Quantification of Antimicrobial Drug Use in Pre-weaned Calves from California Dairies and Calf Ranches

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INTRODUCTION

Antimicrobial drug use (AMD) has been a predominant concern for the rise of antimicrobial resistance (AMR), which is considered a global threat.

Intensive production systems are prone to infectious diseases. In dairy calves, diarrhea and bovine respiratory disease are the main causes of morbidity and mortality which leads to economic loss. Calf health during pre-weaning affects future production, growth, and reproductive efficiency.

The use of AMD to treat, control, or prevent these diseases is common practice, this may contribute to the development and spread of resistance.

This study was done immediately after the implementation of the veterinary feed directive starting January 2017, and prior to the implementation of the California Senate Bill 27, which came into effect January 2018. Both of these regulations increased veterinary oversight in the distribution and use of antimicrobials in livestock. Therefore this study was done to establish baseline data during this time of regulatory change to evaluate the future impact of these regulations.
METHODS

- A longitudinal study conducted 2017 collected data on disease treatment from a cohort of 310 calves enrolled from four calf ranches and three dairies in California.
- An enrollment survey was completed for each premise to record information on farm demographics and calf management practices including feeding regimen and type of diet along with medications added to milk.
- All treatments given to calves from day 0 to day 60 were recorded on treatment cards attached to calf hutches.
- Antimicrobial drug use was quantified based on the treatment incidence and amount of active antimicrobial substance administered.
- A logistic regression model following a manual causal diagram-based model building approach and a Goodness of Fit test using the Akaike Information Criterion was used to determine the associations between treatment and management practices.
RESULTS

Fig 1. Disease incidence among enrolled calves during the pre-weaning period.

There were 4 different diseases noted during the study period, with the most common diseases being pneumonia (44.12%) and diarrhea (41.18%). Swollen leg and ear infection were rarely seen. A small number of treatments administered for undiagnosed conditions (11.7%).

Fig 2. Quantification of antimicrobial drugs use in pre-weaned calves based on active substance

The active substance in the antimicrobial drugs used was quantified using treatment incidence metrics, and the outcome indicated the most used compounds were Enrofloxacin, Ceftiofur, and Florfenicol. Penicillin, and Tulathromycin were used moderately, and Sulfonamides and Tetracyclines were least used.
Fig 3. Quantification of antimicrobial drug use in pre-weaned calves based on premise type

Quantification using the treatment incidence metric for each premise revealed that there was marked variation between different premises. However, the total AMD usage between dairies and calf ranches were comparable.
RESULTS

This causal diagram displays the potential variables from our data that could have affected treatment, and it is categorized based on disease, diet, and herd characteristics. We determined the significance of each variable using univariate analysis and excluded those that were not significant.

Table 1. Logistic regression showing associations between treatment and antibiotics added to milk.

<table>
<thead>
<tr>
<th>Antibiotic Treatment</th>
<th>OR</th>
<th>Std. Err</th>
<th>P- Value</th>
<th>Confidence Interval</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Antibiotics added to milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neomycin</td>
<td>1.97</td>
<td>1.47e-12</td>
<td>0.000</td>
<td>1.973</td>
<td>1.973</td>
<td></td>
</tr>
<tr>
<td>Neomycin + Tetra</td>
<td>4.32</td>
<td>7.51e-07</td>
<td>0.000</td>
<td>4.323</td>
<td>4.323</td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td>2.25</td>
<td>2.30e-12</td>
<td>0.000</td>
<td>2.25</td>
<td>2.25</td>
<td></td>
</tr>
<tr>
<td>2. Vitamins</td>
<td>0.42</td>
<td>1.86e-12</td>
<td>0.000</td>
<td>0.422</td>
<td>0.422</td>
<td></td>
</tr>
<tr>
<td>3. Med. Milk Replacer</td>
<td>0.12</td>
<td>2.17e-08</td>
<td>0.000</td>
<td>0.125</td>
<td>0.125</td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>1.57</td>
<td>6.85e-12</td>
<td>0.000</td>
<td>1.579</td>
<td>1.579</td>
<td></td>
</tr>
</tbody>
</table>

The final logistic regression model showed high odds of treatment for farms that gave antibiotics in milk, such as neomycin, tetracycline, and both neomycin and tetracycline. Whereas farms that give vitamins and medical milk replacer had lower odds of treatment.
DISCUSSION

Pneumonia and diarrhea were the most indications for disease treatment in pre-weaned calves. This outcome was in agreement with previous reports from National Animal and Health Monitoring System (NAHMS). Enrofloxacin, Ceftiofur, and Florfenicol had the highest usage. Across the herds, Enrofloxacin and Florfenicol were primarily used to treat pneumonia, which explains the higher usage. Ceftiofur was primarily used to treat diarrhea, which similarly explains the trend of higher usage. Total usage between premise types was similar, although individual farms had marked variability in usage. This data provides baseline information for future monitoring of AMD in pre-weaned calves.

Logistic regression analysis showed associations between treatment and management practices. Higher odds of treatment were associated with farms adding antibiotics in milk, probably due to the practice of supplementing treatments with antibiotics in milk to manage diseases. Lower odds of treatment were associated with farms that used medicated milk replacer, since the use of medicated milk replacer was more likely to follow the labeled dosage, and hence more effective in controlling the disease. The lower odds for treatment on farms that supplemented calf diet with vitamins could be explained by the role of vitamins in boosting the calf immune system in early life to reduce the chances of disease.
CONCLUSION

- The farms that supplemented calves with vitamins had less chance of treatment due to improved calf health and reduced need for antimicrobial drugs.
- This data serves as baseline information on AMD usage in pre-weaned dairy calves and can guide the development of outreach materials on antimicrobial stewardship.
- Future research directions would be to compare this AMD usage data with antimicrobial resistance profile bacteria from calf sources to determine any associations between drug use and resistance.
ABSTRACT

Antimicrobial drug (AMD) usage has been a predominant concern for the rise of antimicrobial resistance (AMR), which is considered a global threat. Intensive production systems are prone to infectious diseases. In dairy calves, diarrhea and bovine respiratory disease are the main causes of morbidity and mortality which leads to economic loss. Calf health during pre-weaned dairy calves affects future production, growth, and reproductive efficiency. The overuse of AMDs may lead to AMR, which adversely affects both animal and human health. The study was conducted in July 2017, prior to the implementation of the SB-27 but after the implementation of the Veterinary Feed Directive that came into effect in January 2017. Both of these regulations increased veterinary oversight in the distribution and use of antimicrobials in livestock. The goal of the study is to benchmark AMD usage in California dairy calves and determine specific drug classes used. The longitudinal prospective study surveyed 3 dairies and 4 calf ranches located in the California Central Valley. Calves were enrolled at birth (1 to 3 days old) and followed through the weaning period (60 days). During the follow-up period, disease and treatment record was collected using calf record cards attached to calf hutches. Data from these farms were transferred to Microsoft Excel for cleaning, standardization, and analysis. A total of 310 enrolled calves showed that 44.18% of the disease was due to pneumonia while 41.18% was due to diarrhea. This is in agreement with previous reports from National Animal and Health Monitoring System (NAHMS). A few treatments were undiagnosed (11.7%), while swollen leg and ear infection was rarely seen. Antimicrobial usage was quantified based on active substance and herd type using a treatment incidence. Enrofloxacin, Ceftiofur, and Florfenicol were used the most. A logistic regression model following a manual causal diagram-based model building approach and a Goodness of Fit test using the Akaike Information Criterion was used to determine the association between treatment management and practices. There were higher odds of treatment due to farms supplementing treatments with antibiotics to manage diseases. Those who used medical milk replacer had lower odds of treatment because this feed is formulated according to the labeled dosage, which is stated by the manufacturer. The lower odds for vitamins are probably due to vitamins providing immune support for calves to reduce the chances of disease. The outcome of this study will help inform antimicrobial drug use and stewardship programs for the dairy calves. This will benefit dairy cattle health, farm productivity, food safety, and ultimately, human health.