Effects of In-Feed Chlortetracycline Prophylaxis of Beef Cattle on Animal Health and Antimicrobial-Resistant Escherichia coli

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USMARC Antimicrobial Resistance Research in Animal Agriculture

• What is the contribution of antimicrobial use in food animals to compromised human health outcomes due to resistance?

• How can antimicrobial resistance in animal agriculture be mitigated?
WHO Antimicrobial Classification

Fluoroquinolones, 3rd and 4th generation cephalosporins, macrolides and glycopeptides have been categorized as being highest priority critically important antimicrobials.

Tetracyclines (listed as highly important) are not a first-line treatment option for serious gram negative infections; however, with increasing resistance to other drug classes, tetracyclines are considered as a treatment option.
Multiple paths to achieve the same resistance: Co-selection
Evaluation of chlortetracycline mass treatment of weaned calves

Objective:
To evaluate the effect of chlortetracycline mass treatment in weaned beef calves on the dynamics of tetracycline-resistant (TET\textsuperscript{T}) and third-generation cephalosporin-resistant (3GC\textsuperscript{R}) \textit{E. coli} during the entire feeding period.

Background:
- Chlortetracycline is applied as a mass therapy in the feed of weaning calves to prevent respiratory diseases associated with weaning stress.
- Various studies have indicated that tetracycline resistance in livestock is widespread.
- Previous studies have found positive and negative correlations between CTC treatment and 3GC resistance. These studies were short-term investigations.
- \textit{In vitro} studies suggest a tetracycline metabolite represses TET\textsuperscript{T}.

- Study:
  - 30 calves in 10 pens, 5 treated pens and 5 control pens
  - Collected fecal, pen surface material, and feed samples
  - Treated animals were removed from the study
Experimental design

- 150 calves randomized by sex per treatment
- 30 head per pen
- 5 pens per treatment
- CTC was given for 5 days: FEB 14—18
- Any treated animal was removed from the study
- Samples:
  - Fecal swabs
  - Pen surface
  - Water troughs
  - Feed

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- 30 head per pen
Metrics

• Evaluate the effect of in-feed chlortetracycline mass prophylaxis in beef cattle on:
  – Prevalence and concentration of tetracycline and 3\textsuperscript{rd} generation cephalosporin-resistant \textit{E. coli} in fecal swabs and pen surface samples.
  – Animal health

What constitutes judicious use?
CTC prophylaxis reduced morbidity

Hazard ratio = 27.9: 95% CI = 6.7-116.5
CTC prophylaxis reduced morbidity

Cattle treated for BRD received tildipirosin
(Zuprevo®, macrolide)
Performance

![Graph showing mean body weight over time for CTC and control groups. The graph includes data points for Arrival, 5 dpt, 27 dpt, 75 dpt, and 117 dpt, with error bars indicating variability. The graph compares the performance of CTC and control groups, showing a trend in mean body weight over time.]
Fecal swabs: TET⁺ *E. coli* concentration
3GC<sup>+</sup> E. coli prevalence: Fecal swabs

![Graph showing prevalence of 3GC<sup>+</sup> E. coli over time in fecal swabs with CTC and control groups.](image)
Pen surface samples: TET$^+$ *E. coli* concentration
Summary

Results:
- Increased morbidity in non treated animals (25% vs 1.3%)
  - Sick pulls required treatment with a macrolide
- No difference in tetracycline resistance levels in fecal swabs or pen surface material samples.
- No difference in prevalence of 3GC resistance in fecal swabs for treated and control animals.

Conclusions:
Mass treatment with chlortetracycline:
- is a prudent use of antimicrobials as prophylaxis for weaning related illness.
- minimizes the use of higher value antimicrobials required for therapeutic treatments.
- does not cause increased tetracycline or 3GC resistance when compared to non-treated animals.
Pen surface samples: TET' *E. coli* concentration
Is it selection or enrichment?

- Addition of nutrients to unamended soil