Effectiveness of Zinc, Administered Intra-nasally or Orally to Newly Received Stocker Cattle, Against Bovine Respiratory Disease and Effects on Growth Performance

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Introduction

Zinc, an essential dietary trace mineral, is required for proper cell function and overall health in cattle. Zinc’s role as a cofactor in enzymes involved in DNA synthesis and transcription is applicable to the expression of genes in many cell types, including those involved in immune response (Castro and Sevall, 1993). Zinc also has some antiviral properties, acting as a competitive inhibitor to rhinovirus particles entering the nasal epithelium (Cohen, 2006). Recognizing the potential of Zn, drug companies have developed throat lozenges and intra-nasal sprays for humans, which aim to reduce the severity and duration of cold symptoms by applying the Zn ion directly to the site of rhinovirus infection (Cohen, 2006).

Bovine respiratory disease is costly to beef producers (Bagley, 1997). It can be caused by a combination of stress, viral or bacterial infection (Bagley, 1997). In its upper-respiratory form, it elicits symptoms similar to that of a human cold (Bagley, 1997). The objectives of our research were to determine whether mucosal applications of Zn solutions could positively affect health and average daily gain of cattle susceptible to bovine respiratory disease, and to explore the effectiveness of intra-nasal or drench Zn applications in combating viral and bacterial populations.

Experimental Procedures

For this 43-d study, 88 male beef calves (22 steers and 66 bulls) averaging 501.6 lb initial BW were obtained from regional auction barns in western Arkansas and eastern Oklahoma. Upon arrival (d 0 of the study), cattle were processed routinely. They were assigned a unique ear identification tag and branded. Cattle were vaccinated for respiratory viruses including infectious bovine rhinotracheitis (IBR), bovine respiratory syncytial virus (BRSV), bovine viral diarrhea virus (BVDV), and parainfluenza, (PI, ) (Cattle Master Gold FP5, Pfizer Animal Health, New York, N.Y.) and clostridial diseases (Covexin 8, Schering Plough Animal, Omaha, Neb.). An antihelmhenthic was administered for internal parasites (Cydectin, Fort Dodge Animal Health, Fort Dodge, Iowa), and external parasites were also addressed (Double Barrel VP ear tags, Schering-Plough Animal Health, Summit, N.J.). Cattle were tested for persistent infection with BVDV (PI-BVDV) by collecting ear notch samples for testing using antigen capture ELISA (CattleStats, Oklahoma City, Okla). Bulls were castrated using the Callicrate banding method (No-Bull Enterprises, St. Francis, Kan.). All cattle were stratified by sex and assigned randomly to 8 pens. Pens were assigned randomly to 1 of 3 treatments. These treatments were administered on d 0: 22 calves (2 pens) received 3 mL of a Zn nasal spray solution (10.8 mg Zn as Zn acetate/mL of 0.9% saline solution) into each nostril using a single-use nasal atomizer (MAD100, Wolfe Tory Medical, Inc.; Salt Lake City, Utah); 33 calves (3 pens) received 40 mL of a Zn oral drench (16.25 Zn as Zn acetate/mL of 0.9% saline solution), and 33 calves (3 pens) received no Zn or saline at processing to serve as a negative control. The intra-nasal dose of Zn was designed to mimic the concentration found in products sold for human use. The Zn concentration in the oral drench was used in a previous study by Brazel and Stokka (1996).

Cattle were housed on eight 1.1 acre grass paddocks and were given ad libitum access to bermudagrass hay (14.5% CP, 74.5% NDF, and 34.7% ADF on a DM basis). Cattle were offered a grain supplement at 4 lb as fed/d. This supplement consisted of 68% corn, 28% dried distillers' grain, and vitamin and mineral premixes (analyzed to contain 14.7% CP). The diet met and/or exceeded all nutritional requirements for protein and minerals (including Zn) as set by the NRC (1996).

To monitor morbidity, cattle were observed daily for clinical signs of bovine respiratory disease. Those that were coughing, appeared lethargic, or had ocular or nasal discharge were pulled from the pen to measure their rectal temperatures. If a temperature was ≥104°F, the calf was considered morbid and a pre-planned regimen of antibiotics was administered. A treatment of florfenicol (Nuflor, Schering-Plough Animal Health, Summit, N.J.) was given initially. Morbid

Story in Brief

Male beef calves (n = 88) were purchased from regional auction barns and delivered as a single group. Upon arrival, cattle were assigned to 8 pens. Pens were assigned randomly to 1 of 3 treatments; 2 pens received 3 mL of a nasal spray solution (10.8 mg Zn/mL) into each nostril using a single-use nasal atomizer; 3 pens received 40 mL of an oral drench (16.25 mg Zn/mL), and 3 pens received no Zn at processing (negative control). Appropriate treatments were administered at processing on d 0 of the 43-d study. After treatment, cattle were processed and housed so they did not have fenceline contact with any other pens. Cattle were observed daily for clinical signs of bovine respiratory disease, and rectal temperatures were recorded. Nasal membranes of 4 randomly selected calves/pen were swabbed prior to any treatment on d 0 and then post-treatment on d 1, 2, 4, and 7. Calves treated with intra-nasal Zn at processing had lower average daily gain for the first 28 d as compared to controls (P = 0.02) or oral Zn (P = 0.07). Final BW and morbidity rate did not differ among treatments. Bacterial culture swabs were affected by treatment; fewer (P ≤ 0.04) Escherichia coli, alpha-Streptococcus spp., and Staphylococcus spp. colonies were cultured from cattle receiving the intra-nasal Zn. Bacterial cultures indicated decreased numbers of bacterial microbes in the nasal passages after treatment with intra-nasal Zn. Neither Zn treatment benefitted overall morbidity or performance of stressed cattle.
calves were checked again 48 h later. If the re-check temperature was 104°F or greater, a second antibiotic treatment of enrofloxacin (Baytril, Bayer HealthCare LLC, Animal Health Division, Shawnee Mission, Kan.) was given. After another 48 h, the rectal temperature was checked again. If it was still ≥104°F, the last antibiotic of cefitofer crystalline-free acid (Excenel, Pfizer Animal Health, New York, N.Y.) was administered daily for 3 d. No further antibiotics were administered after the third treatment. The rectal temperatures of all cattle were taken on d 0, 1, 2, 3, 4, and 7 to monitor the overall average rectal temperatures among treatments.

Performance was determined by observing BW gain and supplement intake. Cattle were weighed unshrunk on d 0 and then on d 1, 2, 4, and 7. Viral swabs were packed on ice and immediately shipped via overnight courier to the Oklahoma State University Center for Veterinary Health Sciences (Stillwater, Okla.). Bacterial swabs were taken directly to the University of Arkansas Division of Agriculture Veterinary Diagnostic Laboratory (Fayetteville, Ark.) and cultured 24 h on 5 different media plates. The 5 plates consisted of: a blood agar of 5% sheep blood, a Columbia CNA agar of 5% sheep blood, a chocolate agar, MacConkey agar, and a hekton enteric agar. Laboratory personnel monitored and assigned qualitative scores to these plates the following day.

To monitor viral and bacterial populations, the nasal membranes of 4 calves in each pen were swabbed prior to Zn treatment administration on d 0 and then on d 1, 2, 4, and 7. Viral swabs were packed on ice and immediately shipped via overnight courier to the Oklahoma State University Center for Veterinary Health Sciences (Stillwater, Okla.). Bacterial swabs were taken directly to the University of Arkansas Division of Agriculture Veterinary Diagnostic Laboratory (Fayetteville, Ark.) and cultured 24 h on 5 different media plates. The 5 plates consisted of: a blood agar of 5% sheep blood, a Columbia CNA agar of 5% sheep blood, a chocolate agar, MacConkey agar, and a hekton enteric agar. Laboratory personnel monitored and assigned qualitative scores to these plates the following day.

Performance, rectal temperature, and non-binomial morbidity data were analyzed using the MIXED procedure of SAS (SAS Institute, Inc., Cary, N.C.). The model included treatment; gender (arrived sex), in the feedlot, and for repeated observations (supplement intake and rectal temperatures), the model also included day and its interactions. Degrees of freedom were calculated using the Kenward-Roger procedure. The random statement included pens, and for repeated observations (supplement intake and rectal temperatures), the model also included day and its interactions. Bacterial scores and binomial morbidity data were analyzed using the GENMOD procedure of SAS. The model included treatment, gender, swab (where appropriate), day (where appropriate), and all interactions. Binomial distribution of data and Type 3 analysis were specified. The means were generated using the frequency procedure.

**Results and Discussion**

There were no differences in supplement intake (P = 0.97) or final BW (P = 0.15); however, rates of gain did differ among treatment groups (Table 1). Cattle that received the Zn nasal spray had lower ADG for the first 28 d of the study when compared to the control and oral Zn treatment groups (P < 0.10). On d 42, cattle treated with Zn nasal spray had lower ADG compared to control (P < 0.10), with the oral Zn treatment group being intermediate.

Although we randomly assigned cattle to treatment groups, those receiving the Zn nasal spray had higher initial rectal temperatures [(Fig. 1) (treatment by day interaction, P = 0.01)]. There were no other differences in rectal temperature observed. There was a tendency (P = 0.17) for fewer calves receiving the oral Zn to be treated for bovine respiratory disease with the first antibiotic as compared to calves receiving intra-nasal Zn (Table 1). More calves (P < 0.10) that received intra-nasal Zn had to be treated with a second antibiotic for bovine respiratory disease than calves that received oral Zn, and the control group had the fewest number of calves that required a second antibiotic. However, the average antibiotic treatments/calf and medication costs were not affected by Zn treatment (P ≥ 0.21). One calf on the control treatment, died during the study.

Numerous species of bacteria were cultured (Table 2), 4 of which are notable. *Pasteurella multocida* was by far the most prevalent in the cultures, and its occurrence tended to be affected by a treatment by day interaction (P = 0.07; Fig. 2); nasal swabs from calves that received intra-nasal Zn had lower percentages of *Pasteurella multocida* on d 2 and 4 than other calves. There were also treatment differences for 3 other species of bacteria (Fig. 3). Cattle that received Zn nasal spray had fewer colonies of *Escherichia coli*, alpha-*Streptococcus* spp., and *Staphylococcus* spp.

Unfortunately, there are no virus results to report. It is believed that miscommunication on the correct storage conditions of viral swabs may have compromised the results, as none of the swabs had detectable virus when cultured.

The negative effects of intra-nasal Zn on growth could be due to several factors. In humans, anosmia, or a loss of sense of smell, has been frequently noted as a potential side effect of using Zn nasal sprays (Cohen, 2006). If this were to occur in the cattle, decreased appetites may have also resulted (Grovum, 1998). We observed no differences among treatment groups for grain supplement intake. However, we were unable to measure hay consumption. There may have been differences in total feed intake that went undetected.

It appears that the Zn nasal spray had some antimicrobial effects. The question remains as to whether or not this was a positive outcome. Two of the more notable species found, *P. multocida* and *E. coli*, are gram-negative bacteria. As such, they release endotoxins upon their death, potentially leading to inflammation in the host animal (Tizard, 2000). Additionally, by altering the natural flora of the mucosal membranes, the cattle may have become more susceptible to infection by pathogenic microbes. Eliminating the normally non-pathogenic bacteria of the nasal passages may have been detrimental.

In conclusion, bacterial cultures indicated a reduced number of microbes in the nasal passages of cattle that received Zn nasal spray. However, neither Zn application appeared to have a positive effect on ADG or bovine respiratory disease in stressed cattle.

**Acknowledgments**

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**References**


Table 1. Growth performance and morbidity data for cattle receiving no zinc treatment (Control), zinc solution as a drench (Oral), or zinc solution as a nasal spray (Nasal).

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Oral</th>
<th>Nasal</th>
<th>SE</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Initial body weight, lb</td>
<td>503.8</td>
<td>501.6</td>
<td>501.6</td>
<td>8.58</td>
<td>0.96</td>
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<tr>
<td>Final body weight, lb</td>
<td>589.6</td>
<td>578.6</td>
<td>563.2</td>
<td>8.36</td>
<td>0.15</td>
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<tr>
<td>Supplement intake, lb/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>D 1 to 10</td>
<td>2.38</td>
<td>2.42</td>
<td>2.35</td>
<td>0.053</td>
<td>0.76</td>
</tr>
<tr>
<td>D 1 to 42</td>
<td>3.62</td>
<td>3.63</td>
<td>3.62</td>
<td>0.013</td>
<td>0.79</td>
</tr>
<tr>
<td>ADG, lb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D 1 to 28</td>
<td>2.02(^{a})</td>
<td>1.65(^{a})</td>
<td>1.43(^{b})</td>
<td>0.143</td>
<td>0.04</td>
</tr>
<tr>
<td>D 1 to 42</td>
<td>2.05(^{a})</td>
<td>1.78(^{a,b})</td>
<td>1.47(^{b})</td>
<td>0.134</td>
<td>0.06</td>
</tr>
<tr>
<td>Morbidity, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated with first antibiotic</td>
<td>73</td>
<td>70</td>
<td>77</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Treated with second antibiotic</td>
<td>19(^{a})</td>
<td>33(^{b})</td>
<td>36(^{c})</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Treated with third antibiotic</td>
<td>3</td>
<td>9</td>
<td>14</td>
<td></td>
<td>0.39</td>
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<tr>
<td>Antibiotic treatments/calf</td>
<td>0.7</td>
<td>1.3</td>
<td>1.3</td>
<td></td>
<td>0.25</td>
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<tr>
<td>Medication cost, $/calf</td>
<td>10.14</td>
<td>18.44</td>
<td>18.50</td>
<td>3.63</td>
<td>0.22</td>
</tr>
</tbody>
</table>

\(^{a,b,c}\) Means within a row without a common superscript are different \(P < 0.10\)

Table 2. A list of bacteria cultured from the nasal membrane swabs of cattle receiving no zinc treatment, zinc solution as a drench, or zinc solution as a nasal spray.

- Pasteurella multocida
- beta- Escherichia coli
- Escherichia coli
- alpha- Streptococcus sp.
- Staphylococcus sp.
- Bacillus sp.
- Moracella lacunata
- Serratia marcescens
- Lactose-E. coli
- Pseudomonas aeruginosa
- Enterobacter sp.
Fig. 1. Average rectal temperatures of cattle receiving no zinc treatment (Control), zinc solution as a drench (Oral), or zinc solution as a nasal spray (Nasal). Treatment by day interaction (P = 0.01). A = Nasal vs. Oral and Control (P < 0.05). B = Nasal vs. Oral (P < 0.05).

Fig. 2. Percentage of cattle receiving no zinc treatment (Control), zinc solution as a drench (Oral), or zinc solution as a nasal spray (Nasal) with positive nasal membrane swabs for *Pasteurella multocida*. Treatment by day interaction (P = 0.07).
Fig. 3. Percentages of different bacterial species found on nasal membranes swabs of cattle receiving no zinc treatment (Control), zinc solution as a drench (Oral), or zinc solution as a nasal spray (Nasal).