The effect of antibiotic use on resistance in commensal E. coli from pre-weaned calves on a dairy farm in Washington State

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Antibiotic use in dairy calves

- Treatment protocols for observed syndromic diarrhea and respiratory cases
- Antibiotics are used to protect animal well-being (focus on preventing mortality)
- Management goal to use antibiotics carefully (focus on preventing mortality)

Specific aims

- Document antibiotic use in pre-weaned calves
- Determine ABR patterns in commensal E. coli recovered from pre-weaned calves
- Evaluate impact of antibiotic use on ABR and analyze age and temporal trends in ABR patterns

Study design

- Repeated sampling within age cohorts (not necessarily the same animals) on a single farm
- Study conducted from June 2016 to January 2017
- Initial sampling interval 6 week, then 2 weeks thereafter
- Calves 1 – 11 weeks old
- Collected a total of 9 – 11 fecal samples from calves at each sampling
  - one randomly selected calf from each age category
  - all treatment history from a selected calf

E. coli isolation & ABR testing

- Direct fecal culture on MAC agar
- 4 isolates picked per sample & E. coli confirmed using biochemical tests
- ABR testing using an agar micro-dilution assay with 13 antibiotics
- ABR determined as susceptible, intermediate and resistant & reclassified as susceptible and resistant

Data analysis

- Latent class analysis (LCA) of ABR data to create parsimonious (not perfect) groups to reflect resistance patterns to the tested antibiotics
- Latent regression analysis to determine associations of age and antibiotic treatment with resistance class
90% calves received antibiotic treatment

- 14 sampling dates, 140 fecal samples collected & 545 E. coli isolates characterized
- Treatment Frequency (60 day pre-weaning period)
  - 36/140-26% received a single antibiotic treatment
  - 37/140-26% received 2 treatments
  - 30/140-21% received 3 treatments
  - 23/140-16% 4-6 treatments
  - 14/140-10% no treatments
- Median age: 1x (9 days), 2x (15 days), 3x (25 days)

Antibiotics used

- Sulfamethoxazole used most frequently (59%) for 1st treatment.
- Combination of ampicillin and sulfamethoxazole used (69%) for 2nd treatment.
- Enrofloxacin most commonly used for 3rd treatment.
- Enrofloxacin, florfenicol, or tulathromycin used if more than 3 treatments

5 resistance classes

- LCA modeled 11 antibiotics (AN and AMC not used) & optimized at 5 resistance classes
- 13% of the isolates had high probability of resistance to tetracycline -- T
- 22% resistant to chloramphenicol (C), streptomycin (S), sulfisoxazole (Su) & T -- CSSuT
- 23% extensively drug resistant (XDR) including nalidixic acid (Nal) resistance -- XDR-Nal'Cip'Xnl'
- 18% XDR including Xnl resistance -- XDR-Nal'Cip'Xnl'
- 24% XDR including Nal, Cip & Xnl resistance -- XDR-Nal'Cip'Xnl'

Latent regression analysis

- Association between age, treatment intensity and ABR class
- 2 – 3 week olds more likely in XDR-Nal'Cip'Xnl' class than 1 week olds (most likely to be in T class)
- Calves that received 3 or 4-6 treatments more likely to be in XDR classes than untreated calves or calves that received 1 – 2 treatments

Fluoroquinolone resistance associated with enrofloxacin use but ceftiofur resistance not associated with ceftiofur use

- 45 calves (32%) treated with enrofloxacin
- E. coli from enrofloxacin treated calves more likely to be resistant to ciprofloxacin (OR 2.5, 95% CI 1.7 – 3.7) and/or nalidixic acid (OR 2.8, 95% CI 1.9 – 4.0) than E. coli from calves not treated with enrofloxacin
  - (these also had greatest cumulative number of treatments)
- 3 calves (2.3%) treated with ceftiofur but 27% of E. coli resistant to ceftiofur

Biological Summary and Conclusions

Antibiotic Use and Intensity Matters

- 90% of calves in this study received an antibiotic at least one time and XDR was the prevalent ABR pattern
- Resistance class membership was age dependent
- Cumulative treatment intensity was associated with XDR
  - Enrofloxacin use was associated with fluoroquinolone resistance (NAL or CIP)
  - Ceftiofur resistance not associated with related antibiotic class use, i.e. ceftiofur
Reflections on Biological Conclusions

- Off farm employees tasked with keeping calves healthy
- Role of veterinarian was to provide treatment protocols but use decisions are in the hands of employees
- Diagnostic and Treatment decisions are based on observation, experience, and belief with a focus to keep calves alive
- The progression of treatment decisions reflects progression of the farm treatment protocols
- The options available to employees for managing calf well being is not limited to antimicrobials but the belief in their efficacy to “heal” is unshakable

5 observed resistance classes

[XDR-Nal>Cip×κr, T, XDR-Nal>Cip×κr; CSSuT, XDR-Nal>Cip×κr]