in the control group received no additional treatment. Every cow in the trial was treated IM with 500mg of PGF2a on day 20. The second IVP4 was withdrawn from the vagina of each cow on day 21, followed by estrus detection.

Results

Mean interval from IVP4 device withdrawal to onset of estrus, total number of mounts and duration of estrus were similar between the three groups (44.6±3.1 hours, 24.4 ± 8.6 mounts and 9.5 ± 1.1 hours for interval from IVP4 withdrawal to onset of estrus, total number of mounts, and duration of oestrus, respectively; p>0.31. Every cow in the GnRH or ODB group had three follicular waves, compared to only one of the five cows in the control (p<0.001). Six cows in the GnRH group formed accessory CLS after treatment, compared to none of the cows in the control and groups (p=0.02). Emergence of a new follicular wave occurred on day 15.1±0.4 in the GnRH group, while those of control or ODB groups emerged on day 16.6 ±0.9 and 17.5±0.5 days, respectively (p=0.02). Maximum diameter of the ovulatory follicles of cows in the three groups did not differ (15. 0 ±0.8, 15.3 ± 1.2, 14.5 ±0.6 mm for control, GnRH and ODB groups, respectively p=0.83).

Significance

In summary, treatment of cycling cows with GnRH or ODB at the time of CIDR device insertion during diestrus (day 13) caused follicular turnover and a synchronized emergence of a new follicular wave. This follicular wave emerged earlier in GnRH than in ODB-treated cows. Following the synchronized emergence of a new wave, there was a synchronized onset of estrus and ovulation. The onset of estrus and ovulation were not influenced by treatment. ODB caused atresia of every second dominant follicle, while GnRH could not consistently ovulate this second dominant follicle. The inability of GnRH to consistently cause follicular turnover may be a limitation to its use.

Re-examination of the Etiology of Fatal Undifferentiated Fever/Bovine Resipratory Disease

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Introduction

Prevention and control of undifferentiated fever (UF)/bovine respiratory disease (BRD) in Canadian feedlots remains an important component of optimizing the cost of production. Current prevention and control strategies for UF/BRD are directed towards the common etiologic agents involved in UF/BRD of feedlot calves that are described in the veterinary literature. A variety of diagnostic tools, including bacterial and viral culture and serology, have been used over the years to establish that the described etiologic agents are involved in UF/BRD of feedlot calves. Recent diagnostic developments, such as immunohistochemistry (IHC), allow for more standardized and potentially more sensitive diagnostic detection methods. Previous studies have been conducted using IHC to determine the etiologic agents involved in feedlot mortality. However, general extrapolation of the results from these studies has been limited because of sampling methods used (ad hoc or convenience sampling), populations studied (usually animals with chronic disease), pathologic lesions sampled (a wide variety of multi-systemic diseases) and the confirmatory approach to IHC use (IHC used to con-

firm the presence of specific etiologic agents in lesions identified with histopathology). By combining the diagnostic advantages of IHC with a structured case selection process to provide samples from naturally occurring cases of fatal UF/BRD throughout the continuum of the disease process, a standardized determination of the involvement of various etiologic agents and pathologic processes in the pathogenesis of fatal UF/BRD can be made. Moreover, descriptive information collected with this type of approach could be used to assess whether or not the etiologic agents involved in fatal UF/BRD of feedlot calves have changed from those described in the literature.

Improving our understanding of the etiologic agents involved in the pathogenesis of UF/BRD is critical to developing rational preventive and therapeutic strategies. Unfortunately, there are minimal amounts of current, standardized, cross-sectional data throughout the continuum of the disease process that adequately describe the etiologic agents and pathologic processes involved in fatal UF/BRD.

The project described herein was conducted to determine the microbiological agents and pathological processes involved in fatal UF/BRD, as well as to determine if specific microbiological agents are associated with different pathological presentations of fatal UF/BRD.

Materials and Methods

During the fall of 2004, fall-placed feedlot calves that were diagnosed on gross postmortem examination with BRD as the predominant cause of death were pathologically examined in detail using laboratory support.

Animals diagnosed with BRD lesions using gross pathological examination were selected for sampling using a defined protocol that included multiple feedlots, a specified target population, specific pathological findings, a defined treatment history and a defined time interval from feedlot arrival to death. Animals dying with peracute, acute, subacute and chronic BRD, as well as control animals with no BRD and animals with bronchiolar BRD, during the first 60 days of the feeding period, were selected as sampling groups for the study. Up to 25 animals were enrolled in each BRD sampling group, and up to 25 animals were enrolled in the control sampling group. In order to maximize study resources and ensure that only appropriate target animals were included in the study, a two-stage enrollment process was utilized. Conditional enrollment in the study was performed in the field by the attending FHMS veterinarian, and the required study samples were collected. However, prior to laboratory sample submission, the FHMS research team reviewed digital images and animal treatment histories for each conditionally enrolled animal to determine final inclusion in the study.

The pathological processes were characterized using gross postmortem observations, digital imaging and histopathology. Immunohistochemistry was performed on three samples taken from the cranioventral, midlateral and caudodorsal sampling locations of the lung (Prairie Diagnostic Services (PDS), Saskatoon, Saskatchewan). Each lung sample was analyzed using IHC to detect the presence of *Mannheimia haemolytica* (MH), *Mycoplasma bovis* (MB), *Histophilus somni* (HS), bovine viral diarrhea virus (BVDV), infectious bovine rhinotracheitis virus (IBRV), bovine respiratory syncytial virus (BRSV) and parainfluenza-3 virus (PI3V). A standardized IHC scoring system was developed by the PDS IHC team and applied to the study lung samples by a single technician. In addition, skin samples were tested for BVDV using IHC to identify animals that were persistently infected with BVDV. Histopathology was performed using a standardized histopathology lesion categorization and scoring system developed by the PDS pathology team and applied to the study lung samples by a single pathologist. The IHC and histopathology assessments for each sample were independently performed, and laboratory personnel were blinded as to group status of each sample. Results of the gross postmortem, IHC and histopathology examinations were entered into an electronic spreadsheet and verified.

Frequency distributions and descriptive statistics were calculated, and cross-tabulations were used to evaluate simple associations between variables. Spearman rank-sum correlations were used to evaluate simple associations between IHC scores and histopathology lesion scores. Chi-square tests were used to evaluate simple associations between categorical variables. Linear regression was used to evaluate simple associations using sampling group (peracute, acute, subacute, bronchiolar, chronic and control) as independent variables and sums within animals for IHC scores and/or histopathology scores as the dependent variables.

Results

Samples were collected from a total of 99 animals at 17 feedlots, representing 13 peracute, 24 acute, 25 subacute, 10 bronchiolar, 18 chronic and nine control samples. Histopathology findings were categorized into one of 11 categories, with fibrinous pleuritis, fibrinonecrotizing pneumonia, acute/subacute interstitial pneumonia, suppurative bronchopneumonia and hemorrhage being the most commonly described lung lesions in each animal. In terms of histopathology lesion scores across sampling groups, the distribution of scores for suppurative bronchopneumonia, fibrinonecrotizing pneumonia, fibrinous pleuritis and hemorrhage were highest in the cranioventral sampling location, slightly lower in the midlateral sampling loca-

tion and markedly lower in the caudodorsal sampling location. Conversely, acute/subacute interstitial pneumonia was lowest in the cranioventral sampling location, higher in the midlateral sampling location, and markedly higher in the caudodorsal sampling location.

In terms of IHC findings from lung tissues at the animal level, MH and MB were the most commonly identified pathogens, with positive IHC rates for MH of 85%, 100%, 92%, 30% and 39% in the peracute, acute, subacute, bronchiolar, and chronic sampling groups, respectively, and positive IHC rates for MB of 54%, 46%, 67%, 70% and 94% in the peracute, acute, subacute, bronchiolar, and chronic sampling groups, respectively. Pathogens such as BVDV and HS were found less commonly, with positive IHC rates for BVDV of 8%, 42%, 40%, 20% and 17% in the peracute, acute, subacute, bronchiolar, and chronic sampling groups, respectively, and positive IHC rates for HS of 15%, 0%, 4%, 60% and 33% in the peracute, acute, subacute, bronchiolar, and chronic sampling groups, respectively. On average, the other pathogens studied in this project were identified in less than 10% of each sampling group. Only one animal was identified as positive on IHC for PI3V; however, this animal was persistently infected with BVDV. In the control sampling group, one animal tested positive for BRSV on IHC.

Distributions of IHC scores for all pathogens were very similar between the cranioventral and midlateral sampling locations, with the exception of MB, which demonstrated higher 3+ IHC scores in the cranioventral sampling location than in the midlateral sampling location. In the caudodorsal sampling location, distributions of IHC scores for all of the viral pathogens were very similar to the distribution of IHC scores in cranioventral and midlateral sampling locations. Conversely, distributions of IHC scores for all of the bacterial pathogens were markedly lower in the caudodorsal sampling location than in the cranioventral and midlateral sampling locations.

Several significant ($P < 0.10$) associations were detected between pathogens and between pathogens and histopathology lesions during the analyses. Using the least conservative cut-off values for the IHC data, 96% (25/26) of samples positive on IHC for BVDV were also positive for MH, and 80% (12/15) of samples positive on IHC for HS were also positive for MB. Conversely, none of the 15 samples positive on IHC for HS were positive for either MH or BVDV. In addition, there was no significant association (P; 0.10) between MH and MB, as detected by IHC. There were strong positive ($P < 0.05$) associations between IHC staining for MH and the occurrence of fibrinonecrotizing pneumonia, fibrinous pleuritis, and hemorrhage and strong positive ($P < 0.05$) associations between IHC staining for MB and the occurrence of chronic suppurative pneumonia and bronchiectasis. There were moderate positive ($P < 0.05$) associations between IHC staining for HS and occurrence of suppurative pneumonia and chronic suppurative pneumonia.

Regardless of the cut off values used to define pathogen-positive animals or histopathology-positive animals, two or more pathogens were detected in 40-60% of study animals and four or more categories of histopathology lesions were detected in 53-87% of study animals.

Significance

Results of this study demonstrate that several etiologic agents and pathologic processes are involved in fatal BRD of feedlot cattle, with MH (peracute, acute, and subacute cases) and MB (subacute, bronchiolar, and chronic cases) identified as the predominant pathogens in the vast majority of fatal BRD cases. In addition, the results of this study identify some interesting associations between etiologic agents that warrant further investigation. Moreover, if IHC tests for other agents, such as *Pasteurella multocida* and *Actinomyces pyogenes*, become available, the resulting data may improve interpretation of the current study results. Finally, the descriptive nature of the study results provide a standardized, cross-sectional benchmark of feedlot BRD pathology throughout the continuum of the disease process that can be used to assess comparative changes over time.