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SEROEPIDEMIOLOGY OF RESPIRATORY DISEASE IN FEEDLOT CALVES IN WESTERN CANADA

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Une étude séroépidémiologique a été conduite dans un feedlot de l'ouest canadien pour analyser les relations entre les titres sérologiques de Pasteurella haemolytica anti-leucotoxine (PHAL), Haemophilus somnus (HS), herpesvirus-1 bovin (BHV-1), herpesvirus-1 bovin glycoprotéine G-IV (G-IV), virus BVDV (BVDV), Mycoplasma bovis (MB) et Mycoplasma alkalescens (MA), et la mordidité et mortalité des veaux à l'engrais récemment sevrés. Du sang a été prélevé à l'arrivée des veaux au feedlot (arrivée), lors du choix des cas et des témoins (sélection), ainsi qu'à 33 jours de la période d'engraissement (convalescent), sur 100 animaux traités pour pathologie respiratoire (cas) et 100 animaux sains (témoin). Les titres sérologiques "convalescent" étaient significativement plus élevés ($p<0.05$) que les titres "arrivée" pour tous les agents infectieux. L'augmentation des titres PHAL et MA était supérieure ($p<0.05$) pour les cas que pour les témoins. A l'inverse, l'augmentation des titres HS et G-IV était inférieure ($p<0.05$) pour les cas que pour les témoins. Les titres BVDV "arrivée" et "sélection" étaient inférieurs ($p<0.05$) pour les cas que pour les témoins. Les titres "sélection" MA et MB étaient supérieurs ($p<0.05$) pour les cas que pour les témoins. Les titres "convalescent" HS étaient inférieurs ($p<0.05$) pour les cas que pour les témoins. La séroconversion pour PHAL était associée ($p<0.05$) avec un risque augmenté de pathologie ($OR=2.84$); cependant, la séroconversion pour G-IV était associée ($p<0.05$) avec un risque diminué de pathologie ($OR=0.42$). Un titre "arrivée" BVDV plus élevé était associé ($p<0.05$) avec un risque diminué de pathologie ($OR=0.84$). L'augmentation du titre MA après l'arrivée était associée avec un risque augmenté de pathologie ($OR=1.10$). Un titre "arrivée" HS plus élevé et une augmentation de ce titre ensuite étaient associés tous les deux avec un risque diminué de pathologie ($OR=0.76$ et $OR=0.78$). Le titre sérologique "arrivée" BHV-1 était associé significativement ($p<0.05$) avec le risque de mortalité ($OR=1.30$).

INTRODUCTION

In recently weaned beef feedlot calves, bovine respiratory disease (BRD) represents up to 50% of all mortality and is believed to be responsible for the majority of animals treated for undifferentiated fever (UF) in the early feeding period (1,2). However, recently published information indicates that death due to BRD is not the leading cause of death in feedlot animals in western Canada (1,3,4). In these studies, the overall number of animals dying from all forms of hemophilosis (including myocarditis, pleuritis, polyarthritis, thrombotic meningoencephalitis, and septicemia) is greater than the number of animals dying from pasteurellosis. These studies suggest that hemophilosis has become the most significant cause of mortality in beef feedlot calves in western Canada. If mortality rates are indicative of morbidity rates, then it is plausible that the majority of animals with UF in the feedlot may be suffering from hemophilosis as opposed to pasteurellosis. Unfortunately, it is unknown whether animals which become sick early in the feeding period are suffering from pasteurellosis, hemophilosis, or other infectious agents, such as bovine herpesvirus-1, bovine viral diarrhea virus, or *Mycoplasma* spp, alone or in combination.

OBJECTIVE

The objective of this study was to investigate the relationships between *Pasteurella haemolytica* anti-leukotoxin (PHAL), *Haemophilus somnus* (HS), bovine herpesvirus-1 (BHV-1), bovine herpesvirus-1 G-IV glycoprotein (G-IV), bovine viral diarrhea virus (BVDV), *Mycoplasma bovis* (MB), and *Mycoplasma alkalescens* (MA) antibody titres and morbidity and mortality in recently weaned beef calves.

MATERIALS AND METHODS

The trial was conducted in a commercial feedlot in Alberta, Canada which has a capacity of 22,000 animals. The animals were housed in open air, dirt floor pens arranged side by side with central feed alleys and 10% porosity fencing. There were approximately 305 animals per pen.

The animals utilized in the study were recently weaned, crossbred beef steer and bull calves purchased from auction markets throughout western Canada. The animals were seven to ten months of age, weighed between 227 and 400 kg, and were housed in four pens.

EXPERIMENTAL DESIGN

Arrival blood samples were obtained from 1,219 animals at entry to the feedlot. Thereafter, Selection blood samples were obtained on a daily basis from animals which subsequently developed UF (Case) and healthy animals with no fever (Control).

Each pen of animals was observed once or twice daily by experienced feedlot personnel. Animals deemed to be "sick", based on subjective criteria such as general appearance and attitude, gauntness, reluctance to move, etc., were taken to a hospital facility. Animals with a lack of abnormal clinical signs referable to organ systems other than the respiratory system and a rectal temperature greater than or equal to 40.3°C were defined as

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having UF and selected to the Case group for the study. These animals were treated with subcutaneous tilmicosin (Micotil®, Provel, Division Eli Lilly Canada Inc., Scarborough, Ontario) at a dose of 10 mg/kg body weight. After selecting the "sick" animals from each pen, the feedlot personnel returned to that pen and selected apparently "healthy" animals to serve as potential candidates for the Control group. These animals were moved to the hospital facility and examined. Animals with a lack of abnormal clinical signs, a rectal temperature of less than 40.3°C, and no previous treatment history were selected to the Control group.
Candidates for the Case and Control groups were selected daily until significant morbidity decreased (approximately day 24 of the feeding period). At approximately day 33 of the feeding period, Convalescent blood samples were obtained from all animals in the study population.

SAMPLING AND SEROLOGY
Arrival, Selection, and Convalescent samples were collected from 316 Cases and 341 Controls. From these samples, 100 Cases and 100 Controls were randomly selected for the determination of antibody titres to PHAL, HS, BHV-1, G-IV, BVDV, MB, and MA.

STATISTICAL ANALYSIS
Analyses were performed using three different outcome measures: Arrival, Selection, and Convalescent antibody titres, morbidity (Case versus Control), and mortality. Seroconversion was used as a measure of exposure to specific infectious agents and was defined as an increase of at least two logarithms between the Arrival and Convalescent samples.
The effects of morbidity on antibody titres were evaluated over time utilizing analyses of variance for the change in log antibody titre from the Arrival to Convalescent samples and analyses of variance for repeated measures for the Arrival, Selection, and Convalescent titres. Arrival antibody titre, pen, days on feed at the time of selection as a Case or Control, and Arrival weight were controlled for in the analysis for each infectious agent.
Logistic regression was performed to determine if Arrival antibody titre, the change in log antibody titre from the Arrival to Convalescent samples, or seroconversion for each infectious agent, Arrival weight, Arrival rectal temperature, days on feed at the time of selection as a Case or Control, or pen might be associated with UF or mortality. Univariate analyses were performed on each factor and multivariate models were explored using both backward and stepwise selection algorithms. Odds ratios and 95% confidence intervals (95% CI) were calculated for each factor. Variables representing Arrival antibody titre were allowed to simultaneously enter models with variables representing change in antibody titre or seroconversion. The Arrival antibody titre for a specific agent was forced into models whenever change in titre or seroconversion for that agent were included; however, it was subsequently removed if not statistically significant ($p \geq 0.05$). For each infectious agent, variables representing the magnitude of change in log antibody titre and seroconversion were allowed to simultaneously enter models as it was not clear which might be more important. Arrival weight, Arrival rectal temperature, and days on feed at the time of selection as a Case or Control were forced into all final models and subsequently removed if not statistically significant ($p \geq 0.05$).

RESULTS
Results of analyses of variance for the change in log antibody titre from the Arrival to Convalescent samples are shown in Table I. The Convalescent antibody titres of all infectious agents were significantly higher ($p<0.05$) than the Arrival antibody titres. Increases in PHAL and MA titres were higher ($p<0.05$) in Cases than Controls; whereas, increases in HS and G-IV titres were lower ($p<0.05$) in Cases than Controls (Table I).
Results of analysis of variance for repeated measures on the Arrival, Selection, and Convalescent samples is presented in Table II. Antibody profiles for PHAL, HS, BHV-1, BVDV, MB, and MA showed significant ($p<0.05$) change over time, difference between Cases and Controls, or interaction between the change over time in Cases and Controls (Table II). Arrival and Selection BVDV antibody titres were lower ($p<0.05$) in Cases than Controls; however, Selection MA and MB antibody titres were higher ($p<0.05$) in Cases than Controls. Convalescent HS antibody titres were lower ($p<0.05$) in Cases than Controls.

Table I
Summary of changes in antibody titres from the arrival to convalescent samples Analysis of variance for the change in log titre

Parameter	Case	Control	p-value
Pasteurella haemolytica anti-leukotoxin	1.64 ± 0.18	1.14 ± 0.17	0.0493
Haemophilus somnus	0.65 ± 0.19	1.27 ± 0.18	0.0195
Bovine herpesvirus-1	3.32 ± 0.31	4.00 ± 0.30	0.1149
Bovine herpesvirus-1 G-IV glycoprotein	0.55 ± 0.25	1.27 ± 0.24	0.0425
Bovine viral diarrhea virus	2.86 ± 0.25	2.24 ± 0.24	0.0834
Mycoplasma bovis	3.35 ± 0.17	3.14 ± 0.16	0.3841
Mycoplasma alkalescens	2.44 ± 0.35	1.45 ± 0.34	0.0463

Table II
Summary of change in antibody titres from the arrival to convalescent samples Analysis of variance for repeated measures

	p-value		
Parameter	Time	Case/Control	Time* Case/Control
Pasteurella haemolytica anti-leukotoxin	0.0829	0.6505	0.0401
Haemophilus somnus	0.2844	0.0405	0.1732
Bovine herpesvirus-1	0.0240	0.1042	0.6128
Bovine herpesvirus-1 G-IV glycoprotein	0.9179	0.2427	0.0825
Bovine viral diarrhea virus	0.0398	0.0136	0.0005
Mycoplasma bovis	0.0275	0.0034	0.0761
Mycoplasma alkalescens	0.9358	0.1289	0.0539

In the multivariate analysis, two final models were selected (Table III). Four variables were included in both models and the strength of association of each variable was similar between models. The risk of morbidity was greater among animals that seroconverted to PHAL when compared to animals that did not seroconvert (OR 2.84). Conversely, the risk of morbidity was less among animals that seroconverted to G-IV when compared to animals that did not seroconvert (OR=0.42).
Each one log increase in BVDV Arrival antibody titre was on average associated with a 20% reduction in morbidity risk (OR=0.84). Each one log increase in MA antibody titre from the Arrival to Convalescent samples was on average associated with a 10% increase in morbidity risk (OR=1.10). The backward selection model contained two additional variables that were not included in the stepwise model. Each one log increase in Arrival HS antibody titre was associated with a 32% reduction in morbidity risk (OR=0.76). Each one log increase in HS antibody titre from the Arrival to Convalescent samples was associated with a 30% reduction in morbidity risk (OR=0.78).

Table III
Summary of multivariate analyses for morbidity

	Model A (Backward Selection)		
Parameter	Odds Ratio	95% CI	p-value
Intercept	N/A	N/A	0.0042
Pasteurella haemolytica anti-leukotoxin seroconversion	2.83	1.44 - 5.57	0.0027
Haemophilus somnus arrival titre	0.76	0.62 - 0.92	0.0052
Haemophilus somnus change in log titre	0.78	0.64 - 0.94	0.0099
Bovine herpesvirus-1 G-IV glycoprotein seroconversion	0.43	0.19 - 0.99	0.0471
Bovine viral diarrhea virus arrival titre	0.83	0.74 - 0.94	0.0025
Mycoplasma alkalescens change in log titre	1.10	1.01 - 1.20	0.0216
	Model B (Stepwise Selection)		
Parameter	Odds Ratio	95% CI	p-value
Intercept	N/A	N/A	0.6838
Pasteurella haemolytica anti-leukotoxin seroconversion	2.85	1.48 - 5.49	0.0018
Bovine herpesvirus-1 G-IV glycoprotein seroconversion	0.41	0.18 - 0.90	0.0270
Bovine viral diarrhea virus arrival titre	0.85	0.76 - 0.95	0.0044
Mycoplasma alkalescens change in log titre	1.09	1.01 - 1.19	0.0270

1. The change in log titre is from the arrival to convalescent samples.

Each one log increase in Arrival BHV-1 antibody titre was associated with a 30% increase in the risk of mortality (OR=1.30, 95% CI=1.07-1.58).

DISCUSSION AND CONCLUSIONS

The results of this study demonstrate that feedlot calves in western Canada are exposed to PHAL, HS, BHV-1, G-IV, BVDV, MB, and MA early in the feeding period. The association of PHAL seroconversion with morbidity provides additional evidence that pasteurellosis is a major component of UF (5). The sparing effect of G-IV seroconversion in naturally occurring disease challenge is consistent with previously published experimental models pertaining to the protective immunity of the G-IV glycoprotein (6). In addition, the increased risk of mortality with higher Arrival BHV-1 titres may be due to the production of non-protective antibodies in previously infected animals. The sparing effects of higher Arrival HS titres and increases in HS titres after Arrival on the occurrence of UF are logical given that hemophilosis has become the most significant cause of mortality in beef feedlot calves in western Canada (1,3,4). The association of lower Arrival BVDV titres with an increased risk of UF has been previously described and may be due to the immunosuppressive effects of BVDV infection (5,7). Interestingly, Control animals expressed seroconversion to BVDV without evidence of UF. The increased risk of morbidity associated with increases in MA titres has been previously described with other *Mycoplasma* spp (8). However, the role of *Mycoplasma* spp as a primary or secondary pathogen in UF is not fully understood (7,8).
Finally, the results of this study indicate that protective immunity to PHAL, HS, G-IV, BVDV, and *Mycoplasma* spp may be necessary to reduce the occurrence of UF in feedlot calves in western Canada.

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