized β-lactam antibiotic milk primarily affects growth during the nursing period.

Body measurements are important indicators of calf growth and development, reflecting skeletal development and management level. Hill et al. provided reference data for Holstein calves: body height 86.4-93.1 cm and body oblique length 82.3-91.0 cm. In this study, body height and oblique length at 60 days of age were within these reference ranges, indicating normal development in both groups. Additionally, body height at 60 days of age and heart girth at

90 and 180 days of age were significantly greater in the experimental group, likely related to the higher body weights and average daily gains observed in this group. Overall, feeding pasteurized β-lactam antibiotic milk promoted calf growth.

3.3 Effects of Pasteurized β-Lactam Antibiotic Milk on Fecal Score and Diarrhea Rate

Calf diarrhea is a common disease characterized by watery feces, elevated temperature, lethargy, rapid weight loss, and potentially death. Causes include nutritional and infectious factors. Excessive microbial counts of *E. coli* and *Salmonella* in raw milk are primary causes of calf diarrhea, making raw milk a potential source of infection. Studies have shown that pasteurization significantly reduces microbial populations and diversity in milk, decreasing disease risk and mitigating pathogen impacts on calf health. Sandra et al. found that pasteurized waste milk improved calf growth while significantly reducing morbidity and mortality. Song et al. and Yang et al. reported that feeding pasteurized milk improved calf health and reduced diarrhea incidence.

In this study, fecal scores and diarrhea rates during 3–10 days and 3–60 days of age were significantly lower in the experimental group, while no significant differences were observed during 11–30 days and 31–60 days of age, though reductions of 6.57% and 5.76% were still observed. This indicates that pasteurization eliminates some health risks from antimilk microorganisms, which may explain the differences in average daily gain between groups. The limited reduction in diarrhea rate may be due to secondary contamination of pasteurized antimilk during storage, where protein and milk fat quality deteriorate and microbial counts increase. The decrease in diarrhea rate with age is consistent with Dong et al., likely because digestive organs and immune function mature with age, and the high-temperature pelleting process of starter feed kills pathogenic microorganisms, reducing diarrhea incidence. Overall, feeding pasteurized β-lactam antibiotic milk promoted calf growth and maintained better health status.

3.4 Effects of Pasteurized β-Lactam Antibiotic Milk on Gastrointestinal Development

Rumen function is directly related to animal growth performance. Volatile fatty acids are important substances that stimulate rumen development and functional establishment. Typical indicators for evaluating rumen development include papilla height, papilla width, and rumen wall thickness, which are influenced by diet composition. Zhou et al. found that dietary β-glucan supplementation significantly increased rumen papilla height and width. Li reported that a 22% crude protein level in milk replacer promoted rumen papilla development compared with 18% and 26% levels. Li Yu showed that increasing plant protein levels in milk replacer stimulated rumen papilla growth. Evans et al. found that large feed particles floating in the rumen stimulated rapid development of rumen dorsal sac epithelial cells. In this study, no significant differences were found in papilla height, papilla width, or mucosal thickness of the dorsal and ventral rumen sacs between groups at 60, 90, or 180 days of age, indicating that neither milk type significantly affected rumen morphological development. This may be due to the esophageal groove directing milk directly to the abomasum, minimizing rumen exposure. Previous reports indicate that concentrate, forage, solid feed type, and feeding behavior are the main factors affecting rumen development. Since both groups consumed the same starter pellets and Chinese wildrye under identical management conditions, this may explain the lack of difference in rumen morphological development.

In young ruminants with underdeveloped rumens, the small intestine is the primary site for nutrient digestion and absorption, and its structural development directly affects digestive function. Digestive and absorptive capacity is positively correlated with villous height, crypt depth, and mucosal thickness. Villous height is significantly correlated with the number of intestinal epithelial cells, with longer villi indicating stronger nutrient absorption capacity. Crypt depth reflects the proliferation rate and maturity of crypt cells. The V/C ratio is a comprehensive indicator of small intestinal function. Improved mucosal structure enhances digestive and absorptive function, reduces diarrhea rates, and accelerates growth, while decreased V/C ratios indicate damaged intestinal mucosa, reduced absorptive function, and impaired growth. Healthy young animals have V/C ratios of 3–4, indicating strong absorptive capacity. In this study, V/C ratios ranged from 2.88 to 5.53 in both groups, indicating effective nutrient absorption. However, feeding pasteurized antimilk significantly increased duodenal villous height at 60 days of age, significantly decreased duodenal crypt depth at 90 days of age, and significantly increased duodenal V/C ratio at 60 days of age. Additionally, jejunal villous width at 90 days of age and V/C ratio at 90 and 180 days of age were significantly higher in the experimental group, while jejunal crypt depth was significantly lower at 60, 90, and 180 days of age. These small intestinal morphological differences suggest that pasteurized antimilk benefited duodenal and jejunal development, possibly related to the lower diarrhea rates observed in this group. However, pasteurized antimilk had no significant effect on ileal parameters at any time point, indicating that it primarily affected duodenal and jejunal development with minimal impact on ileal development.

4 Conclusions

1. Feeding pasteurized β-lactam antibiotic milk can reduce calf diarrhea incidence, maintain intestinal health, and promote growth.
2. From a gastrointestinal morphological perspective, feeding pasteurized β-lactam antibiotic milk significantly increased duodenal villous height and V/C ratio and jejunal V/C ratio compared with β-lactam antibiotic milk, indicating that pasteurized antimilk primarily affects duodenal and jejunal development.

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Note: Figure translations are in progress. See original paper for figures.