Plasma 3-methylindole and Blood 3-methyleneindolenine in Feedlot Cattle

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Introduction

Bovine respiratory disease complex (BRD) results from an interaction of stressors, animal susceptibility and respiratory pathogens. Well known factors that increase the likelihood of BRD development include young animals, long transportation distances and dehydration. Rumen-generated toxins, such as 3-methylindole (3MI), may also be an important BRD-propagating factor.

Animals challenged with both bovine respiratory syncytial virus (BRSV) and 3MI developed more severe respiratory disease than animals challenged with BRSV or 3MI alone.¹ Further, animals with greater serum 3MI concentrations at feedlot arrival had greater odds of being treated for respiratory disease than animals with lower serum 3MI.²

3-methylindole must be metabolized to induce toxicity. Enzymes responsible for the bioactivation of 3MI are P450s and prostaglandin H synthetase (PHS).^{3,5} These enzymes are found in high concentrations in the bovine Clara cells. The putative pneumotoxic metabolite of 3MI thought responsible for 3MI-induced disease is 3-methyleneindolenine (3MEIN).⁴ Pulmonary injury is prevented if bioactivation of 3MI is blocked.

Materials and Methods

Blood samples were collected from 64 yearling steers four times a week for three weeks; followed by three times a week for a further five weeks; then once a week for the remainder of the study. Plasma was analyzed from all animals for 3MI concentration. Whole-blood samples from 32 animals collected during the first eight weeks were analyzed for 3MEIN-adduct concentration.

Results and Conclusions

Plasma 3MI concentrations unexpectedly decreased during the first 54 days on feed which is the period of greatest risk for BRD development in feedlot cattle. After day 54, plasma 3MI concentrations increased. However, this increase occurred during the phase of feeding in which it is believed cattle are at lowest risk of BRD.

Blood 3MEIN-adduct concentrations increased and peaked on day 33. Overall, the three greatest mean values were observed on days 16, 23, and 33. Concentrations then decreased substantially. Hence, increased blood 3MEIN-adduct concentrations were associated with the greatest-risk period for BRD.

Even thought 3MEIN is a metabolite of 3MI, plasma 3MI and blood 3MEIN concentrations were negatively correlated. This may indicate that the activity of the enzymes that convert 3MI to 3MEIN is more important than the concentration of 3MI in the pathogenesis of BRD.

References

- 1. Bingham HR, et al: Am J Vet Res 60:563-70, 1999.
- 2. Bingham HR, et al: Am J Vet Res 61:1309-14, 2000.
- 3. Bray TM, Emmerson KS: Anu Rev Pharmacol Toxicol 34:91-115, 1994.
- 4. Thorton-Manning J, et al: J Pharmacol Exp Therap 276:21-9, 1996.
- 5. Yost GS: Chem Res Toxicol 2:273-9, 1989.

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