



Clinical Effect of NSAID Treatment of Calves with Early Signs of Respiratory Disease

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ABSTRACT

To reduce the antibiotic treatment of calves with BRD, detection of diseased calves early in the disease process is necessary. If BRD can be treated before turning into bacterial infection, the need for antibiotic treatment could be reduced. Therefore, the objective of this study was to investigate if calves with subtle clinical signs of respiratory disease improve their respiratory score, when treated with NSAID early in the disease process. Thirty-four calves with subtle clinical signs of BRD in a veal herd, were included in the study. On Day 1, seventeen calves were randomly assigned to receive either Finadyne Transdermal or Metacam subcutaneously for three days and seventeen calves received no treatment. When taking account of age and antibiotic treatment, there was a positive effect on respiratory score when receiving NSAID, the respiratory score was on average 1.77 less at day 5, for the NSAID treated calves compared to calves not receiving NSAID treatment. We found that treatment with NSAID in the early process of respiratory disease could decrease the short-term respiratory score in young veal calves. This together with others findings, suggests that starting with NSAID treatment in calves with respiratory disease and only add antibiotics if the disease develops further might be an option to consider.

Keywords: Respiratory disease; Calves; NSAID; Early treatment

INTRODUCTION

Bovine Respiratory Disease (BRD) is a frequent and antibiotic consuming disease in calves all over the world. It is generally accepted that BRD starts as a primary viral infection and in some calves, proceed into a secondary bacterial infection. To reduce the need for antibiotic treatment of calves with BRD, detection of diseased calves early in the disease process is necessary. If the respiratory infection could be solved before turning into bacterial infection, the need for antibiotic treatment could be reduced. Calves experience pain in relation to bovine respiratory disease [1] and treatment with Non-steroidal Anti-inflammatory Drugs (NSAID) reduce pyrexia and the percentage of consolidated lung tissue in naturally occurring BRD [2]. If pyrexia and pain is reduced, the general well-being of the calves is improved, they eat more and display normal behavior, and one could speculate that the resilience against a secondary bacterial infection would be greater. The reduction

of lunge consolidation with NSAID treatment [2,3] could also reduce the likelihood of a secondary bacterial infection. Treatment with NSAID in the very early state of respiratory disease in calves, could hopefully prevent some of the viral infections from developing into a secondary bacterial infection.

The beneficial effect of NSAID treatment in combination with antibiotic treatment for BRD is widely known, but only a few studies have investigated the effect of treating calves with BRD with NSAID only. A study found that with NSAID treatment alone, 25% of the calves recovered from fever due to respiratory disease and 60% improved from antibiotics alone, however worth noticing was that there were no differences in long-term benefits from not having received antibiotics as first treatment [4]. Another study found that the group of calves receiving NSAID only as treatment for BRD, had higher odds of repeated treatment with NSAID and antibiotics [5]. In a study of fattening calves 67% of calves with early signs of BRD recovered fol-

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lowing NSAID treatment alone [6]. This suggests that it could be considered to treat with NSAID only in the very beginning of BRD and only add antibiotics to calves where disease persists or worsens. The objective of this study was therefore to investigate if calves with subtle clinical signs of respiratory disease improve their respiratory score, when treated with NSAID early in the disease process.

MATERIALS AND METHODS

Data was collected in one Danish conventional veal calf herd. The calves were either Holstein-Friesian or Holstein-Friesian/beef cattle crossbreed. Each calf underwent a clinical exam six days in a row. In total 87 calves showing signs of BRD infection were sampled for the study. The clinical signs recorded were general demeanor, cough, nasal discharge, ocular discharge, respiration type and lung auscultation. Temperature was measured rectally with a digital thermometer. On day 1, the calves with clinical signs of respiratory disease were randomly selected to either receive NSAID alone on day 1, 2 and 3, or no treatment. This was a randomized selection not based on the clinical examinations. The NSAID treatment was either 0.5 mg/kg meloxicam (Metacam®, Boehringer Ingelheim) administered subcutaneously or 3.33 mg/kg flunixin meglumine topically (Finadyne Transdermal®, MSD Animal Health) administered along the back of the calf, according to the manufacturer's manual. Antibiotic treatment was initiated by the farmer according to his treatment protocol and noted by the researchers. The antibiotic treatment was 10 mg/kg oral doxycycline twice daily for 3 days and administered as group medication, to all calves in a pen if more than 5 calves out of 15 calves in the pen showed signs of depression and anorexia. If 1 or 2 calves showed depression and anorexia, they were individually treated with penicillin procaine intramuscular (Ethacilin Vet., MSD Animal Health).

The first clinical examination was used to determine if the calf could be included in the study. If the calf had one or several of the following clinical signs on Day 1, it was excluded from the study: Cough and/or serous-mucoid/purulent nasal discharge and/or abdominal respiration and/or harsh auscultation sounds and/or a rectal temperature >39.6 and/or were depressed. Based on the clinical examinations, a respiratory score was calculated for all included calves on each of the five study days. See details on how each clinical sign corresponds to a score that was added together, resulting in an overall score (Table 1). All variables were considered statistically significant at a level of $p < 0.05$. The respiratory score at day 2-6 was compared directly between calves receiving NSAID treatment and calves not receiving NSAID treatment. To take account for age and antibiotic treatment a linear model was built, with respiratory score as outcome and explaining variables were age and treatment-group (no treatment, NSAID, antibiotics) and the interaction between NSAID and antibiotic treatment.

RESULTS

In total, 34 calves were included in the study. The average age was 35 days, with a minimum age of 13 days and maximum of 61 days. Of these, 17 received NSAID on day 1, 2 and 3, while 17 calves did not receive any NSAID treatment. The maximum respiratory score was 8, with an average of 2.3. 15 calves re-

ceived antibiotics during the study period and 19 did not. This gave the following combinations of treatment: No treatment (11), NSAID (17), antibiotics (14) and antibiotics+NSAID (8). When comparing the NSAID treated calves (NSAID only and NSAID+AB) with calves receiving no NSAID treatment (no treatment, AB only), there was not a statistically significant difference in age or mean respiratory scores at day 1, 2, 4 or 6. But at time point 3 the mean respiratory score for the NSAID treated calves was 1.8, while it was 3 for the calves receiving no NSAID treatment ($p=0.03$) and at time point 5 the mean respiratory score for the NSAID treated calves was 1.8, while it was 3.5 for the calves receiving no NSAID treatment ($p=0.003$) (Figure 1). When taking account of age and antibiotic treatment at day 5, there was still a positive effect on respiratory score when receiving NSAID, as the respiratory score was on average 1.77 less at day 5, for the NSAID treated calves compared to calves not receiving NSAID treatment (Table 2). The group of calves who received antibiotics (+/-NSAID), had a non-statistically significant average higher respiratory score of 1.62 at day 5 (Table 2).

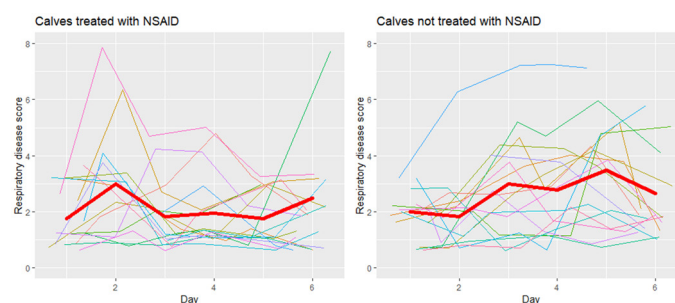


Figure 1: The individual and mean (thick red line) respiratory score of the group of dairy calves receiving NSAID treatment on day 1-3 (left) and the group of calves receiving no NSAID treatment (right). Each calf has individual color and dots from the same calf are connected with lines. To be able to differentiate the calves from each other, jitter is applied, so not all dots are placed at exactly the timepoint they were sampled

Table 1: The clinical signs of bovine respiratory disease in calves recorded in this study corresponding to a respiratory score

General demeanor	Respiratory score
Normal	0
Mildly depressed	1
Depressed	2
Cough	
No	0
Yes	1
Nasal discharge	
No	0
Serous	1
Serous-mucoid	2
Mucopurulent	3
Ocular discharge	
No	0
Serous	1
Respiration type	
Thoracoabdominal	0
Abdominal	1
Auscultation	
Normal	0

Increased inspiratory sounds	1
Increased in-and expiratory sounds	2
Rough and abnormal sounds	3
Rectal temperature	
< 39.7	0

≥ 39.7 and <40.2	1
≥ 40.2	2

Table 2: Results of the final model describing explanatory variables of respiratory score at day 5. The adjusted R2 was 0.22

Fixed effects	Estimate	S.E.	Confidence interval	P-value
Treatment group (n)				
No treatment (Intercept)	1.76	1.30		
+NSAID	-1.77	0.65	-3.04-(-0.5)	0.01
+AB	1.62	0.89	-0.12-3.36	0.08
+Interaction (NSAID and AB)	-0.20	1.02	-2.2-1.8	0.84
Age	0.03	0.03	-0.03-0.09	0.27

DISCUSSION AND CONCLUSION

Based on our results, we don't propose that treatment with NSAID could replace antibiotic treatment totally, but if calves with early signs of respiratory disease are detected early enough in the disease course, the use of antibiotics could probably be reduced. Mahendran et al. found that 25.7% of calves with pneumonia related fever recovered from NSAID treatment alone [4]. Although many of the NSAID treated calves required additional antibiotic treatment, there were no long-term negative effects of not having received antibiotic treatment at the start. Another study found a reduction in antibiotic use of 66.7%, when treating early clinical signs of BRD with NSAID [6]. This together makes it worth trying on a larger scale to start with NSAID treatment in calves with respiratory disease and only add antibiotics if the disease develops further. On the other hand, another study found that calves receiving only NSAID in case of respiratory disease, might be more likely to require additional NSAID and antibiotic treatment, than calves who received antibiotics or antibiotics and NSAID as start treatment [5]. The NSAID used in that study was Finadyne Transdermal and it was only applied once. This could be an explanation why Mahendran did not show an effect of NSAID, while we did as NSAID was applied for three consecutive days in our study [5]. Overall, this suggests that if the use of early NSAID treatment should be successful, it might not be enough to do it once and the calves needs to be detected very early in the disease process.

Unfortunately, we had to exclude 53 calves due to a high respiratory score at Day 1. From an animal welfare perspective, it is concerning that on a random day in this veal calf herd, many calves were showing severe signs of clinical disease. In this herd, as well as in many other veal herds in Denmark, calves are transported from the dairy herd to the veal herd at an early age and often mixed with other calves from different dairy herds. This practice will undoubtedly often lead to a high infection pressure on the calves.

A limitation of this study is that we have only followed the calves for a very short period and cannot evaluate how the NSAID treatment influenced the probability of BRD relapse, growth etc. Ideally, more calves should have been included, as

this would have made it possible to include more variables in the model and generate more robust results. This study was performed in a conventional herd, and we did not have influence on the use of antibiotics, other than it was recorded what treatment was added by the farmer. The farmer used oral antibiotics that were added to the milk in the trough, consequently all calves in the same pen received antibiotics, despite not all the calves displaying clinical symptoms of BRD. It would have been desirable if we were to control the antibiotic treatment as well, and only administer to single calves that needed further treatment.

Together with previous findings, our study suggests that starting with NSAID treatment in calves with respiratory disease and only add antibiotics if the disease develops further might be an option to consider.

ETHICAL APPROVAL

The study protocol was approved by the Danish Animal Experiments Inspectorate (Approval number, 2021-15-0201-01099; Approval date, 18-12-2021).

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CONFLICT OF INTEREST STATEMENT

None of the authors has any financial or personal relationship that could inappropriately influence or bias the content of the paper.

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