Comparison of tilmicosin and gamithromycin for treatment of undifferentiated fever in backgrounded winter-placed feedlot calves

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Abstract

A study was conducted in Alberta, Canada utilizing 2 feedlots to compare clinical efficacy of tilmicosin to gamithromycin for the initial treatment of undifferentiated fever in backgrounded winter-placed feedlot calves. There were no significant differences ($P > 0.05$) in undifferentiated fever relapse rates and crude case fatality or bovine respiratory disease/histophilus fatality rates between the 2 treatments. As a result, the cost-benefit was based on the difference in treatment cost between the 2 drugs. Using current drug costs and a treatment weight of 750 lb (340 kg), tilmicosin had an economic advantage of $2.23\text{CAN}$ per head over gamithromycin.

Key words: bovine respiratory disease, undifferentiated fever, tilmicosin, gamithromycin

Introduction

Various therapeutic antimicrobials are used to treat bovine respiratory disease (BRD) and undiffer-
coccidiosis as per label claims. Tylosin phosphate was included in the starter ration to reduce the incidence of liver abscesses as per label claims. All pens of cattle were fed rations 3 times daily on an *ad libitum* basis using truck-mounted mixers on load cells.

**Study Animals**

Backgrounded steer calves used in the study arrived from January through April 2012. These animals were approximately 6 to 10 months of age, and body weights ranged from 700 to 800 lb (318 to 364 kg). These calves were purchased through the auction market or directly from a backgrounding feedlot. The history of these calves prior to feedlot arrival was not known, which is typical in purchased feedlot cattle.

Upon arrival at the feedlot, animals were given a modified-live infectious bovine rhinotracheitis and bovine viral diarrhea virus (types 1 and 2) vaccine, 8-way clostridial bacterin, *Histophilus somni* bacterin, *Mannhemia haemolytica* leukotoxoid vaccine, ivermectin, and an anabolic implant. All processing products were administered as per label dosage and route. No metaphylactic antimicrobials were used at induction processing. All animals were uniquely identified with a numbered feedlot ear tag and CCIA (Canadian Cattle Identification Agency) tag.

**Experimental Design**

The sample size used was 390 animals per treatment group. Based on a historical initial BRD treatment rate of 15 to 20%, the trial had a power of 80% and a 95% confidence interval to show at least an 8% difference in rate of 15 to 20%, the trial had a power of 80% and a 95% ment group. Based on a historical initial BRD treatment...

A diagnosis of the initial case of UF (undifferentiated fever) was made on an animal if the following criteria were satisfied: 1) the case abstract, which appeared on the computer screen, indicated no previous treatment history for UF; 2) there was an absence of clinical signs attributable to organ systems other than the respiratory tract; 3) there were signs referable to the respiratory system such as depression, inappetence, rapid or labored breathing, nasal discharge, or coughing; and 4) animals met the temperature criteria (≥104.0°F; ≥40°C). If all these criteria were met, then the animal was treated and designated as UF. All treated animals were returned to their home pen the same day of treatment unless they were severely compromised, defined as those animals that could not walk back to their home pen due to weakness or severe disease. Cattle that were severely compromised were housed in the hospital pen until they could be returned home; if not, they were euthanized. Severely compromised animals were humanely euthanized as per the feedlot veterinarian’s euthanasia protocol if they were in severe respiratory distress or could not rise by themselves or were severely emaciated and dehydrated.

A diagnosis of a relapse case of UF (first or second) was made on the individual animal if the following criteria were satisfied: 1) the case abstract indicated previous treatment for UF, 2) there was an absence of clinical signs attributable to organ systems other than the respiratory tract, and 3) there were signs referable to the respiratory system such as depression, inappetence, labored or rapid breathing, nasal discharge, and/or coughing. An animal was considered a relapse for disease regardless of the time interval from previous treatment to subsequent treatment. This case definition of UF relapse rates is typical in western Canadian feedlot medicine. Animals that relapsed were treated according to the feedlot’s standard treatment...
protocol; all steers that relapsed were treated with the same protocol, regardless of initial therapy.

A calf was defined as a chronic if pulled as a third UF relapse. Such individuals were sent to the chronic pen and no further treatment for that disease was administered because it was unlikely to improve the animal’s health, and there were concerns about treatment cost and development of antimicrobial resistance. If calves were moribund at any time, they were humanely euthanized. Calves gaining weight that could not be returned to their home pen because they could not compete with peers for feed and water were sent to a rail pen for fattening and slaughter.

Animals that either died naturally or were euthanized during the trial period were necropsied by feedlot veterinarians to determine the cause of death. The cause of death was based on gross pathology.

Data Analysis

Data were analyzed using analytical software programs (SAS™ System for Windows, Release 9.1; SAS Institute, Cary, North Carolina, USA). UF relapse rates were the proportion of UF cases previously pulled. Crude case fatality was the proportion of UF cases that died for any reason and BRDHS case fatality was the proportion of UF cases that died from respiratory disease (fibrinous and/or bronchopneumonia) or histophilosis (i.e. myocarditis, pericarditis, endocarditis, pleuritis, arthritis) based on gross necropsy findings.

Myocarditis, pericarditis, endocarditis, and pleuritis (without pneumonia) are classic lesions observed in histophilosis. Arthritis, with or without bronchopneumonia may be caused by *H. somnus* and/or mycoplasma, but for the purposes of this study it was included in the category BRDHS since this syndrome may be caused by *H. somnus* and both microorganisms are potentially responsive to the antimicrobials being tested here.

Differences in UF relapse rates and case fatality rates between tilmicosin and gamithromycin were analyzed using generalized linear mixed modeling techniques (PROC GLIMMIX) to account for the clustering of calves within pens and feedlots, with both variables treated as random effects. A binomial data distribution and logit link function were used in the modeling procedure. Calculation of Wald-type confidence intervals was done by using pseudo-likelihood estimation. The parameter estimates and 95% confidence intervals were estimated using an interior point algorithm and the Markov chain marginal bootstrap method, respectively. The significance of each factor was assessed using both Wald and Likelihood ratio tests.

Results and Discussion

A total of 784 animals were allocated to the trial, 393 animals in the tilmicosin group and 391 animals in the gamithromycin group. Results are presented in Table 1. There were no statistically significant differences (*P* > 0.05) between cattle treated with tilmicosin or gamithromycin in UF relapse rates, crude case fatality rates, BRDHS case fatality rates or post-treatment intervals. In the tilmicosin group, 6 animals died from BRDHS; specifically, 2 from chronic pneumonia, 2 from fibrinous pneumonia, and 2 from myocarditis. In the gamithromycin group, 8 animals died from BRDHS; 3 from chronic pneumonia, 2 from myocarditis, 1 from endocarditis, 1 from pericarditis, and 1 from arthritis.

The PTI between initial treatment and first UF relapses was 30 days for the tilmicosin group and 42 days for the gamithromycin group (data not shown). The PTI between first UF relapse and second UF relapses was 12 days for the tilmicosin group and 10 days for the gamithromycin group. In this study, relapses were defined as any retreatment of UF regardless of the time interval between initial treatment and subsequent retreatment following the minimum PTI of 5 days set for the therapeutic drugs being tested. It is not known with certainty when an animal is repulled for retreatment of UF whether it is actually a new occurrence of UF or failure of previous treatment. In western Canada, a proportion of UF cases are not respiratory disease, but instead are septicemia from histophilosis, and the time interval from initial treatment to retreatment and/or fatal disease can be quite long.

Failure to see differences between the macrolide drugs in UF relapse and case fatality rates suggests that these two antimicrobials performed equally in backgrounded calves in western Canada at low to moderate risk of UF. It is not known how clinical efficacy of these two antimicrobials would compare in higher-risk cattle, or in cattle where the post-treatment interval for the drugs was eliminated or extended beyond 5 days. The PTI for tilmicosin can be extended from 5 to 7 days without any negative health effects. There is no published feedlot trial data in North America evaluating the clinical efficacy of gamithromycin for treating BRD/UF using different PTIs.

Macrolide antimicrobials are the most common class of metaphylactic antimicrobial used in fall-placed
calves in western Canada that are medium to high risk of UF. It is not known if using a macrolide antimicrobial at arrival processing in these backgrounded winter-placed calves would have affected clinical efficacy of tilmicosin and gamithromycin when used as the therapeutic drug to treat initial cases of UF. There are no published studies comparing the clinical efficacy of tilmicosin as a therapeutic drug to another class of antimicrobial following tilmicosin metaphylaxis at feedlot arrival. A few studies have evaluated the therapeutic treatment success of tilmicosin in calves with or without tilmicosin metaphylaxis and found no difference in the therapeutic treatment success rates between those given tilmicosin on arrival and non-medicated controls. Two feedlot trials found that florfenicol was more effective than tulathromycin as an initial therapeutic drug following metaphylactic treatment with tulathromycin or tilmicosin. It is not known if the lower therapeutic efficacy of tulathromycin was due to development of antimicrobial resistance following previous metaphylactic treatment with a macrolide. Further research is needed to answer these questions, preferably in commercial feedlots using controlled field trials so that the data has both internal and external validity; thus, the results provide objective data for bovine practitioners in decision making.

**Conclusions**

The cost-benefit between the 2 antimicrobials for initial treatment of UF here was simply the difference in treatment cost between tilmicosin and gamithromycin, since there were no significant differences in relapse rates or mortality. Using current market prices and a treatment weight of 750 lb (340 kg), using tilmicosin for therapeutic treatment of UF had an economic advantage of $2.23CAN per head over gamithromycin.

**Endnotes**

- DG Professional, ITS Global, Okotoks, Alberta, Canada
- Rumensin®, Elanco, a Division of Eli Lilly Canada, Inc.
- Tylan®, Elanco, a Division of Eli Lilly Canada, Inc.
- Super Calc 3, IBM PC
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- Zactran®, Merial Canada Inc.
- M750 thermometer, GLA Agricultural Electronics, San Luis, Obispo, CA

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**References**


