EFFECTS OF ON-ARRIVAL, DELAYED VACCINATION AND SUPPLEMENTAL

LYSINE ON PERFORMANCE, ANTIBODY TITER, TEMPERATURE AND

METABOLIC PROFILES IN RESPONSE TO MODIFIED-LIVE VIRAL

RESPIRATORY VACCINATION

by

Katherine Parsons Sharon

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Katherine Parsons Sharon

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Dr. Glenn Duff

Approved for the Department of Animal and Range Science

Dr. Glenn Duff

Approved for The Graduate School

Dr. Ronald W. Larsen

STATEMENT OF PERMISSION TO USE

Katherine Parsons Sharon

April, 2013

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ABSTRACT

Improved vaccination efficacy and reducing virulence of bovine herpesvirus-1 could reduce respiratory disease incidence in feedlot cattle. Further, reduced virulence of herpesviruses by lysine supplementation is documented. The objective of this work was to evaluate the effects of timing as well as supplemental lysine associated with the administration of a modified-live respiratory viral vaccine on performance, feed intake, antibody titer response, and the febrile response. Thirty-six heifers were randomly assigned to treatments included no vaccine (CON), vaccination on d 0 (DO), and a d 14 (D14) of a 28 d receiving period. Daily feed intakes were recorded and body weight measured weekly. Temperature data loggers were attached to a blank controlled intrauterine drug release devices recording vaginal temperatures every 5 min. No differences (P > 0.10) among treatments were observed for performance. Daily intake was decreased for D14 versus D0 on d 14 (P < 0.01) and 15 (P < 0.10) and decreased (P < 0.05) on d 15 for the average of vaccinated calves versus CON. Vaginal temperature was increased (P < 0.10) on d 1 for D0 versus D14 heifers and increased (P < 0.05) for D14 versus D0 on d 14, 15 and 16. Sixty-four neonatal Holstein bull calves were used in a completely randomized design. Calves were fed milk replacer supplemented with either 17 g/d lysine (LYS) or an equivalent amount of casein (CAS) for 42 d. Calves were vaccinated with either an IN or an IM modified-live vaccine on d 36. Calves were weighed weekly and bled on d 35, 36, 37 and 42. Temperature data loggers were attached to rectal probes and temperatures were recorded every 5 min from d 28 to d 42. No differences (P > 0.10) were determined for average performance, rectal temperature, or IBR antibody titers between treatments. Serum urea nitrogen and the ratio of serum lysine:arginine increased (P < 0.05) for LYS compared to CAS calves. These results suggest that time vaccination alter feed intake and febrile response and supplementing lysine impacts nitrogen metabolism but does not alter the response to IBR vaccination in neonatal Holstein calves.

CHAPTER 1

INTRODUCTION

Bovine respiratory disease (BRD) is a multifactorial complex, affecting the lower

respiratory tract (pneumonia) or upper respiratory tract (rhinitis, tracheitis or bronchitis).

Both viral and bacterial pathogens contribute to BRD, therefore both antibiotics and

vaccination protocols are used to combat this widespread problem. Although many

treatment techniques are available BRD is still the most prominent health problem in the

cattle industry. Vaccination is a common practice aimed at prevention; although,

procedures do not always guarantee prevention and can even contribute to BRD, such as

vaccinating already sick cattle. Although mortality is a concern in feedlot cattle,

morbidity may have a greater cost. Expenses of morbid cattle include medication costs,

labor, and a decrease in cattle performance well beyond the time of infection. Predictions

of sick animals are not entirely possible and a decrease in performance may be

contributed to disease incidence as well as overall poor immunity. Vaccination aimed at

pathogens contributing to BRD are widely available, yet vary in efficacy. Vaccine

processing strategies differ including vaccine type (intranasal vs. intramuscular) and

timing (arrival or delayed) and have yielded conflicting results in terms of effectiveness.

Similarly, antibiotic treatments vary (injectable or oral) and concern of resistance

continues. Newly received cattle in the feedlot are at greatest risk for respiratory disease

due to the combination of stress, commingling and pathogen presence. Processing is a

central procedure for beef cattle and when performed correctly is essential for overall

heard health. Common processing practices can include dehorning, castration, parasite control, implantation, and vaccination. Therefore, prudent measures to increase overall heard health and decrease disease incidence is essential for top performance. The objective of this project was to investigate vaccination protocol and a potential technique to increase vaccine efficacy.

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CHAPTER 2

LITERATURE REVIEW

The Overall Problem of Bovine Respiratory Disease

Bovine respiratory disease (BRD) continues to be the most important health factor
in feedlot cattle in North America, accounting for the majority of morbidity and mortality
in feedlot cattle (Woolums et al., 2005). Additional economic impacts include reduction
in performance, carcass quality, and medical and labor costs (McNeill et al., 1996;
Holland et al., 2010). Although preventative measures are available, morbidity rates due
to BRD have continued to increase (Loneragan et al., 2001).

Bovine respiratory disease is a complex of syndromes both viral (parainfluenza-3,
bovine rhinotracheitis, bovine viral diarrhea virus, coronavirus, rotavirus and bovine
respiratory syncitial virus) and bacterial (*Haemophilus somnus, Pasteurella multocida,
and Mannheimia haemolytica*), as well as mycoplasmal origin (Ellis, 2010). Although a
pathogenic disease, BRD is aggravated by many external factors. Shipping and
processing can increase the risk factors for BRD both immunologically and
environmentally. Immunological competence can be compromised due to stress from
commingling, nutritional change, shipping distance and weather (Cernicchiaro et al.,
2012). The majority of morbidity during the feeding period occurs within the first three
weeks after arrival and 15% to 45% of incoming calves require treatment (Kelly and
Janzen, 1986). Epidemiological risk factors may increase during these times including
virulence, type, and mode of transmission of microbes, latent and carrier status of

animals, and infectious period. Environmental factors include temperature, climate, humidity, ventilation and stocking density. Although, interventions including vaccination, processing procedures, antimicrobials, and nutrition have reduced morbidity and mortality, BRD is still the most common disease of feedlot cattle (Taylor et al., 2010).

Beyond treatment, performance of sick cattle may decrease due to BRD. Economic effects of BRD include decreased ADG, death loss, treatment costs and reduced carcass quality (Smith, 2004; Schneider et al., 2009; Taylor et al., 2010). Calves treated for BRD commonly have lower average daily gain (ADG) compared to healthy animals (Fulton et al., 2002; Snowder et al., 2006; Schneider et al., 2009) and infected calves have been reported to return up to $54.01 less than non-infected calves (Schneider et al., 2009). McNeill et al. (1996) and Schneider et al. (2009) found cattle treated for BRD to have less desirable carcass qualities including reduced hot carcass weight (HCW), subcutaneous fat cover, muscling, marbling score and quality grade compared to untreated cattle. Further, identifying infected cattle is difficult and often inaccurate as indicators such as depression, abnormal appetite, and labored breathing can be very subjective. Cattle that do not exhibit clinical symptoms may go untreated resulting in decreased performance, such as suppressed gains (Wittum et al., 1996). Untreated cattle also can develop lung lesions; Schneider et al. (2009) found 60.6% of cattle never treated for BRD had lung lesions. Also, Thompson et al. (2006) reported 68% of untreated cattle had pulmonary lesions, associated with decreased ADG.

In summary, bovine respiratory disease impacts both herd health and performance, increasing economic expense. Improved measures of processing and

vaccination protocol are important components in reducing BRD, promoting cattle health and improving performance.

Pathogenesis of Bovine Respiratory Disease

Pathogenesis of BRD is a combination of one or more bacterial and viral infectious agents along with stress including weaning, shipping and processing (Heddleston and Wessman, 1975; Taylor et al., 2010). These bacteria can be routinely found in the upper region of the respiratory system (Frank and Briggs, 1992; DeRosa, 2000). A viral infection reduces the body's immune mechanisms, specifically in the pulmonary system (Bielefeldt Ohmann and Babiuk, 1984; Jones and Chowdhury, 2007; Ellis, 2010). This reduction in immune defense leads to bacterial aerosolization and colonization in the lower part of the lungs (Yates, 1982; Bielefeldt Ohmann and Babiuk, 1984; Jericho et al., 1986). This interaction allows for the definition of 'complex' for BRD. Bacterial pathogens involved in BRD are important to the pathogenesis of this disease.

Viral Pathogens in Bovine Respiratory Disease

The mucosal respiratory tract in cattle may be infected by bacterial and/or viral pathogens resulting in obstruction of airflow to the lungs (Baker et al., 1997). Viral agents can also alter or destroy structural integrity as well as resident immune factors in the lung (Bielefeldt Ohmann and Babiuk, 1984; Ellis, 2010). This results in immune

vulnerability and the potential for a secondary bacterial infection (Gardner and Kung, 1980; Bielefeldt Ohmann and Babiuk, 1984).

Multiple viral pathogens and their interactions with bacteria contribute to BRD. These viral pathogens include bovine herpes virus type I (BHV-1), bovine respiratory syncytial virus (BRSV), bovine viral diarrhea virus (BVDV), and parainfluenza-3 (PI3) (Yates, 1982). Bovine herpes virus-1 is a significant contributing pathogen in bovine respiratory disease complex (Yates, 1982; Jones and Chowdhury, 2007). Cattle infected with BHV-1 may suffer from upper respiratory tract disorders, conjunctivitis, and immune suppression. Bovine herpesvirus-1 has an incubation time of 2 to 6 days (Yates, 1982). An acute infection of this virus can lead to infectious bovine rhinotracheitis (IBR). Symptoms of IBR include fever, anorexia, coughing, excess salivation, nasal discharge, conjunctivitis, and nasal lesions. After an infection from exposure of high or low doses, BHV-1 establishes lifelong latency in the trigeminal ganglia and the pharyngeal tonsil (Pastoret et al., 1982; Nandi et al., 2009). Latency can also be established from a modified-live attenuated vaccination (Jones et al., 2000). Elevated stress levels or immune suppression can initiate reactivation of the virus from latency (Pastoret et al., 1982). Stress and immune suppression can cause reactivation and lead to BRD (Yates, 1982). This reactivation results in viral production and shedding, leading to an acute and communicable disease (Jones et al., 2000). Acute infections, either from initial exposure or from reactivation, will lead to high virus production. Shedding of the virus can be in ocular, oral or nasal cavities and shedding can last for 7 to 10 days after the infection (Jones, 2003). Cattle can become infected with the virus by contact with another animal

or surface an infected animal has come into contact with. Although immunosuppression results from BHV-1, a systemic infection is commonly avoided by an effective immune response from the host, with recovery typically occurring 1 to 5 days following the onset of clinical symptoms. Despite the short duration of immune suppression induced by BHV-1, a secondary bacterial infection can occur during this time (Yates, 1982). As a result BHV-1 can initiate bovine respiratory disease (Yates, 1982; Jones and Clowdhury, 2007). Not only will exposure to BHV-1 lead to BRD but a reactivated latent virus can initiate BRD as well (Nandi et al., 2009).

While many commercial vaccines that target BHV-1 are available, immunosuppression can result from vaccination. As a result, these vaccines can cause disease in young calves and have the potential to induce BRD (Jones and Clowdhury, 2007). Modified live attenuated virus (MLV) or killed whole virus (KV) vaccinations are available against BHV-1. Modified live attenuated vaccinations are effective in inducing an effective immune response, although concerns of latency establishment and reactivation are a concern. Killed whole virus vaccines are safe, but often do not produce sufficient immunity and require more than one injection to produce acceptable antibody response (Jones and Clowdhury, 2007). Both types of vaccinations may create management issues such as morbidity in the case of MLV vaccines or cost of reworking cattle for a second vaccination in the case of a KV vaccine. An increase in IBR outbreaks in feedlot cattle after vaccination has been observed (Ellis et al., 2005). Whether this is a result of the vaccination or a field strain is unknown. Because of observed side effects

and deficient immune development, alternative approaches to prevent BHV-1 leading to IBR are of growing interest.

Bovine respiratory syncytial virus (BRSV) can cause disease in all ages of cattle, although young calves often experience the most severe disease, clinical signs can last 1 to 2 weeks (Antonis et al., 2010). Cattle infected with BRSV often contract a secondary bacterial infection, contributing to BRD (Baker and Frey, 1985). This virus can be isolated from cattle with or without clinical signs (Collins et al., 1970). Immunity following an infection or vaccination is short-lived, lasting only 3 to 4 months; recurrent infections are common among vaccinated and non-vaccinated calves (Martin and Bohac, 1986).

Bovine viral diarrhea virus (BVDV) has been isolated alone as well as in combination with other pathogens in cattle diagnosed with BRD. Disease transmission in feedlots is elicited by persistently infected (PI) cattle (O'Connor et al., 2005). Further, cattle in the presence of a PI-BVDV animal have been reported to increase the risk of antimicrobial treatment by 43% compared to cattle not exposed (Loneragan et al. 2005). This virus is important in terms of persistently infected animals compromising overall herd health.

Bovine parainlfluenza-3 (PI3) virus is associated with respiratory disorders that range from asymptomatic to severe pneumonia, with most symptoms being mild (Frank et al. 1973). Infection can result from aerosol transmission and direct contact of the virus, and is frequent in areas of overcrowding and poor ventilation (Hoerlein et al., 1959). Viral pathogens are an essential area to target in bovine respiratory disease. Improving

the efficacy directly through vaccination, or through alternative methods would be an

opportune route in decreasing BRD rates in feedlot cattle.

Prevention

Processing and its Relation
to Bovine Respiratory Disease

Common processing practices of feedlot cattle, including vaccination, castration,

implantation of growth hormones, anthelmintics, and dehorning are performed at or

shortly after arrival. Vaccination and antibiotic protocols are important to overall feedlot

health. Although necessary, stresses due to processing and shipping in combination with

exposure to pathogens can increase BRD incidence (Daniels et al., 2000). Despite

improved vaccines and antibiotics on the market, BRD rates are still increasing

(Loneragan et al., 2001). Newly arrived feedlot cattle are at the highest risk for

developing respiratory disease (Jensen et al., 1976; Kelly and Janzen, 1986). Therefore,

timing and methods of processing may be significant concerning morbidity due to

respiratory disease. Castration is an expected stress imposed on bull calves entering a

feedlot. Daniels et al. (2000) found calves castrated on-arrival compared to those

castrated before entry into the feedlot had a 92% increase in morbidity incidence and

3.5% compared to 0% mortality. In the same study, previously vaccinated calves also had

better ADG during the 21 d receiving period. Administration of preventative treatments

including antibiotics is common in newly received cattle. Treating high-risk cattle with

antibiotic medication proves to be an effective method for reducing morbidity (Galyean

et al., 1995; Daniels et al., 2000; Duff et al., 2000a). Although necessary, processing is

one of the major stresses that cattle are exposed to (Fordyce et al., 1985). This may limit effectiveness of vaccination, and increase risk for BRD, again improved vaccine efficacy is essential.

Vaccination Protocols in Receiving Cattle

Health management, namely vaccination programs, is essential to successful cattle production. The investment of disease prevention is much less than disease treatment (van Shaik et al., 1996). The goal of vaccines is to increase protection for calves against disease as the calf enters into an adult herd. Although vaccinations do not prevent 100% of disease for every animal, they can increase overall herd health and economic return (Nyamusika et al., 1994). Both modified-live virus (MLV) vaccines, which have the ability to replicate, and killed (inactivated) vaccines, that are not capable of replication, are available. Modified-live vaccines are beneficial as they result in a rapid, wide spectrum of protection, but can result in abortions and infertility as well as disease problems in overly stressed cattle. Killed vaccines are more stable in storage and there is no risk of spread between animals, killed vaccines result in a slower onset of immunity as well as greater risk of allergic reactions. Many management practices can reduce vaccine efficacy, including processing techniques and nutritional status of cattle.

Routine vaccination against respiratory disease includes the viral pathogens of IBR, BRSV, BVDV, and PI3. These vaccines are generally administered intramuscularly (IM) as a combination of IBR-BRSV-BVDV-PI3 while IBR-PI3 can also be delivered intranasaly (IN). Common practices include vaccinating cattle within 48 h of arrival, or a

delayed vaccination, administered 2-3 weeks after arrival. Often times, calves arriving to the feedlot may suffer from stress resulting from transportation and processing procedures. A combination of stress and immune challenges may result in morbidity and poor performance (Smith, 2004). Effects of stress due to shipping, environment, and commingling can persist up to 15 d after arrival and continue to negatively impact the immune system and decrease vaccine efficacy (Loerch and Fluharty, 1999; Purdy et. al. 2000). Therefore, time of vaccination may be significant for protection against pathogens contributing to BRD.

Vaccines are given to increase antibody titers, which should encourage protection of the host against viral and/or microbial pathogens. Although an increase in antibody titer production from a vaccination occurs, disease protection is not always adequate (Loan et al., 1998). Overall immunity acquired after vaccination against respiratory disease pathogens is variable; Hodgins et al. (2002) reported only 75% of vaccinated animals are protected from BRD. Further, vaccination in time of stress may reduce immunity gained from vaccination (Kehrli et al., 1999). The relationship of vaccine timing and morbidity is an area of ongoing research. Most veterinarians and animal health professionals support vaccinating cattle against BRD on arrival, while some argue that vaccination should be delayed to allow animals to recover from the stresses of shipping. In groups of cattle where morbidity is high, on-arrival vaccination protocol is common (Hansen et al. 1992). However, several studies observed no difference in morbidity when vaccinating receiving cattle on arrival (Bateman, 1998; Duff et al., 2000b; Richeson et al., 2008; Richeson et al., 2009) and Martin et al. (1982) reported

increased mortality risk when cattle were vaccinated with a respiratory vaccine within the first 14 d of arrival. Cattle may be exposed to pathogens after arriving to a feedlot. For this reason, on arrival vaccination and the rapid onset of immunity may be beneficial (Todd et al., 1971; Sutton, 1980).

Increased performance may be an advantage of vaccination. Kreikemeier et al. (1996) reported calves that were vaccinated before weaning and revaccinated on arrival to the feedlot had a greater body weight (BW) gain than calves receiving a vaccination upon arrival and revaccinating after 21 d at the feedlot. However, timing of vaccination has also shown neutral outcomes concerning performance. Delayed versus on arrival vaccination has been shown to have no effect on animal performance by several groups (Lofgreen et al., 1983; Duff et al., 2000b; Richeson et al., 2009). Further, Chirase et al. (2001) observed that calves receiving a saline subcutaneous injection had greater ADG than calves injected subcutaneously with a 7-way clostridial vaccine. And Spurlock (1997) observed that repeated vaccination, or repeated immune stimulation, can have a negative effect on growth of an animal. Vaccination timing and its effects on performance may be attributed to overall health state of incoming animals, type of vaccination, and stress animals are subjected to.

Vaccinating against certain respiratory disease pathogens shows variation concerning morbidity and performance. Wildman et al. (2008) reported high-risk cattle receiving a modified-live viral vaccine containing IBR, BVDV types I and II, and *Mannheimia haemolyltica*, and *Pasteurella multicoda* bacteria toxoid experienced less mortality and increased ADG compared to cattle receiving a IBRV, BVDV type I, BRSV,

and PI3 as well as *Mannheimia haemolyticia* vaccination. Not only vaccine type, but also route of vaccine administration may affect performance in receiving cattle. Respiratory vaccines administered intranasaly (IN) have demonstrated advantages in ADG (Duff et al., 2000b). Again, method of vaccination may depend on health state of calves and timing of vaccination. Intranasal vaccines may be beneficial when vaccinating on-arrival because of immediate protection (within 24 hours; Kucera and Beckenhauer, 1978). Kucera and Beckehhauer (1978) reported IN temperature-sensitive IBR vaccine to deliver protection within 24 h. An IM IBR vaccination is also capable of providing protection against a virulent virus within 48 h (Sutton, 1980).

Maternal antibodies may play a significant role in vaccination efficacy in young animals (McGuire et al., 1976; Lamiare et al., 2000). These maternal antibodies can persist in calves for up to 230 days after birth (McGuire et al., 1976). Menanteau-Horta et al. (1985) found calves with maternal antibodies still present had reduced active immunity formation from an intramuscular IBR modified-live viral vaccination. However, after a second IBR vaccination, titer levels rose rapidly. Kryubov et al. (1978) found similar reactions in calves vaccinated with a modified-live IBR vaccination in calves with maternal antibodies present.

It can be considered that vaccination type and timing can have effects on both morbidity and performance, although reports have been inconsistent as to a superior routine. A lack of consistency of vaccine efficacy and performance may be affected by health state of calves, commingling, susceptibility to pathogens due to stress, and to the dynamic complex of BRD.

Nutritional Status and Respiratory Disease

Nutritional status is important for all bodily functions including immunity (Chandra, 1997; Lochmiller and Deerenberg, 2000). Cattle exposed to stress and/or pathogens require adequate nutrition to maintain health (Cole, 1996). This topic is specifically relevant in receiving cattle, which may be greatly affected by nutrition, as they will be exposed to stress and pathogens as well as likely reductions in nutritional consumption after arrival. These factors often have added significant, as previous nutrition of receiving cattle is generally unknown. Receiving cattle may have lower dry matter intake (DMI) due to factors such as herd hierarchy and stress, resulting in a depressed nutritional state (Gibb et al., 2000). Consequently, it is essential for to provide appropriate nutrition to receiving cattle. Sick cattle often have reduced feed intake, accentuating reduced nutritional status (Lofgreen et al., 1983). Cattle with poor nutritional reserves may be unable to withstand a pathogenic infection, leading to BRD. Further, additional dietary energy has shown evidence of improved immune cell function (Stabel et al., 2003). Dietary energy may play an important role in reducing the incidence and severity of respiratory disease in receiving cattle.

Similarly, protein intake may also influence pathogen resistance. Protein is required for proper cellular development, including immune-related cells. Jakab et al. (1981) reported protein deficient mice were unable to clear influenza virus from their lungs. Moreover, protein deficient animals may have impaired cellular immune function (Chandra, 1997; Dai et al., 1998). Adequate protein consumption is most likely an important factor for maintained health in receiving cattle.

Immune function can be improved through trace mineral supplementation (Underwood and Shuttle, 1999). Some specific nutrients that have been shown to aid disease resistance include vitamin A, D, E and C and elements selenium, copper and zinc (Itze, 1984; Chew, 1987; Reinhart and Hustmyer, 1987). Arthington and Havenga (2012) reported injectable trace minerals to increase the humoral immune response. Work by Cole (1985), Pritchard and Mendez (1990) and Galyean et al. (1999) found steers which were preconditioned with trace minerals reduced BRD incidence and severity. Although trace minerals and the relationship to immunity has received much attention, the effects of nutritional plane and its effects on immunity and health in response to a BRD challenge has received little research.

Nutritional status may also influence febrile response (Scrimshaw et al. 1991; Scrimshaw and SanGiovanni, 1997). Fever can induce amino acid mobilization from tissues such as muscles, used in cellular immune function (Scrimshaw et al., 1991). Fatty acids may also be utilized during a fever (Long et al., 1977). Basal metabolic rate can increase up to 30% during a febrile response (Cooper et al., 2000). Further, Scrimshaw and SanGiovanni (1997) reported malnourishment results in a reduced ability to produce central immune factors. As a result, nutritional state of cattle may be important for recovery as well as future performance.

Because of the significance of nutrition and immune function, vaccination should not be treated as the singular solution in cattle health. Therefore, meeting nutritional requirements in receiving cattle is an important factor in maintaining herd health.

Lysine and the Potential Role in Respiratory Disease

Bovine herpes virus-1 (BHV-1) is a major contributor to BRD (Yates, 1982). Bovine herpesvirus-1 is unique in that ultimately all animals are exposed and infected to BHV-1 early in life. Following inoculation, animals may exhibit clinical signs or be asymptomatic (Jones et al., 2000). Subsequently, the virus will become latent within nerve cells (Nandi et al., 2009). In stressed animals the virus may exit latency and replicate to produce infectious virus (Pastoret et al., 1982). The replicating virus can induce disease (IBR) and/or spread to susceptible animals. Vaccines are readily available for BHV-1, the goal being to maintain enough immunity to avoid reactivated, clinical disease, although this is not always the case, as sufficient immunity may not last throughout life, and another infection. Further, vaccination does not provide protection against latent infection (Jones et al., 2000). Shortcomings in vaccination encourage additional methods of prevention.

Herpes virus-1 requires arginine to replicate (Griffith et al., 1981). Lysine is a natural inhibitor of arginine (Maggs et al., 2000); as lysine levels increase, arginine levels will decrease. Lysine as a combatant for herpes replication in felines and humans has been evaluated. In vitro studies of lysine have shown a replication-inhibiting capability of the herpes virus (Maggs et al., 2000). With previous research in other species, lysine has potential to combat a herpes virus infection in stressed cattle. Lysine supplementation may decrease virulence of a herpes virus infection, and/or increase efficacy of current vaccines. A decrease in IBR outbreaks may reduce BRD severity and frequency.

CHAPTER 3

SUPPLEMENTAL LYSINE DOES NOT AFFECT ANIMAL PERFORMANCE,
ANTIBODY TITER, OR RECTAL TEMPERATURE IN RESPONSE
TO A MODIFIED-LIVE VIRAL RESPIRATORY VACCINE
IN NEONATAL HOLSTEIN CALVES

<u>Contribution of Authors and Co-Authors</u>

Manuscript in Chapter 3

Author: Kate P. Sharon

Contributions: Collected and analyzed data. Performed lab work. Wrote first draft of the manuscript.

Co-Author: Glenn C. Duff

Contributions: Conceived and implemented the study design. Analyzed statistics. Edited drafts of manuscript.

Co-Author: Jeff W. Dailey

Contributions: Constructed and supplied temperature probes.

Co-Author: Jeff A. Carroll

Contributions: Constructed and supplied temperature probes.

Co-Author: Jonathan K. Hilmer

Contributions: Conducted mass spectrometry analysis.

Co-Author: Brian Bothner

Contributions: Provided methods of mass spectrometry lab work as well as instruments for analysis.

Manuscript Information Page

K. P. Sharon, G. C. Duff, J. W. Dailey, J. A. Carroll, J. K. Hilmer and B. Bothner

Abstract

Infectious bovine rhinotracheitis (IBR), caused by bovine herpesvirus-1, is a contributing pathogen to bovine respiratory disease. Lysine has been shown to reduce virulence of herpesviruses in felids and humans. Our objective was to evaluate the effects of supplemental lysine on serum IBR antibody titer and rectal temperature in response to a modified-live intranasal (IN) or intramuscular (IM) respiratory-virus vaccination. Sixty-four neonatal Holstein bull calves (7 ± 2 d of age; BW = 37 ± 4.2 kg) were used in a completely randomized design. Calves were fed milk replacer supplemented with either 17 g/d L-lysine monohydrochloride (LYS; 28 calves) or an equivalent amount of casein (CAS; 28 calves) for 42 d. Calves were then vaccinated with either an IN IBR-parainfluenza virus-3 (PI3; Nasalgen, Merck, Summit, NJ) or an IM (IBR-PI3-bovine viral diarrhea type I and II, bovine respiratory syncytial virus; Express 5, AgriLabs, St. Joseph, MO) modified-live vaccine on d 36. A control group (8 calves) received no supplement or vaccination. All calves were housed in individual calf pens (1.2 x 2.1 m). Daily feed intakes were monitored and BW measured weekly. Calves were bled on d 0, 35, 36, 37 and 42. Temperature data loggers were attached to rectal probes and temperatures were recorded every 5 min from d 28 to d 42. All data was analyzed using the Proc Mixed procedures of SAS (SAS Institute Inc., Cary, NC) with calf as the experimental unit, and a model that included treatment, calf (treatment), day and treatment x day. No significant differences were determined for average performance, rectal temperature, or IBR antibody titers with either IN or IM vaccinations between LYS and CAS treated calves (P > 0.10). However, serum urea nitrogen and the ratio of serum

lysine:arginine increased (P < 0.05) for LYS compared to CAS calves. These results suggest that supplementing lysine impacts nitrogen metabolism but does not alter the response to IBR vaccination or animal performance in neonatal Holstein calves.

Key Words: Holstein calves, bovine herpesvirus-1, lysine, vaccination

Introduction

The susceptibility of the respiratory tract to bacterial disease following a viral infection is a matter unresolved. Bovine herpesvirus-1 (BHV-1) is one of the foremost infections contributing to bovine respiratory disease (BRD; Nandi et al., 2009). An infection of BHV-1 can lead to infectious bovine rhinotracheitis (IBR), suppressing the immune system and increasing the risk for a secondary bacterial infection (Yates, 1982). Herpes viruses are difficult to eradicate due to the establishment of latency after exposure (Jones et al., 2000 Nandi et al., 2009). Times of stress, such as those experienced during shipping and processing, can stimulate the virus to emerge from latency, inducing disease and further spreading the virus (Pastoret et al., 1982). Bovine herpesvirus-1 is very common; cattle herds of over 400 head may have BHV-1 prevalence of over 85% (Raaperi et al., 2010). Vaccines are readily available for BHV-1 that attempt to provide enough immunity to avoid reactivation of the disease. Although vaccination is common, humoral immunity is not always sufficient and reactivated-induced disease puts cattle at risk for developing BRD (Jones and Chowdhury, 2007).

There is evidence that lysine supplementation decreases the incidence and severity of herpesvirus-associated disease (Griffith et al., 1981; Maggs, 2000). *In vitro*

studies have shown lysine has a replication-inhibiting capability of the herpes virus (Maggs et al., 2000). Since IBR is the result of a herpes virus infection, there may be an altered response to the common IBR vaccination when lysine is supplemented at concentrations exceeding requirements of 17 g/d (Hill et al., 2007). The objective of this study was to investigate the effects of a lysine supplementation on a modified-live viral respiratory vaccine.

Materials and Methods

Procedures were reviewed and approved by the Montana State University Agriculture Care and Use Committee, 2012-AA01.

Animals, Treatments and Diets

Sixty-four Holstein calves (7 ± 2 d of age; BW = 37 ± 4.2 kg) were used in a completely randomized design. Sixteen calves were purchased from a commercial Montana dairy and were transported (approximately 30 min 30 km) to the Montana State University facility after receiving their morning feeding. Forty-eight calves were purchased from a commercial Idaho calf ranch and were transported (approximately 6 h and 660 km) after their morning feeding and to the Montana State University facility. Upon arrival, calves were weighed and randomly assigned to treatments including: **LYS**, lysine supplemented, **CAS**, casein supplemented, and **CON,** control (no supplementation). Calves received either an **IN**, intranasal, or **IM**, intramuscular modified-live viral respiratory vaccination. **CON** calves received no vaccination. Calves were housed in individual pens (1 x 2 m) fitted with feed and water buckets and nose

guards to eliminate calf-to-calf contact. Pens were concrete-surfaced covered with rubber mats. Crates were maintained inside at the Bozeman Agriculture and Teaching (BART) Farm with a mean temperature of 15° C.

All calves were fed a commercial milk replacer (Vigortone, Nurture Pinnacle, Brookville, OH; DM: 95.7%;, CP: 26.6%; crude fat: 18.7%; ash: 6.4%) at 0.45 kg/d per calf twice daily at 0700 and 1900 for 42 d. Milk replacer was mixed based on weight and at a concentration of 12% powder (as-fed) (Milk Master, PolyTank & Polydome, Litchfield, MN). Milk replacer was fed using 2 L nursing bottles (Calf Nurser Bottle, Merrick, Inc., Vadnais Heights, NM) with a rubber teat (Milk Bar Bottle Nipple, Coburn Company, Whitewater, WI) and individual bottle holders in each pen. **LYS** calves received 8.5 g of L-lysine monohydrochloride (Global Bio-Chem, Hong Kong, China) twice daily allocated to individual bottles and mixed with milk replacer. **LYS** calves received a total of 17 g·head^{-1}·d^{-1} of lysine. **CAS** calves received 8.5 g of casein allocated to individual bottles and mixed with milk replacer twice daily. **CAS** calves received a total of 17 g·head^{-1}·d^{-1} of casein. **CON** calves received no supplementation. After each feeding, bottles and teats were washed with a soap, bleach, and water mixture.

Additionally, calves were offered a commercial starter feed (Dairy Starter Pellet; Payback Feed, Sioux Falls, SD; DM, 97.8%; ADF, 8.9%; NDF, 21.9%; and CP, 19.9%) beginning on d 3 with an initial offering of 0.2 kg·head^{-1}·d^{-1}. Amounts were increased to ensure free choice consumption. Daily allotments of grain were fed starting at 0730 in buckets. Daily refusals were weighed prior to feeding. Offered and refused feed was

weighed back daily. Each calf was supplied with a water bucket. Water was changed twice daily. Water buckets were washed with a soap, bleach, and water mixture weekly.

Data Collection

Rectal temperatures were constantly recorded by means of an indwelling rectal temperature probes starting on d 28 and ending on d 42. Temperature data loggers were attached to the rectal probes. Temperatures were recorded every 5 min and averaged every hour for the duration of the study for statistical analyses.

Calves were vaccinated on d 35 at approximately 1000 via intranasal inoculation with 2 mL of a modified-live respiratory vaccine containing BHV-1 and PI3 (Nasalgen, Merck Animal Health, Summit, NJ) or intramuscularly with 2 mL of a pentavalent, modified-live respiratory vaccine containing BHV-1, BVDV1a, BVDV2a, PI3 and BRSV (Express 5, Boehringer Ingelheim Vetmedica, Inc., Saint Joseph, MO). Control calves (CON) received no vaccination.

Body weights were obtained on d 0, 1, 7, 14, 21, 28, 35, and 42 prior to the 1900 feeding. Grab samples of the grain and milk replacer diet were collected weekly for analysis. Ingredient samples were analyzed for NDF and ADF, CF, fat and CP (Dairy One Laboratory, Ithaca, NY).

Incidence of any illnesses was recorded daily for each animal. Calves that showed signs of morbidity were treated immediately. Treatment regimen consisted of administration of tulathromyocin (Draxxin; Pfizer Animal Health) at a rate of 1.1 mL/45.3 kg (2.5 mg/kg) and flunixin meglumine (Banamine; Merck Animal Health) at a rate of 1.0 mL/45.3 kg (2.2mg/kg). All treatments including d of treatment, type of

treatment, and amount of dosage were recorded. Documentation of death was recorded by animal ID and date of death.

Blood samples were collected via jugular venipuncture on d 0, 7, 14, 21, 28, 35, 36, 37, 39 and 42 in vacuum tubes (Kendall Monojet; Covidien, Mansfield, Massachusetts) for all calves. Blood collection was conducted prior to the 1900 h feeding. Serum was centrifuged at 2,100 x g for 15 min at 20°C and then stored frozen at -20 °C until analyzed. Frozen serum was transported to the Montana State University Veterinary Diagnostic Lab (Bozeman) for determination of serum neutralizing antibodies for BHV-1, PI3, BVDV type I, BVDV type II, and BRSV. Serum samples were analyzed for SUN content by a commercial assay kit (Urea Nitrogen Direct; Cat. # 0580-250; Stanbio Laboratory, Boerne, TX). Additionally, serum samples were analyzed for serum lysine and arginine concentrations by means of mass spectrometry.

Calculations and Statistical Analysis

All data was analyzed using the Proc Mixed procedures of SAS (SAS Institute Inc., Cary, NC). Calf was treated as the experimental unit. Performance data were analyzed with a model that included treatment, block and calf. Temperature, antibody titer data, serum lysine and arginine, and SUN data were analyzed with a model that included treatment, calf (treatment), day, and treatment x day. Significance was indicated when $P < 0.05$.

Results

No differences (P > 0.10) were observed for initial BW, final BW, ADG, DMI or overall G:F across treatments (LYS, CAS, and CON) (Table 1). No differences were observed among treatments (LYS, CAS, and CON) in vaccinated calves for IN (Figure 2) or IM (Figure 3) for rectal temperature (P > 0.10) or IBR antibody titer levels (P > 0.10) (Figure 4). Serum urea nitrogen (Figure 5) and the ratio of lysine:arginine (Figure 6 and 7) was greater for LYS compared to CAS calves.

Discussion

Rectal temperature did not differ among vaccinated and non-vaccinated calves. Ellis et al. (2010) reported reduced efficacy of an IN vaccination to a bovine respiratory syncytial virus challenge in seropositive animals compared to seronegative animals. Seropositive results derived from maternal antibodies may inhibit response to vaccination early in life (Tizard, 2009). Although vaccinations were administered four weeks after arrival, maternal antibodies may have been a factor, reducing the immune response, febrile and antibody titer response, in vaccinated animals.

IBR antibody titers showed no difference among supplemented and control calves, or vaccinated and non-vaccinated calves. Maternal antibodies should have dissipated by the time of vaccination. Schipper et al. (1978) reported one-third of calves failed to develop antibody titers receiving an initial IBR vaccination.

These results suggest that supplemental lysine will not alter febrile response or IBR antibody titer levels after a modified-live respiratory vaccine but will alter SUN and serum lysine:arginine concentrations in neonatal calves.

Acknowledgements

Table 1. Effect of supplemental lysine on performance of neonatal Holstein calves.

Item	Treatments[1]			SEM[2]
	CAS	LYS	CON	
Calves	28	28	8	-
BW, kg[3]				
Initial	36.5	36.7	34.4	1.1
Final	56.9	59.3	52.4	2.6
Performance, d 0 to 42[3]				
ADG, kg	0.45	0.46	0.43	0.07
DMI, kg	0.66	0.70	0.60	0.13
G:F	0.94	0.65	0.69	0.25

[1]Treatments were supplementation: CAS = 17 g/d casein; LYS = 17g/d L-lysine monohydrochloride; CON = no supplementation

[2]Pooled SEM

[3]No difference (P > 0.10)

IN Vaccination Temperature Response
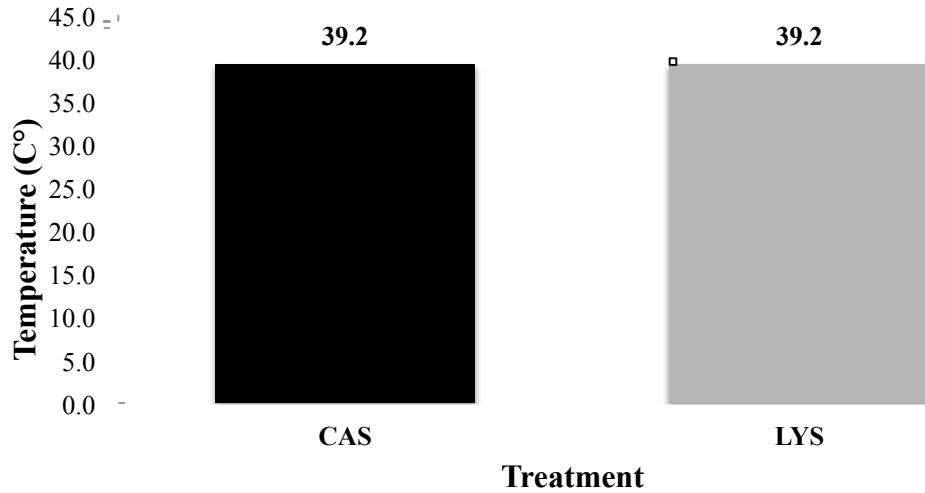
Figure 1. Effects of IN modified-live IBR-PI3 viral vaccination on rectal temperature in calves receiving supplemental lysine, supplemental casein or no supplementation in neonatal Holstein calves. Averaged rectal temperature was not significant among treatments (P > 0.10).

IM Vaccination Temperature Response
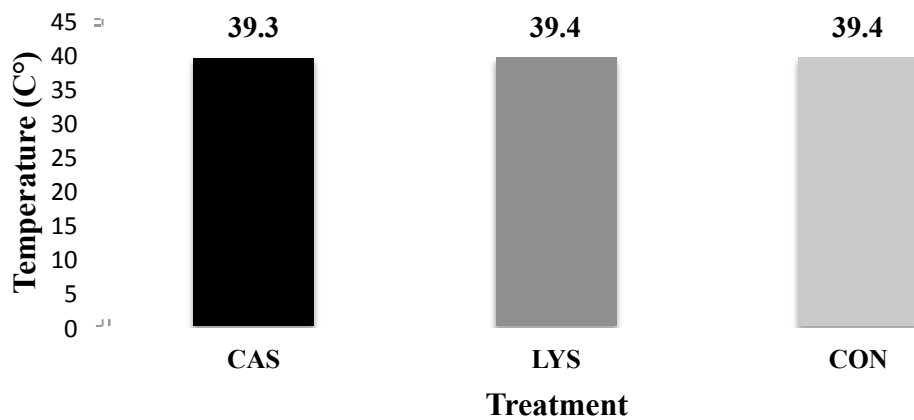
Figure 2. Effects of IM modified-live IBR-PI3 viral vaccination on rectal temperature in calves receiving supplemental lysine, supplemental casein or no supplementation in Holstein calves. Averaged rectal temperature was not significant among treatments (P > 0.10).

IBR Antibody Titers
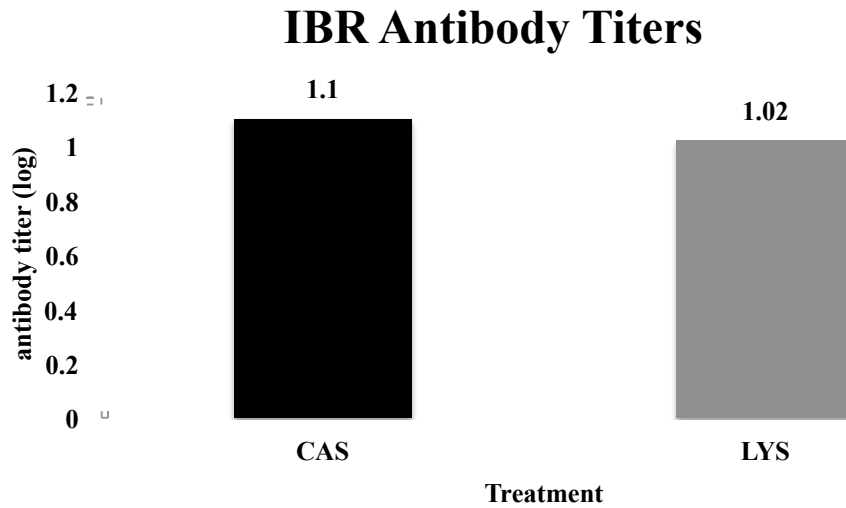
Figure 3. Overall effects of supplemental lysine or casein on IBR antibody titers following a modified-live viral respiratory vaccination in neonatal Holstein calves. No difference ($P > 0.10$) between CAS and LYS calves was detected.

Serum Urea Nitrogen
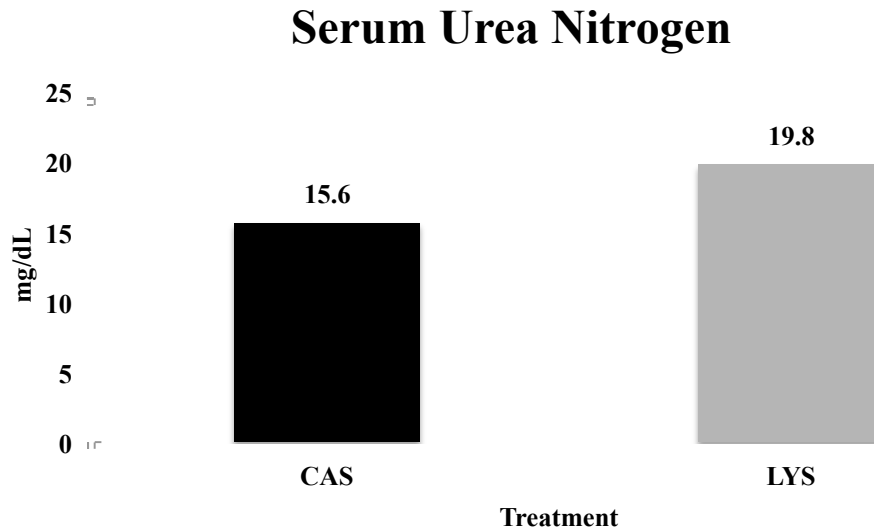
Figure 4. Effects of supplemental lysine or supplemental casein on serum urea nitrogen in neonatal Holstein calves. Overall SUN was greater ($P > 0.05$) in LYS compared to CAS calves.

Serum Lysine and Arginine
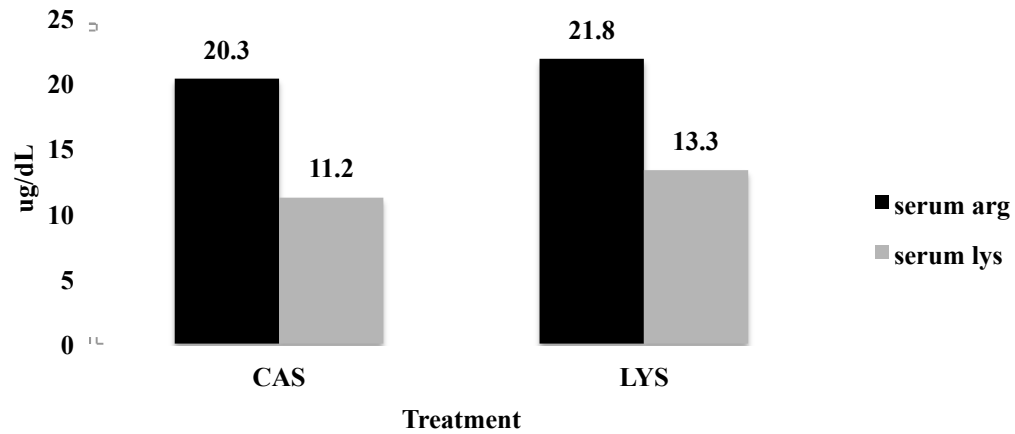
Figure 5. Overall effects of supplemental lysine or supplemental casein on serum lysine and arginine levels in neonatal Holstein calves. No difference ($P > 0.10$) between CAS and LYS calves was detected for serum lysine or serum arginine.

Serum lysine:arginine
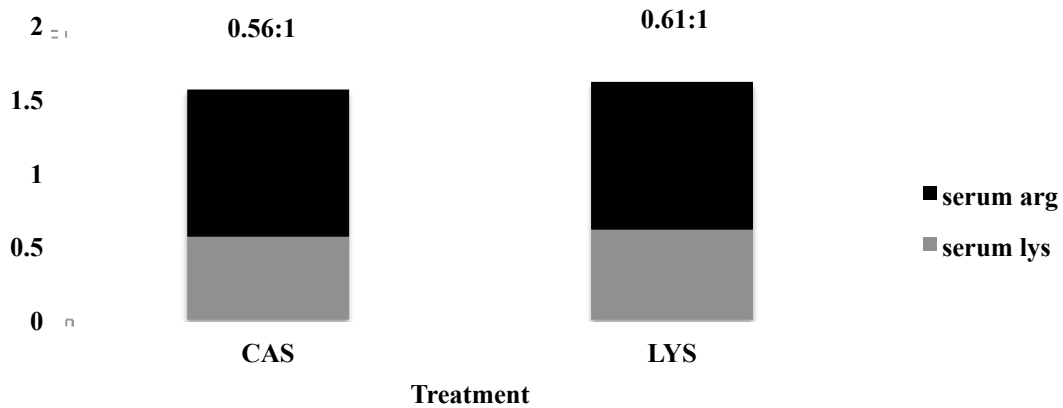
Figure 6. Effects of supplemental lysine on serum lysine:arginine ratio in neonatal Holstein calves. Serum lysine:arginine ratio was greater ($P < 0.05$) in LYS compared to CAS calves.

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CHAPTER 4

EFFECTS OF TIMING OF A MODIFIED-LIVE RESPIRATORY VIRAL
VACCINATION (DAY 0 VERSUS DAY 14 OF A RECEIVING
PERIOD) ON PERFORMANCE, FEED INTAKE,
ANTIBODY TITER RESPONSE,
AND FEBRILE RESPONSE
OF BEEF HEIFERS

Contribution of Authors and Co-Authors

Manuscript in Chapter 4

Author: Kate P. Sharon

Contributions: Collected and analyzed data. Fed animals. Performed lab work. Wrote first draft of the manuscript.

Co-Author: Glenn C. Duff

Contributions: Conceived and implemented the study design. Analyzed statistics. Edited drafts of manuscript.

Co-Author: John A. Paterson

Contributions: Assisted with nutritional components of animal diet.

Co-Author: Jeff W. Dailey

Contributions: Constructed and supplied temperature probes.

Co-Author: Jeff A. Carroll

Contributions: Constructed and supplied temperature probes.

Co-Author: Eric A. Marceau

Contributions: Performed feed analysis lab work.

Manuscript Information Page

Abstract

The objective of this study was to evaluate the effects of timing associated with the administration of a modified-live respiratory viral vaccine (BHV-1, BVDV, PI3, BRSV) on d 0 or on d 14 of a receiving period on performance, feed intake, antibody titer response, and the febrile response in beef heifers. Our hypothesis was that vaccine timing will alter the febrile response and feed intake of feeder cattle. Thirty-six heifers (Angus and Angus crosses; initial BW = 265 ± 20 kg) were ranked by BW and assigned to treatment pens (9 pens total) in a completely randomized design. Treatments (3 pens/treatment with 4 heifers/pen) included no vaccine (CON), vaccination on d 0 (DO), and a delayed vaccination on d 14 (D14) of the receiving period. Heifers were fed in 6 x 12 m pens equipped with GrowSafe feeding systems. Daily feed intakes were recorded and BW measured on d -1, 0, 14, 27, and 28. Temperature data loggers were attached to a blank controlled intrauterine drug release devices (CIDR; contained no active compound) that recorded vaginal temperatures every 5 min for the experiment; vaginal temperatures were then averaged for every h before data analysis. All data were analyzed using pen as the experimental unit. No differences ($P > 0.10$) among treatments were observed for initial BW, final BW, ADG for d 0 to end, or overall G:F. A treatment x d interaction ($P < 0.05$) was observed for feed intake. Daily intake was decreased for D14 versus D0 on d 14 ($P < 0.01$) and 15 ($P < 0.10$) and decreased ($P < 0.05$) on d 15 for the average of vaccinated calves versus CON. Eating rate (grams consumed/eating duration) was decreased ($P < 0.05$) on d 14 for D14 versus D0. No differences ($P > 0.10$) among

treatments were noted in the number of eating events/d. A treatment x d interaction ($P <$

0.01) was observed for vaginal temperature. Vaginal temperature was increased

($P < 0.10$) on d 1 for D0 versus D14 heifers and increased for D14 versus D0 on d 14 (P

< 0.01), 15 ($P < 0.05$) and 16 ($P < 0.05$). Our results suggest that time of administration

of a modified-live respiratory viral vaccine can alter feed intake and vaginal temperature

in feeder heifers.

Key Words: Beef heifers, respiratory vaccines, feed intake, febrile response

Introduction

Bovine Respiratory Disease (**BRD**) is the most common and costly problem in

feedlot cattle in North America, resulting in a $750 million annual loss to the industry

(Chirase and Greene, 2001). This disease accounts for approximately 75% of morbidity

and over 50% of mortality in feedlot, adding major costs to producers. (Taylor et al.,

2010). Calves treated for BRD once returned $40.64 less than uninfected calves, treated

twice returned $58.35 less, three or more times returned $291.93 less (Fulton et al.,

2002).   Bovine respiratory disease is a secondary infection that typically follows an

infection such as bovine herpes virus-1 (BHV-1) that causes broad immunosuppression in

infected cattle. Other important viruses that could lead to BRD include bovine viral

diarrhea virus (BVDV), bovine parainfluenza-3 (PI3), and bovine respiratory syncytial

virus (BRSV).   General health preventative management practices typically include

vaccinating against these pathogens in the form of a combined vaccine of BHV-1, PI3,

BRSV and BVDV.

Immunological competence is arguably the most important subject in newly received cattle. Cattle encountering stress due to shipping, processing, environmental factors, and commingling may become immune-compromised. Immune-compromised cattle exhibit reductions in performance as well as being incapable of building an ample immune response to a vaccination. As the industry attempts to implement alternative management practices to offset the detrimental effects of BRD, there is a renewed interest in evaluation of various vaccination protocols in order to maximize vaccine efficacy. Chirase and Greene (2001) reported decreased BW gain in calves receiving a vaccination on-arrival as compared to calves receiving a delayed vaccination. Alternatively, Richeson et al. (2009) found no differences in ADG between calves vaccinated on-arrival and calves receiving delayed vaccination. Inflammation is a necessary and normal immune response to injury or infection (Sheldon and Verhulst, 1996). Cooper et al., (1992) described inflammation in the form of febrile response following vaccination. In vivo research has shown increased skeletal muscle degradation as a result of inflammation (Cai et al., 2004). Therefore, standard vaccinations may contribute to negative effects on carcass quality due to associated inflammation (Eley and Tisdale, 2007). There is a shortage of data relating febrile response and its relationship to performance in cattle. Therefore, the focus of this study was to assess the effects of a pentavalent, modified-live vaccine containing BHV-1, BVDV1a, BVDV2a, PI3 and BRSV administered on d 0 or d 14 on growth performance, feed intake, febrile response and serum antibody titers.

Materials and Methods

Procedures were reviewed and approved by the Montana State University Agriculture Care and Use Committee, 2012-AA01.

Thirty six crossbred heifer calves (Angus and Angus crosses; average initial BW = 265 ± 20 kg) were used. Twenty-two heifers were purchased from a commercial Montana feedlot and 14 heifers originated at the Montana State University ranch. Purchased calves were in transit for approximately 3 h and hauled 330 km to the Montana State University facility. Candidate animals were not PI-BVD tested prior to the study, but were previously vaccinated with a modified-live vaccine containing BHV-1, BVDV, PI3, and BRSV. Montana State University calves were weaned approximately 2 mo. prior to study initiation and were fed grass hay. Upon arrival, heifers were weighed unshrunk. Heifer BW was ranked and heifers were assigned random numbers then assigned to treatment pens (3 pens/treatment with 4 heifers/pen). Each pen contained 1 or 2 purchased calves, the remaining being Montana State University ranch calves. Pens were randomly assigned to treatments including: **CON**, control (no vaccination), d 0 vaccination (**D0**) and a 14-d delayed vaccination (**D14**). Pens were concrete-surfaced covered pens (6 x 12 m) with two pens sharing an automatic watering system. Each pen contained one GrowSafe feed bunk.

All heifers were weighed on consecutive days at the beginning and the end of the study. In addition, D0 and D14 heifers were weighed on d 14 of the experiment. Vaginal temperature was constantly recorded by means of an indwelling vaginal temperature probe starting on d 0 and ending on d 28. Temperature data loggers were attached to a

blank controlled internal drug-releasing device (CIDR; contained no active compound). Temperatures were recorded every 5 min and averaged every hour for the duration of the study for statistical analysis.

Calves were fed 70% concentrate diets containing corn/barley grain mix, grass hay, and a pelleted protein supplement (Payback Feed, Beef Grower 20-7 R400, Sioux Falls, SD). Proximate analysis of the diet was: DM, 81%; ADF, 39.2%; NDF, 50.6%; CF, 37.5%; and CP, 10.9%. Diets were mixed daily in a Butler-Oswalt Ensil-Mixer 1830 (Dodge City, Kansas). Daily allotments of diets were fed in GrowSafe feeders starting at 0730 h. Feed samples were collected weekly and analyzed for DM. Grab samples of the concentrate diet was collected weekly for analysis. Diet samples were dried at 100° C for approximately 24 h, ground to pass through a 2-mm screen in a Wiley Mill (Thomas Scientific, Swedesboro, NJ), and analyzed for NDF and ADF, CF, and CP.

Heifers were vaccinated subcutaneously on either d 0 (D0) or d 14 (D14) at approximately 1000 with 2 mL of a pentavalent, modified-live respiratory vaccine containing BHV-1, BVDV1a, BVDV2a, PI3 and BRSV (Express 5, Boehringer Ingelheim Vetmedica, Inc., Saint Joseph, MO) and 2 mL of an 8-way clostridial bacterin (Vision 8 Somnus, Intervet, Summit, NJ). Control heifers (CON) received no vaccination and were processed with D0 and D14 heifers on d 0 and d 28 but were maintained in pens on d 14.

Blood samples were collected via jugular venipuncture on d 0 for all treatments, on d 14 for D0 and D14 treatments, and on d 28 for all treatments. Serum was centrifuged at 2,100 x g for 15 min at 20°C, serum was stored frozen at -20 °C until analyzed. Frozen

serum was transported to the Montana State University Veterinary Diagnostic Lab (Bozeman) for determination of serum neutralizing antibodies for BHV-1, PI3, BVDV type I, BVDV type II, and BRSV.

Performance data were analyzed with a model that included treatment and pen using Proc Mixed procedures of SAS (SAS Institute Inc., Cary, NC). Feeding behavior and febrile response were first analyzed using GLM procedures of SAS with a model that included treatment, heifer (treatment), day, and treatment x day. When a treatment x day interaction was observed, the data were analyzed by day using Proc Mixed procedure. Contrasts were used to separate treatment means. Contrasts included 1) control versus the average of vaccinations and 2) on arrival versus delayed vaccination.

Results

No morbidity or mortality was observed for any of the cattle during the study. No differences ($P > 0.10$) were observed among treatments (D0, D14, and CON) for initial BW, final BW, ADG, overall G:F or number of trips to GrowSafe bunk (Table 1). No differences were observed among treatments (D0, D14, and CON) for vaccine titers ($P > 0.10$) with the exception of BHV-1 D0 versus D14 on d 14 ($P < 0.05$) and BHV-1 titers for CON versus vaccinated heifers on d 28 ($P < 0.05$; Table 2). A treatment x day interaction ($P < 0.05$) was observed for daily feed intake. Daily DMI was decreased for D14 versus D0 on d 14 ($P < 0.01$) and 15 ($P < 0.10$) and decreased ($P < 0.05$) on d 15 for the average of vaccinated calves versus CON (Figure 1). Eating rate (g consumed/second) was decreased ($P < 0.05$) on d 14 for D14 versus D0 (Figure 2). A

treatment x d interaction (P < 0.01) was observed for vaginal temperature. Vaginal temperature was increased (P < 0.10) on d 1 for D0 versus D14 heifers and increased for D14 versus D0 treatments on d 14 (P < 0.01), 15 (P < 0.05) and 16 (P < 0.05; Figure 3).

Discussion

Common feedlot management practices involve vaccinating cattle for BRD upon arrival with modified-live viral and bacterin-toxoid vaccines. Cattle are exposed to antigenicity through all stages of life, therefore sufficient, consistent immunity is important in times of stress, such as shipping and processing (Klasing and Barnes, 1988). All heifers were in an apparent healthy state upon arrival and had previously received standard respiratory vaccinations. This could have contributed to the lack differences in ADG and BW and serum antibody titers, with the exception of BHV-1. However, high-risk, light weight cattle may have elicited more discrepancy in terms of performance and serum antibody titer levels. Origin and immune state of receiving cattle may influence post-arrival health and therefore vaccine timing may be more significant.

Although no difference in performance, a reduction in feed intake in D14 heifers on d 14 and d 15 suggests that vaccination may impact DMI. Further, Gandra and Scrimshaw (1961) explained even mild immune taxation such as vaccination has been shown to decrease normal feed intake. However, on d 15 a reduction in DMI for the average of the vaccinated heifers compared to the CON group suggests that working cattle even without vaccinating, may affect feed intake.

A link between febrile response and nutrition could serve as an explanation for the increased febrile response observed in the D14 compared to the D0 heifers. Further, D14 heifers may have been in a better nutritional state and thus had the ability to generate an amplified immune response in the form of fever. Although a large demand energetically, fever is a necessary and beneficial response when responding to an increased immune requirement. Energy and body tissue lost due to an immune challenge may be restored more rapidly if cattle are in a sound nutritional state.

No differences were observed among treatments for vaccine titers with the exception of BHV-1. This difference was noted on d 14 for D0 compared to D14 groups and d 28 in CON compared to vaccinated heifers. Previous vaccination with a modified-live respiratory vaccination and health state of candidate animals was likely to have influenced titer levels and accounted for lack of difference. BHV-1 titer distinction may have been exemplified due to lack of previous developed immunity. Efficacy of BHV-1 of the modified live vaccine may have been superior within this group of cattle.

In summary, delaying vaccination altered feeding behavior for approximately 3 d versus altered feed intake for 1 d when the vaccine was administered during the start of the receiving period. Although delayed vaccination resulted in reduction in feed intake no difference in performance or serum antibody titers among treatments was noted. This information can affect the timing and type of vaccinations used in previously vaccinated, healthy receiving cattle.

Implications

Vaccinating cattle with a modified live respiratory vaccine will increase body temperature and alter feed intake for a short duration; thus, managers can use these data when determining which vaccination protocols to utilize on various groups of receiving cattle. It's important to note that the short durations of febrile response and decreased feed intake observed in the current study didn't result in overall losses in ADG or gain efficiency.

Acknowledgments

Table 1.   Effects of vaccination timing (on arrival versus delayed 14 d) on performance of beef heifers during a 28-d receiving period

Item	Treatments[1] CON	D0	D14	SEM[2]	P-value contrast[3] CON vs. Vacc	D0 vs. D14
Pens (heifers)	3 (12)	3 (12)	3 (12)	-	-	-
BW, kg[4]						
Initial	262	268	266	5.96	0.51	0.84
d 14	-	286	279	5.20	-	0.32
Final	299	303	301	5.60	0.66	0.76
Performance, d 0 to 28						
ADG, kg	1.3	1.2	1.2	0.10	0.58	0.88
DMI, kg[5]	7.9	7.1	7.4	0.41	0.16	0.64
Trips[6]	15.6	14.3	15.5	0.27	0.57	0.44
G:F	0.13	0.14	0.13	0.01	0.82	0.53

[1] Treatments were day of vaccination: CON = control, no vaccination; D0 = heifers received respiratory (BHV-1, PI3, BVDV, BRSV) vaccination on d 0 of the receiving period; and D14 = heifers received respiratory (BHV-1, PI3, BVDV, BRSV) vaccination on d 14 of the receiving period; Vacc = all vaccinated heifers (both D0 and D14 groups).

[2] Pooled SEM.

[3] Contrasts evaluated were CON versus average of vaccinated heifers and d 0 vaccination versus d 14 vaccination.

[4] Heifers were weighed two consecutive d at the beginning and end of the experiment.

[5] A treatment x day interaction (P < 0.05) was observed for intake; therefore, data were analyzed by day. Data are presented in Figure 2.

[6] Number of eating events per day. No treatment x day interaction was observed (P > 0.65)

Table 2. Effects of vaccination timing (on arrival versus delayed 14 d) on serum antibody titers of beef heifers during a 28-d receiving period

Item[6]	Treatments[1,2]			SEM[5]	P-value[4]	
	CON[7]	D0[7]	D14[7]		CON vs. Vacc	D0 vs. D14
d 0						
BHV-	0.3	0.1	0.2	0.13	0.64	0.52
PI3	1.0	1.0	0.9	0.23	0.87	0.66
	1.1	1.3	0.7	0.27	0.33	0.74
	1.1	0.7	1.3	0.29	0.33	0.14
BRSV	1.4	1.6	1.6	0.19	0.80	1.00
d 14						
BHV-	-	1.4	0.4	0.20	-	0.01
PI3	-	1.5	1.7	0.17	-	0.31
	-	1.7	1.4	0.23	-	0.38
	-	1.3	1.4	0.39	-	0.79
BRSV	-	1.7	1.7	0.29	-	0.93
d 28						
BHV-	0.2	1.2	1.2	0.18	0.01	1.00
PI3	1.2	1.7	1.7	0.26	0.26	0.86
	1.4	1.8	1.7	0.32	0.67	0.78
	1.6	1.7	1.6	0.54	0.98	0.86
BRSV	1.4	2.0	2.0	0.21	0.14	1.00

[1] Treatments were day of vaccination: CON = Control, no vaccination; D0 = heifers received respiratory (BHV-1, PI3, BVDV, BRSV) vaccination on d 0 of the receiving period; and D14 = heifers received respiratory (BHV-1, PI3, BVDV, BRSV) vaccination on d 14 of the receiving period; Vacc = all vaccinated heifers (both D0 and D14 groups).

[2] Vaccinated heifers were bled on d 0, 14, and 28. CON heifers were bled on d 0 and d 28.

[3] A treatment x day interaction ($P < 0.05$) was observed for titer.

[4] Contrasts evaluated were CON versus average of vaccinated heifers and d 0 vaccination versus d 14 vaccination.

[5] Pooled SEM.

[6] BHV-1 = infectious bovine rhinotracheitis; PI3 = parainfluenza-3 virus; BVDVI = bovine viral diarrhea type I; BVDVII = bovine viral diarrhea type II; and BRSV = bovine respiratory syncytial virus.

[7] All serum antibody titers are presented in log10 format.
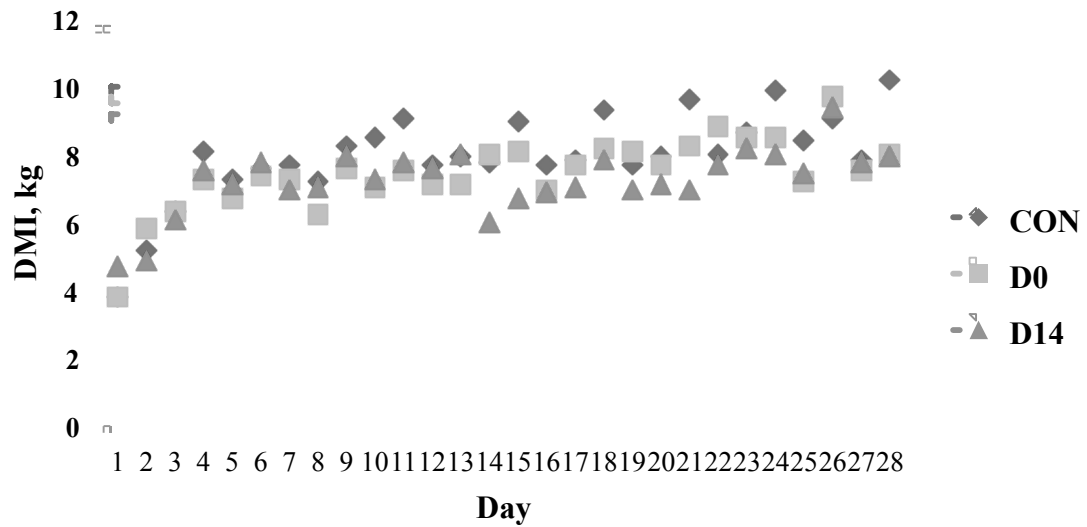
Figure 1. Response in DMI to vaccinations administered on day 0 or day 14 of the receiving period. Daily intake was decreased for D14 versus D0 on d 14 ($P < 0.01$) and 15 ($P < 0.10$) and decreased ($P < 0.05$) on d 15 for the average of vaccinated calves versus CON.
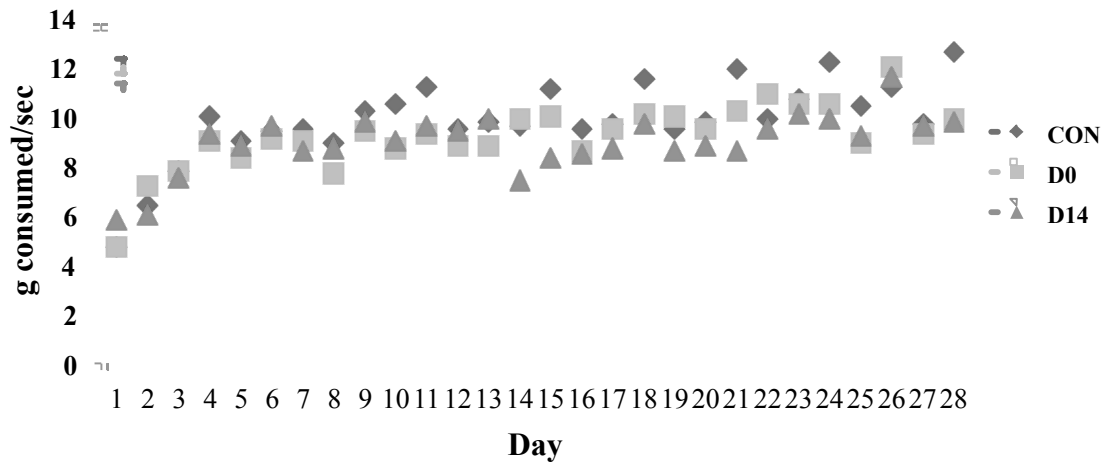
Figure 2. Eating rate (g consumed/s) response to vaccinations administered on day 0 or day 14. Eating rate (g consumed/s) was decreased ($P < 0.05$) on d 14 for D14 versus D0.

Figure 3. Daily vaginal temperature response to vaccinations administered on day 0 or day 14.   Control (CON) heifers were not vaccinated. Vaginal temperature was increased ($P < 0.10$) on d 1 for D0 versus D14 heifers and increased for D14 versus D0 on d 14 ($P < 0.01$), 15 ($P < 0.05$) and 16 ($P < 0.05$).
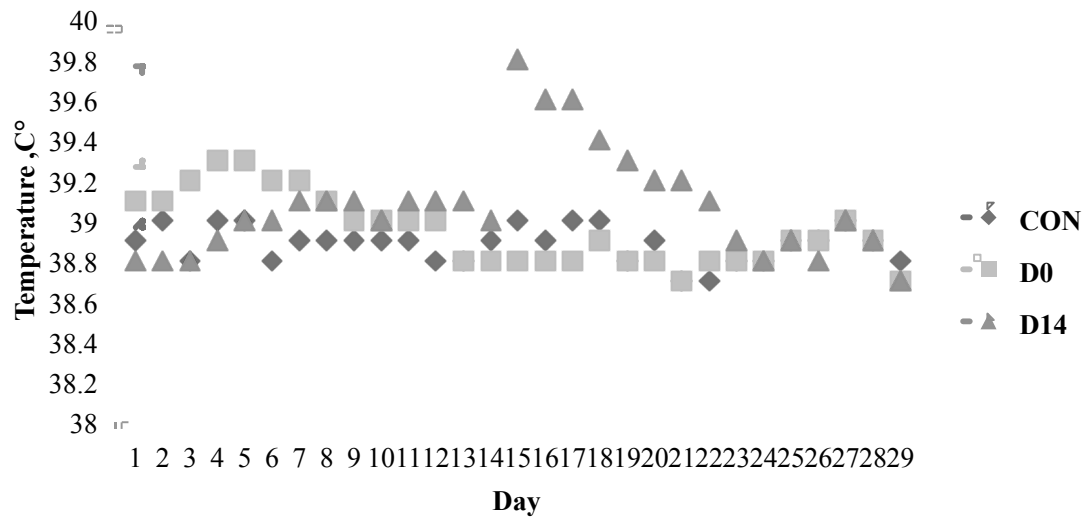
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CHAPTER 5

CONCLUSION

Bovine respiratory disease continues to be a substantial problem in the cattle industry. Multiple factors may have potential for reducing frequency of outbreaks, such as processing practices. Improved processing practices may reduce stress and therefore disease in receiving cattle. Increased efficacy of vaccines and reduced virulence of viral pathogens by means of alternative measures are areas of importance in receiving cattle.

On arrival compared to a delayed vaccination in receiving cattle appear not to effect performance or immunity. Supplemental lysine, similarly, does not appear to affect immunity but will alter serum lysine and serum urea nitrogen levels in neonatal calves.

Improved vaccination effectiveness and a reduction in respiratory disease in receiving cattle is an area requiring continued attention.

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