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Short communication: Investigation of antibiotic alternatives to improve health and growth of veal calves

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ABSTRACT

The inherent disease susceptibility of veal calves results in frequent antimicrobial use. Improvements in antimicrobial stewardship necessitate alternative therapies to improve calf health and growth, while reducing the need for antimicrobials important to human health. This study investigated the effect of 2 alternative therapies, lactoferrin (an iron-binding protein found in colostrum) and cinnamaldehyde (an essential oil of the cinnamon plant) on growth, disease incidence, and mortality risk in special-fed veal calves. On the day of arrival to the growing facility (3 to 7 d of age), calves (n = 80 per treatment) were randomized to 1 of 3 treatments: (1) control (no supplement), (2) lactoferrin (1 g/d in milk replacer for 7 d), or (3) cinnamaldehyde (1 g/d in milk replacer for 21 d). Body weight was measured on the day of arrival (d 0), 21, and 42 d postarrival. Health assessments were performed twice weekly through 21 d, and mortality records were obtained through 6 wk postarrival. A repeated measures ANOVA was used to compare growth between treatment groups, and a Poisson regression model (PROC GENMOD, SAS v. 9.4, SAS Institute Inc., Cary, NC) was used to test differences between groups in the incidence of diarrhea (fecal score ≥ 2 with and without depression and temperature) and disease through 3 wk postarrival. Body weight and average daily gain were similar between treatments. Neither lactoferrin nor cinnamaldehyde had an effect on diarrhea incidence. However, the risk of navel inflammation was significantly lower for calves that received cinnamaldehyde compared with calves in the control group. Mortality through 6 wk postarrival was low, with 4, 1, and 0 deaths from the control, lactoferrin, and cinnamaldehyde treatment groups, respectively. Additional research is needed to investigate various doses of these alternative therapies on calf health and growth, in addition to different routes of administration.

Key words: calf diarrhea, growth, lactoferrin, cinnamaldehyde

Short Communication

The early management of special-fed veal calves (calves marketed at 16 or 20 wk of age; Terosky et al., 1997) presents a particular challenge to calf health and welfare. Calves often travel long distances and are co-mingled with other animals during transport and auction, likely increasing their susceptibility to disease (Taylor et al., 2010). Special-fed veal calves arrive to growing facilities with varying degrees of dehydration, depression, and navel inflammation (Pempek et al., 2017), and diarrhea and respiratory disease are leading causes of morbidity and mortality in special-fed veal calves (Pardon et al., 2013). Strategies to reduce morbidity and early mortality sometimes include prophylactic and therapeutic use of antibiotics in milk or medicated milk replacer (**MR**), and thus, antimicrobial use in the veal industry is higher than other animal industries (Pardon et al., 2012). Antimicrobials categorized as "highest priority critically important," including third generation cephalosporins and fluoroquinolones, are routinely used in calves to treat respiratory or enteric infections (WHO, 2017). However, recent regulations mandate that calves no longer be fed medically important antibiotics continuously in milk or MR (Mzyk et al., 2017). Thus, improved antibiotic stewardship necessitates research on alternative therapies for reducing morbidity and mortality in special-fed veal calves.

Lactoferrin, an iron-binding glycoprotein in colostrum (Rybarczyk et al., 2017), and cinnamaldehyde, a natural phenylpropanoid compound in the bark of the cinnamon tree (Chapman et al., 2017), are 2 antibiotic alternatives that have been investigated for use in livestock. Lactoferrin supplementation in pre-weaned dairy calves has been shown to increase ADG (Joslin et al., 2002; Robblee et al., 2003) and reduce diarrhea (Robblee et al., 2003) and mortality (Habing et al., 2017); however, other studies have shown no significant effect (Cowles et al., 2006). Prior studies have evaluated cinnamaldehyde supplementation and have found

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a positive effect on DMI and milk production in lactating dairy cows (cinnamaldehyde and eugenol blend; Wall et al., 2014) or no significant effect on growth in weaned dairy calves (Chapman et al., 2017). However, no data are available describing the effects of lactoferrin and cinnamaldehyde supplementation in special-fed veal calves.

The objective of this study was to investigate the effect of lactoferrin and cinnamaldehyde on the health, growth, and mortality of special-fed veal calves. We hypothesized that supplementing calves with lactoferrin and cinnamaldehyde would improve BW and ADG, reduce the incidence of diarrhea and other health outcomes, and reduce calf mortality.

This study was conducted from June through July 2016 with 2 special-fed veal cohorts (n = 120 calves per cohort) on 1 commercial farm in Ohio, in accordance with the guidelines administered by the Institutional Animal Care and Use Committee (Animal Use Protocol: 2015A00000131). Holstein bull calves (approximately 3 to 7 d of age) were purchased from livestock auctions in Massachusetts, Pennsylvania, and New York, and transported to the growing facility in Ohio. Calves were managed as all-in, all-out production units, and each cohort was filled within 24 h. Calves were housed in individual stalls (2.13 m × 0.61 m) with coated metal slatted flooring (Tenderfoot, Tandem Products Inc., Minneapolis, MN). Stalls were separated via removable metal dividers with horizontal partitions to provide visual access to other calves, and temperature and humidity in each room were mechanically controlled. Calves were vaccinated with Inforce 3 (intranasal; Zoetis, Parsippany, NJ) before milk feeding on the day of arrival to the growing facility. Calves were fed MR (22% protein, 18% fat) via bucket twice daily at approximately 0500 and 1600 h; calves received 220 g of MR powder reconstituted in warm water to yield 1.47 kg of MR per feeding on d 1, which was gradually increased to 454 g of MR powder reconstituted to yield 2.95 kg of MR per feeding on d 21. Water was offered via metal nipple.

A randomized complete block design was used where calves were randomized (Microsoft Excel, Redmond, WA) to 1 of the 3 treatment groups in blocks of 3, with a randomly assigned within-block order of treatments. The control group (**CON**; n = 80 calves) received MR without supplementation. The lactoferrin treatment group (**LAC**; n = 80 calves) received 1 g of lactoferrin powder (The Tatua Co-operative Dairy Company Ltd., Morrinsville, New Zealand) once daily added to the MR during the evening feeding for 7 d (Robblee et al., 2003). The cinnamaldehyde treatment group (**CIN**; n = 80 calves) received 1 g of cinnamaldehyde blend powder (Healthy Aging, Columbus, IN; zhang102@gmail.com), per manufacturer recommendation, once daily added to the MR for 21 d. Eighty calves was calculated to provide sufficient power ($\beta = 0.20$) to identify significant ($\alpha = 0.05$) differences in growth and disease frequency between treatment and control groups. Eighty calves provides sufficient power assuming a final 6-wk weight of 74 and 71 kg (SD = 6 kg) in the treatment and control group, respectively (SD = 6 kg). The sample size is additionally sufficient to identify significant differences in disease frequency, assuming rates of 0.1 and 0.2 in the treatment and control groups, respectively, 5 observations per calf, and a calf-level intraclass correlation coefficient of 0.20 (Dohoo et al., 2009).

All calves (n = 240 total calves) were assessed following arrival to the growing facility, and then twice per wk for 3 wk. Three experimenters (1 postdoctoral researcher, 2 experienced veterinary students) performed data collection. A blood sample from the jugular vein was collected from each calf directly following arrival to estimate passive transfer and packed cell volume (Pempek et al., 2017). Health assessments were conducted between 0700 and 1200 h, following the morning milk feeding. To limit the awareness of the experimenters to treatment assignments, health assessments were conducted before treatment administration at the evening milk feeding, and treatment assignment was only identifiable on the datasheet available during administration (O'Connor et al., 2010). Although the same experimenter conducted health examinations and administered treatments, the experimenter was generally unaware of treatment assignments due to separation of treatment and outcome records, and the volume and frequency of data collection. However, the inability to achieve complete blinding may be viewed as a limitation to this study. Further, the inability to calculate intra- and inter-observer reliability is an additional limitation to our study due to the subjectivity of the health assessment.

The health assessment included rectal temperature, and scores for diarrhea (4-point scale; Lago et al., 2006), depression (5-point scale; adapted from Perino and Apley, 1998), respiratory disease (4-point scale; Lago et al., 2006), navel inflammation (4-point scale; adapted from Fecteau et al., 1997), and dehydration (skin tent test, 2-point scale; Wilson et al., 2000); see Pempek et al. (2017) for detailed scoring criteria. Scores for health outcomes were dichotomized using biologically relevant cut-off points. Health outcomes were considered clinically normal if fecal score = 0 or 1 (normal or semiformed), depression score = 0 or 1 (no signs of depression or noticeable depression without apparent signs of weakness), navel inflammation score = 0 or 1 (normal, pencil-sized to the approximate width of pointer finger), and skin tent score = 0 (skin remains tented for $\leq$4 s).