The Efficacy of Bacitracin Methylene Disalicylate when Fed in Combination with Narasin in the Management of Necrotic Enteritis in Broiler Chickens

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ABSTRACT The efficacy of bacitracin methylene disalicylate (BMD) in the management of necrotic enteritis (NE) when fed in combination with narasin was investigated in a floor-pen study of 2,000 broiler chickens using a Clostridium perfringens inoculum challenge model. Treatments consisted of 1) nonchallenged-nonmedicated; 2) challenged-nonmedicated; 3) challenged-narasin (70 ppm); 4) challenged-BMD (55 ppm); 5) challenged-narasin (70 ppm) + BMD (55 ppm). Medication was provided in the feed from Day 0 to trial termination on Day 41. C. perfringens challenge occurred from Day 14 to 16. BMD and narasin, fed alone and in combination, reduced (P < 0.05) mortality due to NE when compared to challenged-nonmedicated birds. NE lesion scores (Days 0 through 41) were lower among birds fed BMD and narasin, alone and in combination, compared to challenged-nonmedicated birds. Improvements in NE mortality and NE lesion scores were greatest for the BMD + narasin-medicated birds, followed by the BMD-alone, and then narasin-alone treated birds. BMD and narasin, alone and in combination, provided improvements (P < 0.05) in average daily gains over the entire study (Days 0 to 41). The results of this study demonstrate the effectiveness of BMD and narasin in the management of NE in broiler chickens.

(Key words: necrotic enteritis, bacitracin methylene disalicylate, narasin, Clostridium perfringens, broiler chicken)

INTRODUCTION

Necrotic enteritis (NE) caused by the Gram-positive bacillus Clostridium perfringens is a significant disease of broiler chickens throughout the world. First described in 1961, NE has been traditionally associated with outbreaks in 2-wk- to 6-mo-old chickens, characterized by depression, anorexia, and sudden death (Tsai and Tung, 1981; Frame and Bickford, 1985; Ficken and Wages, 1997). Increasingly, studies examining subclinical NE are suggesting significant economic losses associated with carcass condemnations and reduced production performance (Kaldhusdal and Lovland, 2000; Lovland and Kaldhusdal, 2001). Although not completely understood, NE is believed to have a complex, multi-factorial epizootiology (Ficken and Wages, 1997). Control of this condition depends upon a variety of actions, including reducing exposure to various dietary risk factors, reducing concurrent enteric infections (particularly coccidiosis), managing litter properly, and using feed additives with activity against C. perfringens (Ficken and Wages, 1997).

Certain antibiotics and anticoccidials have been demonstrated to have inhibitory effects on the growth of C. perfringens (Watkins et al., 1997). However, little is known of the joint compatibility of antimicrobials and anticoccidials when fed together for the management of NE. The objective of the present study was to evaluate the efficacy of bacitracin methylene disalicylate (BMD) when fed in combination with narasin in the management of NE in C. perfringens-challenged broiler chickens. The in vivo efficacies of BMD and narasin for the management of NE have been previously demonstrated (Brennan et al., 1996, 2001).

MATERIALS AND METHODS

A randomized complete block design was utilized in this study. A total of 2,000 male 1-d-old Ross × Ross broiler chicks purchased from a commercial hatchery was used. The following five treatments were evaluated: 1) nonchallenged-nonmedicated; 2) C. perfringens-challenged-nonmedicated; 3) challenged-narasin (70 ppm); 4) challenged-BMD (55 ppm); and 5) challenged-narasin (70 ppm) and BMD (55 ppm). Narasin and BMD were admin-

Abbreviation Key: BMD = bacitracin methylene disalicylate; NE = necrotic enteritis.
istered in the feed from the start of the trial (Day 0) to the end (Day 41). Birds were vaccinated for Marek’s disease at the hatchery and received no other medication throughout the study other than narasin and BMD. All experimental procedures were conducted in accordance with the guidelines of the Canadian Council on Animal Care (1993).

The research facility was thoroughly cleaned and disinfected prior to bird placement. Birds were randomly assigned in groups of 250 to one of five adjacent pens (50 birds per pen) in the trial facility (five pens per block). Pens within each block were randomly assigned one of the five treatments. This was repeated eight times (40 pens in total). Each pen had a concrete floor, new wood shavings, and provided 4.2 m² of floor space. Solid plastic barriers extending 30 cm from floor level, followed by 90 cm of welded wire, separated the pens. Lighting program, heating, ventilation, and other management procedures were typical of broiler chicken producers in the local geographic area of Ontario, Canada. Four nipple-type drinkers per pen provided water ad libitum. Replacements were not made for early mortality.

Dry feed was provided ad libitum by one tube-type feeder per pen except during the C. perfringens challenge period, when inoculum-feed mixture was provided in trough-type feeders. Birds were fed broiler starter on Days 0 to 7 and high protein starter on Days 8 to 13 containing fishmeal (a recognized risk factor for naturally occurring outbreaks of NE [Truscott and Al-Sheikhly, 1977]). Feed was withdrawn from all pens for 4 h on Day 14, prior to commencement of the challenge. Broiler starter was subsequently fed until Day 21, and a broiler grower was fed to the end of the trial (Day 41).

The C. perfringens-challenge model was based on that developed originally by Prescott et al. (1978). The challenge inoculum contained approximately \( 1 \times 10^8 \) cfu C. perfringens/mL at the time of administration. The challenge strain was originally isolated from a field case of NE in an Ontario broiler flock (Brennan et al., 1996). The inoculum was administered to birds via feed, using trough-type feeders, in the morning and afternoon commencing on Day 14 a.m. and ending Day 16 p.m.

Birds were observed on a pen basis at least once daily. Birds that were moribund and unable to reach food or water were culled and euthanized by cervical dislocation. All culled or dead birds were necropsied to determine the cause of morbidity or death. A gross pathologic diagnosis of NE was based on the presence of intestinal lesions typical of naturally occurring and experimentally produced NE: focal to confluent areas of bland mucosal necrosis of the small intestine, often forming a pseudomembrane with no gross evidence of inflammatory reaction or haemorrhage. All dead or culled birds were scored for intestinal lesions as follows: 0 = no gross lesions; 1 = thin-walled or friable; 2 = focal necrosis or ulceration; 3 = large patches of necrosis; 4 = severe extensive necrosis (Prescott et al., 1978). Three birds were randomly selected from each pen on Day 17, euthanized, weighed, and scored for NE lesions and coccidiosis lesions, the latter according to criteria established for floor-pen studies in chickens (Johnson and Reid, 1970).

Feed consumption and BW were measured on a pen basis on Days 0, 14, 21, and 41, except during the 3-d challenge period when feed consumption was measured twice daily. One sample of each feed was analyzed for DM, CP, calcium, phosphorus, sodium, narasin, and bacitracin. Permitted analytical variation of drug content for all medicated feeds was ±25% of calculated drug content.

The pen was considered the experimental unit for all statistical analyses. Statistical analyses were conducted using the SAS System (SAS Institute, 1997). Data were analyzed using the MIXED procedure (Littell et al., 1996), which fits both fixed effects (treatment) and random effects (block). Mortality, gross-lesions, feed consumption, and growth parameters were evaluated among treatment groups for three time periods: 0 to 14, 0 to 21, and 0 to 41 d. Mortality data were transformed with the arcsine transformation prior to analyses (Steel and Torrie, 1980).

**RESULTS**

BMD (55 ppm) and narasin (70 ppm), fed alone and in combination, reduced \( P < 0.05 \) mortality due to NE when compared to C. perfringens challenged-nonmedicated birds (Table 1). Improvements in NE-associated mortality among medicated birds in comparison with the two nonmedicated treatment groups, were greatest for the BMD + narasin-mediated birds, followed by those treated with BMD alone, and then those treated with narasin alone. Similarly, overall mortality by Day 41 was lower among treatment groups receiving BMD and narasin, administered alone and in combination, compared to challenged-nonmedicated and nonchallenged-nonmedicated birds. These differences were significant \( P < 0.05 \) for the BMD-treated birds (with and without narasin) compared to the challenged-nonmedicated birds. Non-NE mortality was principally the result of septicemia, which occurred mainly between Days 21 and 41. Cause-specific mortality between 21 and 41 d of age consisted of the following: septicemia, 60%; NE, 1%; urate nephrosis, 10%; sudden death syndrome, 5%; ascites, 6%; proventricular hemorrhage, 3%; leg deformities, 9%; no diagnosis, 4%; other, 3%. Most cases of septicemia involved septic arthritis, osteomyelitis, or both.

NE lesion scores among birds necropsied throughout the 41-d study (birds randomly selected on Day 17 together with all mortalities) were lower among birds receiving BMD and narasin, fed alone and in combination, than among challenged-nonmedicated birds (Table 1). Within medicated groups, improvements were greatest for the BMD + narasin-mediated birds \( P < 0.05 \), followed by birds treated with BMD alone \( P < 0.05 \), and then birds treated with narasin alone \( P > 0.05 \). Improvements \( P < 0.05 \) in mean NE lesion scores on Day 17 were experienced among BMD-treated birds (fed alone and in combination with narasin) compared with challenged-nonmedicated birds.
TABLE 1. Mortality and lesion scores in a study of the efficacy of bacitracin methylene disalicylate (BMD) in combination with narasin for the management of necrotic enteritis (NE) in broiler chickens

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Mean NE lesion scores</th>
<th>Overall mortality (%)</th>
<th>NE Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17 d</td>
<td>0 to 41 d</td>
<td>0 to 14 d</td>
</tr>
<tr>
<td>Challenged</td>
<td>No</td>
<td>0.4 b</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1.8 b</td>
<td>1.36</td>
</tr>
<tr>
<td></td>
<td>Yes Narasin</td>
<td>1.9 a</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>Yes BMD</td>
<td>0.2 b</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Yes BMD + narasin</td>
<td>0.0 b</td>
<td>1.42</td>
</tr>
</tbody>
</table>

a–dMeans within columns with different superscripts are significantly different (P < 0.05).
10 (no gross lesions) to 4 (severe extensive necrosis).
Three birds were randomly selected from each pen on Day 17.
Birds randomly selected on Day 17 together with all mortalities occurring from Days 0 to 41.

BMD and narasin, fed alone and in combination, provided significant improvements (P < 0.05) in average daily gain over the entire study (Days 0 to 41) compared with both nonmedicated treatment groups (challenged and nonchallenged; Table 2). Among the same treatment groups, improvements were also observed by Day 41 in average daily feed intake; these improvements were significant at the 5% level for the BMD-medicated birds (both alone and in combination with narasin). Feed-to-gain ratios were improved by Day 41 among birds receiving BMD and narasin, alone and in combination, when compared with challenged-nonmedicated birds; these differences were significant at the 5% level for the birds treated with BMD + narasin and for the birds treated with narasin only (Table 2). In general, there were only minor differences in growth performance parameters among all three medicated groups (narasin, BMD, BMD + narasin).

All feeds were within tolerance for analyzed drug and nutrient contents. No gross lesions consistent with coccidiosis were observed among necropsied birds.

DISCUSSION

The results of this study demonstrate that BMD and narasin, fed alone and in combination, are effective in reducing morbidity, mortality, and suppression of growth and feed efficiency associated with NE among broiler chickens challenged with *C. perfringens*. Improvements in morbidity and mortality were most pronounced among BMD + narasin-treated birds, followed by the BMD-alone- and narasin-alone-treated birds. The effectiveness of BMD and narasin in reducing mortality, and in improving growth parameters in *C. perfringens*-challenged broilers in the present investigation, is consistent with previous in vivo studies (Brennan et al., 1996, 2001).

Significant reduction in NE lesion scores among medicated birds on Day 17 demonstrate that, in addition to reducing mortality, administration of BMD (alone or in combination with narasin) significantly reduced the clinical impact of challenge among surviving birds. This result suggests that the positive effect of BMD on growth parameters was related to control of NE and not simply a result of growth promoter effect. The fact that NE-associated mortality was decreased by the administration of narasin alone also suggests that the effect of narasin on growth parameters was at least in part due to the control of clinical NE.

Broiler deaths due to NE occurring among nonchallenged birds underscore the vulnerability of birds managed under typical conditions of modern poultry husbandry to this disease. NE is believed to have a complex epizootiology involving many factors, including dietary factors and concurrent infection (Ficken and Wages, 1997). In the present investigation, broilers were fed a high-protein starter containing 50% fishmeal, a recognized risk factor for naturally occurring outbreaks of NE (Truscott and Al-Sheikhly, 1977). *C. perfringens* can often be found in the intestinal tracts of normal chickens, and it has been suggested that *C. perfringens* may be transmitted vertically (Shane et al., 1984; Ficken and Wages, 1997).

TABLE 2. Growth performance measures in a study of the efficacy of bacitracin methylene disalicylate (BMD) in combination with narasin for the management of necrotic enteritis (NE) in broiler chickens

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Average daily gain 1 (kg/bird per d)</th>
<th>Average daily feed intake 1 (kg/bird per d)</th>
<th>Feed conversion 1 (feed:gain ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Challenged</td>
<td>0 to 14 d 0 to 21 d 0 to 41 d</td>
<td>0 to 14 d 0 to 21 d 0 to 41 d</td>
<td>0 to 14 d 0 to 21 d 0 to 41 d</td>
</tr>
<tr>
<td>No</td>
<td>0.022 b 0.031 c 0.049 b</td>
<td>0.024 b 0.043 d 0.090 d</td>
<td>1.103 bc 1.468 b 1.957 ab</td>
</tr>
<tr>
<td>Yes</td>
<td>0.022 b 0.028 d 0.048 b</td>
<td>0.024 b 0.043 d 0.091 cd</td>
<td>1.126 a 1.687 a 2.017 a</td>
</tr>
<tr>
<td>Yes Narasin</td>
<td>0.022 b 0.031 c 0.051 a</td>
<td>0.024 b 0.045 a 0.094 bc</td>
<td>1.088 bc 1.538 b 1.919 b</td>
</tr>
<tr>
<td>Yes BMD</td>
<td>0.026 a 0.036 a 0.053 a</td>
<td>0.028 a 0.051 a 0.100 a</td>
<td>1.117 ab 1.500 b 1.981 a</td>
</tr>
<tr>
<td>Yes BMD + narasin</td>
<td>0.022 b 0.033 b 0.053 a</td>
<td>0.024 b 0.047 b 0.096 ab</td>
<td>1.101 bc 1.494 b 1.900 b</td>
</tr>
</tbody>
</table>

a–dMeans within columns with different superscripts are significantly different (P < 0.05).
1Adjusted for mortalities and removals due to morbidity.
Non-NE mortality was principally the result of septicemia between Days 21 and 41. Most of these cases involved septic arthritis and/or osteomyelitis. Whether or not this was a direct consequence of prior NE in these birds is unknown.

The results of this study thus demonstrate the effectiveness of BMD and narasin in the management of *C. perfringens*-challenge-induced NE in broilers, together with the compatibility of BMD when administered with narasin. Furthermore, given the observed trends in mortality and NE lesion scores among the treatment groups, there is evidence to suggest benefits to medicating with BMD in combination with narasin in the management of NE even in the absence of clinical coccidiosis.

**REFERENCES**


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