Enhancing feedlot cattle health: The roles of animal handling and feed additives in reducing stress and disease

by

Jared Robert Bourek

B.S., Kansas State University, 2016
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AN ABSTRACT OF A DISSERTATION

submitted in partial fulfillment of the requirements for the degree

DOCTOR OF PHILOSOPHY

Department of Diagnostic Medicine/Pathobiology
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Abstract

The health of feedlot cattle is dependent on reducing stress and exposure to disease. Stockmen and veterinarians work together to improve health and disease outcomes in feedlot cattle through biosecurity and improving immunocompetence. Stress for cattle throughout the supply chain can come from many causes such as weather, transportation, maternal separation, digestive disruption, and many more. These stressors can result in an increase in morbidity, antimicrobial use, and subsequently mortality of cattle in feeding operations. With increased consumer pressures for reduced antimicrobial usage in red meat production, there is an increased need to evaluate these stressors to improve outcomes without the use of antimicrobials. Reducing the stress of cattle and increasing disease control directly improves cattle health, performance, and carcass characteristics while indirectly decreasing the need for antibiotics to prevent, control, or treat bacterial diseases of cattle during the finishing phase of the beef supply chain. Therefore, the objectives of these three studies were to address two specific stressors routinely observed during the feedlot phase of cattle production: 1) stress due to human-animal interactions during initial processing which could lead to increased bovine respiratory disease complex in feeder cattle and 2) stress from digestive upset that could result in liver abscesses in feeder cattle which are observed at slaughter. The first objective of this research was to evaluate the effect of handling intensity at the time of initial processing on the immune system of feedlot cattle. The second objective of this research was to evaluate the effects of antimicrobial alternatives on performance and prevalence of liver abscesses at slaughter. The results of this research indicate that aggressive handling causes negative physiological stress responses in newly received beef cattle. Secondly, this research indicates tylosin continues to be an effective fed antimicrobial for the reduction in liver abscesses. Alternative feed additives such

as decoquinate may have a positive effect on the reduction of liver abscess prevalence, and feed additives such as *Yucca schidigera* extract may improve performance at the end of the finishing period. Decreasing stress from the first day to the final day of the feeding period leads to improved health and welfare of fed cattle.

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Approved by:

Co-Major Professor
Michael D. Apley

Approved by:

Co-Major Professor
Daniel U. Thomson

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List of Abbreviations

ADG- Average daily gain
AF – As fed
AH-Aggressive handling
BRD -Bovine respiratory disease
BRSV-Bovine Respiratory Syncytial Virus
BVDV-Bovine Viral Diarrhea Virus
BW-Body weight
CK-Creatine Kinase
d-Day(s)
DM – Dry matter
DMI-Dry matter intake
DOF-Days on feed
dROMS-Derivatives of reactive oxygen metabolites
FDA- Food and Drug Administration
FRAP-Ferric reducing antioxidant power
G:F – Gain to feed ratio
GFI-Guidance for industry
HR-Rate
IBR-Infectious Bovine Rhinotracheitis Virus
IL-1-Interleukin 1
IL-6-Interluekin 6
LSH-Low stress handling
pCO_2-Parital pressure of carbon dioxide
PI3-Parainfluenza 3 Virus
pO_2 – Partial pressure of oxygen
RR- Respiratory rate
SAA-Serum amyloid A
sO_2-saturated oxygen
s-Second(s)
TCO_2- total carbon dioxide
TNF-α -Tumor necrosis factor-alpha
YG – Yield grade

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Dedication

This dissertation is dedicated to my daughter, Jordan. You have shown me how beautiful life can be, how fast someone can learn and grow, and how inherent God's love for creation is within us. May you spend the rest of your life learning with love and joy in your heart.

Preface

Chapter 2 in this dissertation entitled "The effect of handling intensity at time of processing on physiological response, immune response, and vaccination status in beef cattle at the feedlot" was prepared for publication in the *Journal of Animal Science.* Chapters 3 and 4 in this dissertation entitled "Alternative feed additive strategies to reduce antimicrobial use in finishing cattle: 60 day study" and "Alternative feed additive strategies to reduce antimicrobial use in finishing cattle: 120 day study" were prepared for publication in *Translational Animal Science.* The text and figures within these chapters are formatted according to the guidelines specified by the corresponding journal.

Chapter 1 - Literature review

Part 1: Understanding the effect of stress in cattle.

Introduction

Cattle undergo a variety of stressors because of environment, production practices, and management. Weaning, transportation, comingling, environmental changes, animal handling, morbidity, surgical procedures such as castration and dehorning, and digestive stressors create a complex and challenging environment for cattle. Many of these stressors are unavoidable parts of beef production. Nevertheless, many of these stressors negatively impact performance, health, and well-being, ultimately leading to increased morbidity, mortality, and production loss. Physiologically, stress is regulated through two interconnected pathways, the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic adrenal medullary (SAM) axis, and these neuroendocrine systems are primarily involved in maintaining metabolic homeostasis (Mormede et al., 2007). This review will discuss the causes of stress in cattle, the fundamental pathways of the stress response, and the effects of the stress response on immune function, and the effects of stress on cattle health and performance.

Stressors in cattle

Carroll and Forsberg (2007) concluded that stressors in cattle can be broken down into three broad, but intermingling categories: psychological stress, physical stress, and physiological stress. Psychological stressors are those associated with fear, such as maternal separation, commingling, exposure to novel environments, loud noises and restraint are considered psychological stress (Grandin, 1997; Carroll and Forsberg, 2007). Maternal separation from calf is a critical stressor, as Lefcourt and Elsasser found significant increases in epinephrine and norepinephrine after dams were separated from calves for 1 d, with a rapid decline in epinephrine and norepinephrine when re-united (Lefcourt and Elsasser, 1995). The culmination of psychological stress for feeder cattle are maternal separation, entering a novel auction market, commingling with cattle from other ranches, and then arrival another novel environment, altogether or in a short period of time (Araujo et al., 2010).

Physical stressors are associated with thermal stress, hunger and thirst, fatigue, injury, and disease. Heat stress in cattle is the result of heat accumulation from the environment exacerbated by metabolic heat accompanying high feed intake that results in physiological changes and reduced feed intake (Burhans et al., 2022). Transportation of cattle is one of the most common stressors undergone by cattle, and several studies have shown stress compared to cattle not transported (Cole et al.,1988; Carroll and Forsberg, 2007; Chen et al., 2015). Additionally, long haul transportation of beef cattle often results in the extensive deprivation of feed and water and cattle fatigue (Loerch and Fluharty, 1999). Surgical procedures, specifically castration and dehorning, are significant stressors causing physical trauma in addition to the stress of physical restraint (Coetzee et al., 2007; Doherty et al., 2007).

Physiological stress results from deviations in normal endocrine or neuroendocrine function caused by nutrient restriction, glandular disorders, or other endocrine disruptors. Prolonged exposure to high concentrations of glucocorticoids can cause physiological issues, including protein catabolism, immunosuppression, hyperglycemia, and depression (Carroll and Forsberg, 2007).

Physiological pathways of the stress response

The aforementioned stressors initiate the pathway for a stress response (Carroll and Forsberg, 2007; Cooke, 2017). A stress response begins with the central nervous system perceiving a real or potential threat to homeostasis (Moberg & Mench, 2000). The stress response pathway is regulated by the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic adrenal medullary (SAM) axis. The type and duration of stress will influence which stress pathway, or both are initiated. In less than a minute, in acute stress responses, the animal's SAM axis is activated by the hypothalamus releasing catecholamines, such as epinephrine, and norepinephrine that act directly to stimulate biological responses, such as increasing heart rate, respiratory rate, or initiating aggressive, "fight or flight" behaviors (Chen et al., 2015). Later, the HPA is activated. Initiation of HPA begins with a stimulus and the release of corticotropin-releasing hormone (CRH) and vasopressin (VP). Elevated concentrations of CRH and VP in the hypothalamic-hypophyseal portal blood reach the anterior pituitary gland, stimulating corticotrophs to synthesize and secrete of adrenocorticotropic hormone (ACTH) (Burdick et al., 2011). The adrenocorticotropic hormone then stimulates the adrenal cortex to release glucocorticoids, such as cortisol (Mormede et al., 2007; Burdick et al.,2011; Brown and Vosloo, 2017). Cortisol is a primary glucocorticoid in cattle (Mormede et al., 2007), and cortisol plays a vital role in glucose metabolism, immune modulation, as well as heart rate, pupil dilation, vasoconstriction to the skin and gut, vasodilation to the leg muscles, and adaptation to stress (Sapolsky et al., 2000; Carroll and Forsberg, 2007).

Impact of the stress response on immune function

The SAM and HPA axis have many effects on immune function in cattle (Carroll and Fosberg, 2007). The HPA axis plays a critical role in cattle heat stress management (Bagath et al., 2019). The HPA axis results in the production of cortisol, influenced by cytokines induced by the heat shock response, which in turn reduces feed intake and endogenous heat production, while initiating a protective down-regulation of cytokine production to prevent excessive immune suppression (Bagath et al., 2019). Down-regulation of cytokines and immune function is not always a desired effect (Sapolsky et al, 2000). Blecha et al. (1984) found that transportation had a significant effect on circulating lymphocyte function compared to cattle not transported.

Outcomes of the stress response on health

Taylor et al. (2010) discussed several different stressors in the role of Bovine Respiratory Disease (BRD), the most costly disease in North America (Griffin, 1997). Stressors such as transportation, commingling, weather, dehydration, and digestive disturbances play a major role in the health and performance of cattle in feedlots. In what is considered one of the greatest stressors on calves, maternal separation, prolonged vocalization is a key behavioral change. This may irritate the respiratory tract and increase susceptibility to infection (Loerch and Fluharty,1999). Transportation, and the accompanying dietary restriction and water deprivation can have significant impacts on rumen function. Several studies indicated differences in rumen microbial populations or decreased rumen function because of nutrient deprivation (Cole and Hutcheson, 1981; Galyean et al., 1981; Loerch and Fluharty, 1999). Cole and Hutcheson (1981) found that ruminal fermentative capacity was reduced by as much as 75% when cannulated steers were deprived of feed for a 48-h period and was still lower 5 d post compared to no feed and water restriction.

Conclusions

Cattle are subjected to several stressors throughout the production life cycle (Carroll and Forsberg, 2007). These stressors initiate distinct changes in the HPA and SAM axis that directly impact the immune response of cattle and cattle health. More research is needed to understand the relationship between physiological stress pathway and live animal outcomes.

Part 2: Liver Abscesses in Feedlot Cattle

Introduction

Liver abscesses in cattle pose a major health challenge in the beef industry, affecting both economic performance and animal welfare. These abscesses result from bacterial infections that affect the liver, which in turn lead to reduced feed efficiency and lower weight gains (Nagaraja and Lechtenberg, 2007). These abscesses also contribute to carcass condemnation at slaughter, leading to yield loss and carcass trim in advanced cases. The primary causative agent of liver abscesses in feedlot cattle is *Fusobacterium necrophorum*, but other bacteria such as *Trueperella pyogenes* and *Salmonella enterica* also play a role (Nagaraja and Chengappa, 1998; Amachawadi et al., 2017) This review examines the epidemiology, pathogenesis, risk factors, and control strategies related to liver abscesses in feedlot cattle.

Epidemiology

While liver abscesses are observed in many cattle, including neonatal calves and dairy cattle, liver abscesses commonly affect cattle in feedlots. Incidence of liver abscesses found in feedlot cattle at slaughter have been highly variable, typically ranging from 12-32% (Brink et al., 1990) but can be found in up to 90-95% (Nagaraja and Chengappa, 1998). Brown and Lawrence found 13.6% prevalence in feedlot cattle (2010). Rezac et al. found a 20.5% prevalence in feedlot cattle slaughtered in packing plants in Kansas and Texas (2014). In the National Beef Quality Audit Report, 20.9% of livers were condemned at slaughter and liver abscesses accounted for two-thirds of liver condemnations (Mckeith et al., 2012). There is significant variation in total prevalence as well as variation in the severity of abscesses. Liver abscesses are graded based on a severity score of 1-3, or as A-, A, or A+ (mild to severe, respectively) (Brown et al., 1975). Livers with a score of 1 (A-) or 2 (A) do not have a significant effect on performance or carcass quality (Brink et al. 1990; Davis et al., 2007; Brown and Lawrence, 2010; Amachawadi and Nagaraja, 2016). The most significant impact on live cattle performance and condemnation at slaughter are A+ liver abscesses when adhesions to the diaphragm or abdominal organs are found (Brown and Lawrence, 2010). Incidence of A+ varies from 4.6% to 6.1% (Davis et al, 2007; Brown and Lawrence, 2010; Rezac et al, 2014)

Pathogenesis

Liver abscesses are the ultimate result of acidosis or rumen insult. Changes in rumen pH, because of the accumulation of organic acids, lead to inflammation and erosion of rumen epithelium, causing ruminitis. Erosion of the ruminal epithelium can then be magnified by sharp feed particles, ingestion of foreign objects or hair during grooming, allowing for bacterial colonization of the rumen wall. These bacteria, principally *Fusobactierum necrophorum*, enter the portal bloodstream, leading to colonization of the liver (Amachawadi and Nagaraja, 2022). The relationship between rumenitis and abscesses in the liver was first observed by Smith (1944) and later by Jensen and colleagues (1954).

Fusobacterium necrophorum is considered the primary agent and two subspecies, subsp. *necrophorum* and subsp. *fundiliforme,* are the most frequently cultured from liver abscesses (Lechtenberg et al., 1988; Nagaraja et al, 1999 Amachawadi et al, 2017; Amachawadi and Nagaraja, 2022). *Fusobacterium necrophorum* is a Gram-negative, rod-shaped, anaerobic yet aerotolerant bacterium that has several virulence factors such as leukotoxin, endotoxic lipopolysaccharide (LPS), hemolysin, and others that allow it to colonize the rumen wall as well as the liver. *Trueperella pyogenes*, a Gram-positive, facultative anaerobic bacterium, is also considered to be a secondary agent that works synergistically to create an anaerobic environment within the highly oxygenated liver to support the colonization of *F.necrophorum* (Amachawadi and Nagaraja, 2022). More recently, *Salmonella enterica* has also been isolated from liver abscesses in Holstein steers (Amachawadi and Nagaraja, 2015). There have also been studies utilizing 16S rRNA sequencing that indicate *Bacteroides* species play a role in the formation of liver abscesses (Pinnel et al., 2022; O'Hara et al., 2024).

While the rumenitis-liver abscess pathway has been well described, Amachawadi and Nagaraja (2016) suggest that hindgut fermentation may also play a significant role. Five to ten percent of microbial fermentation in cattle occurs in the hindgut, and hindgut acidosis is more likely to occur in cattle fed higher proportions of grain (Gressley et al, 2011). Differences in the epithelium thickness of the hindgut, microbiome, and decreased bicarbonate buffering capacity of the hindgut compared to the rumen suggest hindgut acidosis may play a significant role (Amachawadi and Nagaraja, 2016). More studies on the impact of the hindgut on liver abscess formation are needed.

Risk factors

There are several risk factors for liver abscesses in feedlot cattle. Consumption of high dietary concentrations of rapidly fermentable cereal grains with low concentrations of dietary fiber is the primary risk factor associated with liver abscesses (Reinhardt & Hubbert, 2015; Galyean & Hales, 2022). These diets are highly acidogenic in the rumen and with prolonged exposure or erratic individual animal feeding may predispose the rumen wall to insult (Nagaraja and Lechtenberg, 2007).

Genetics, specifically breed and gender, are additional risk factors associated with liver abscesses. In one review, Amachawadi and Nagaraja reported a higher prevalence in beef steers compared to beef heifers and a higher prevalence in Holstein steers compared to beef cattle (2016; Elanco Liver-Check System, 2014). While the exact cause in greater prevalence of liver abscesses and A+ livers with adhesions to the body wall in Holsteins are not known, it has been attributed to increased days exposed to high-grain finishing diets and higher feed intake compared to beef breeds (Duff & McMurphy, 2007; Reinhardt & Hubbert, 2015).

There are also regional differences within cattle slaughtered, with a higher prevalence of liver abscesses in cattle slaughtered in the central United States, lower prevalence observed in cattle in the midwestern, southern, and desert southwest, and the Pacific Northwest and northern plains being intermediate (Reinhardt & Hubbert, 2015; Elanco Liver Check System, 2014). Liver abscess prevalence can also fluctuate seasonally, as Brown and Lawrence observed cattle slaughtered in the spring have a greater number of liver condemnations (2010). One explanation for the observed seasonal and geographical differences in liver abscess prevalence may be due, in part, to differences in cattle type, as well as hair coat. Grooming, particularly the ingestion of cattle hair, has been found to increase the prevalence of liver abscesses in sheep (Fell et al, 1972). Cattle hair may imbed in the rumen wall, causing trauma and increasing the likelihood of bacterial colonization (Amachawadi and Nagaraja, 2016).

Economic impact

Liver abscesses affect the overall economic performance through loss of edible product, decreased carcass yield, increased carcass trim at slaughter, and reduction of feed utilization by live animals. Montgomery (1992) found that the liver accounts for approximately 2% (by weight) of the carcass itself . At the time of this review, liver contributes to about 2.2% of the total by-product drop value and is valued at about $0.27/cwt at slaughter (USDA ARS, 2025). There is also loss of time and efficiency incurred by the packer, due to excessive trim in the case of adhesions of the liver abscess to the body wall (Nagaraja and Chengappa, 1998). Torres et al. (2024) also reported a 1.2% reduction of ribeye area associated with the presence of liver abscesses. This reduction in muscle deposition is due to the most significant economic impact, the loss of feed efficiency and feed utilization. Decreased average daily gain can be affected by as much as 11%, and a decrease in feed efficiency has been observed as high as 9.7% (Brink et al., 1990). The most significant impact on performance is observed in cattle with A+ liver abscesses found at slaughter. Montgomery (1985) found cattle with A+ liver abscesses had significantly lower hot carcass weight, dressing percentage, and significantly higher trim percentage compared to cattle with no or mild liver abscesses (A or A-). More recently, Lawrence (2022) estimated that reduced carcass weights, diminished grading performance, and the financial loss from the condemned liver and associated viscera ranges from $8 to $189 on a per animal basis.

Control and prevention

The prevention or control of liver abscesses in feedlot cattle has primarily relied on the use of antimicrobial feed additives. There are five antimicrobials (bacitracin methylene disalicylate, chlortetracycline, oxytetracycline, tylosin, and virginiamycin) labeled for the prevention of liver abscesses in feedlot cattle (Feed Additive Compendium, 2013). Of the five labeled antibiotics, tylosin phosphate is considered to be the most effective, while bacitracin is considered to be the least effective (Nagaraja & Chengappa, 1998; Nagarja & Lechtenberg, 2007; Reinhardt & Hubbert, 2014; Theurer & Amachawadi,, 2022). Tylosin phosphate, a macrolide antibiotic, is the most used feed additive for the control of liver abscesses. Tylosin has been shown to reduce the incidence of liver abscesses by up to 40-70% when included in feedlot diets (Nagaraja & Chengappa, 1998). Wileman and colleagues (2009) found that feeding tylosin reduced the risk of liver abscesses from 30 to 8%. Monensin, an ionophore antibiotic, has been used along with tylosin for control of liver abscesses. Monensin alone does not have an effect on liver abscesses, but when used in conjunction with tylosin reduced the prevalence of total and severe liver abscesses (Meyer et al, 2013).

With the growing concern over the use of antimicrobials in feed, other alternative strategies for the control of liver abscesses need to be explored. Roughage level and level of grain processing have been extensively explored. Increasing the amount of physically effective, course roughage typically has a positive effect on the reduction of liver abscesses at slaughter (Reinhardt & Hubbert, 2015). Zinn and Plascencia (1996) reported that increasing ground alfalfa hay from 10% to 30% significantly reduced the prevalence of liver abscesses. Loerch and Fluharty (1998) found that cattle fed increasing amounts of corn silage from 0% to 15% in high-moisture corn diets reduced the prevalence of condemned livers from 29.3% to 14.7%. Conversely, Kreikemeier and colleagues (1990) reported that increasing roughage level in steam-rolled, wheat-based diets numerically increased the prevalence of liver abscesses. Level of grain processing does not appear to affect the prevalence of liver abscesses (Reinhardt and Hubbert, 2015).

Non-antimicrobial feed additives have also been explored for the control of liver abscesses with mixed results (Bryant and Jennings, 2022). Meyer and colleagues (2009) evaluated cattle fed a commercially available mixture of essential oils, with and without tylosin, and found no significant differences in liver abscess prevalence compared to cattle fed a negative control, and a higher prevalence of total and A+ liver abscesses in cattle fed essential oils alone compared to cattle fed tylosin and monensin. Yeast products such as *Saccharomyces cervisiae*, and probiotics such as *Lactobacillus acidophilus* or *Megasphaera elsdenii* have also been studied but have not shown a consistent impact on liver abscess prevalence (Bryant and Jennings, 2022). Vaccination against the causative agents of liver abscesses, namely *F.necrophorum* and *T.*

pyogenes, has been explored with variable results, and there are currently no commercially available vaccines with the label claim to prevent or control liver abscesses in feedlot cattle (Theurer and Amachawadi, 2022).

Conclusion

Liver abscesses in feedlot cattle are a multifactorial condition driven by dietary practices that promote ruminal acidosis. While antimicrobial feed additives have been the primary control method, the growing concern over antibiotic resistance necessitates the exploration of alternative prevention strategies. More research into the role of vaccines, probiotics, and dietary adjustments is needed to provide sustainable solutions to this ongoing issue in feedlot management.

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Chapter 2 - The effects of handling intensity at time of processing on physiological response, immune response, and vaccination status in beef cattle at the feedlot

Abstract

Newly received feeder calves often experience stress upon arrival at the feedlot due to various factors. The objective of this study was to determine if the effects of cattle handling intensity at processing influenced physiological, inflammatory, and immune stress markers in newly received feeder calves. Crossbred heifers (n=80, BW =355+/- 24 kg) from a single cohort were used for this study at a commercial cattle feeding facility in central Nebraska. These heifers were systematically allocated to treatment and observed over a 42-day period to evaluate the effects of 2 handling treatments:

Low stress handling (LSH): Cattle walked calmly through a crowding tub and snake processing facility up to a hydraulic chute. Electric prods and striking were not permitted. Noise from the handlers was kept to a minimum.

Aggressive handling (AH): Cattle moved through the crowding tub and snake processing facility at a lope. An electric prod was applied twice (1 s per impulse) before entering a hydraulic chute. A radio was playing and yelling and whistling were encouraged.

Cattle administered the AH treatment had greater increases in respiratory rates and heart rates than LSH cattle immediately after treatment administration ($P \leq 0.0001$). No differences between LSH and AH cattle were observed for the changes in epinephrine, norepinephrine, and cortisol post treatment ($P \geq 0.12$).AH cattle tended to have a reduction in blood pH compared to LSH cattle ($P=0.09$). AH cattle experienced a greater increase in blood glucose and tended to have a greater increase in blood lactate compared to LSH cattle immediately after treatment (P=0.03, P=0.06, respectively). LSH cattle had an increase in sO2 percentage compared to AH cattle immediately post treatment (P=0.05). Aggressively handled cattle had a greater decrease in SAA concentrations immediately post treatment compared to LSH cattle (P=0.05). Cattle handled aggressively tended to have a greater increase in IL-6 between treatment and 5 days post (P=0.05). These results indicate aggressive handling causes negative physiological stress responses in newly received beef cattle.

Keywords: Animal Welfare; Beef; Feedlot; Low Stress Cattle Handling

Introduction

Newly received feeder calves are often subject to an array of stressors upon arrival at the feedlot due to: weaning, new social hierarchies due to commingling, group relocation, marketing, nutrition, and handling. While many of these factors are out of direct control of the receiving feedlot, handling upon arrival is a controllable aspect. Grandin reported that many detrimental effects of handling stressors on animal performance and health are likely due to fear (Grandin, 1998). Stress has a negative influence on the immune system (Blecha et al., 1984); however, the effects of specific sources of stress or compounded stress on the incidence or consequences related to animal health are not fully understood. The combination of stressful events and creating a new social hierarchy with cattle from different farms allows for the exposure of infectious agents between animals (Duff and Galyean, 2007). This results in an increased pathogen challenge that overwhelms the immune system, which in turn increases the animal's susceptibility to develop disease. Bovine respiratory disease is the leading cause of morbidity and mortality in newly weaned/received cattle. It is prevalent in 95.6% of feedlots over 1,000 head and in 100% of feedlots with 8,000 head or more (National Animal Health Monitoring

System, 2013). Bovine respiratory disease was the most common illness among cattle in feedlots (National Animal Health Monitoring System, 2013).

Viral agents, including infectious bovine rhinotracheitis (IBR), parainfluenza-3 (PI3), bovine viral diarrhea virus (BVDV), and bovine respiratory syncytial virus (BRSV) have been associated with respiratory tract disease in feedlot calves; therefore, vaccination is an integral part of preconditioning programs (Duff and Galyean, 2007). These viral pathogens can predispose animals to a coinfection with bacteria such as *Mannheimia haemolytica, Mycoplasma bovis, Pasteurella multocida,* and *Histophilus somni* (Grissett et al., 2015).

Our objective was to determine the effects of handling intensity during receiving and initial processing on the physiological and immunological responses of beef cattle administered a modified live vaccine. This includes determining if handling intensity caused a change in stress mediators at processing, if handling intensity affected acute phase protein levels, and if handling intensity at initial processing affected overall immune response to vaccination.

Materials and Methods

The procedures used in this study were approved by the Kansas State University Institutional Animal Care and Use Committee (IACUC) protocol #3830. Production Animal Consultation and the contract feedlot additionally approved these procedures.

Experimental Design and Treatments

Crossbred *Bos taurus* heifers (n=80, BW =355+/- 24 kg) from a single North Carolina source were selected from a single cohort of 139 head of cattle that had recently arrived at a commercial feeding facility in central Nebraska. This cohort was placed in a receiving pen and allowed to rest for 3 d prior to the start of the trial. These selected heifers were then used over a 42 d period in a systematic allocation design to evaluate the effects of 2 handling treatments: 1) Low stress handling (LSH) or 2) Aggressive Handling (AH). The treatments were defined as:

LSH: Cattle were walked calmly and quietly through a crowding tub and snake processing facility up to a hydraulic chute (Silencer; Moly Manufacturing, Lorraine, KS). Electric prods were not applied to LSH cattle at any time point during study sampling nor was striking permitted. Noise from the handlers (radio, whistling, yelling) was kept to a minimum.

AH: Cattle were moved through the same crowding tub and snake processing facility at a lope. An electric prod (Hot-Shot, Miller Manufacturing, Eagan, MN) was applied twice (approximately 1 s per impulse) before entering a hydraulic chute. A radio was playing next to the hydraulic chute, and yelling and whistling were encouraged.

Cattle were allocated to treatment in groups of 4 head from the order the animals entered the processing facility. A coin was flipped to determine which treatment would be assigned first, and the 2 treatments were alternated in groups of 4. Low stress handling treatment was randomly selected to start, and the first 4 animals were allocated to the LSH treatment, followed by 4 animals allocated to the AH treatment. This pattern was repeated for the remaining cattle until 40 animals were systematically allocated to treatment groups (20 per treatment group). Due to facility constraints, the remaining 40 animals (20 per treatment group) were allocated to treatment on the following day. Treatment allocation occurred at the same time baseline measurements were taken.

During treatment group allocation and baseline measurement, all cattle were handled calmly and quietly without the use of electric prods to minimize stress that would potentially confound the post treatment measurements. Baseline measurements were taken for body weight, physiological measurements, and blood samples for stress and immunological assays. After baseline measurements, cattle were ear-tagged with an observation number and penned together by treatment group, away from the processing facility. Due to facility constraints, all cattle were penned in either an LSH treatment pen or an AH treatment pen.

Both treatment groups rested for approximately 1 hour after the last animals entered the resting pen. Then LSH cattle were walked calmly back into the processing facility, approximately 100 m, where animals experienced the LSH treatment and then processed based on the feedlot's protocol. Aggressively handled cattle were quickly removed from the resting pen with yelling encouraged, ran back to the processing facility, approximately 100 m, experienced the AH treatment, and then were processed according to the operation's protocol. Cattle were penned together based on the treatment they were allocated so that all AH cattle were placed in 1 pen and all LSH cattle were placed in another, separate pen. All cattle returned to the processing facility in an order different from the original treatment allocation order, and individual animal was the experimental unit for statistical analyses.

Post treatment physiological measurements and blood samples for stress and immunological assays were taken prior to processing. All cattle were vaccinated with a 5 way modified live for Infectious Bovine Rhinotracheitis Virus (IBR), Bovine Viral Diarrhea Virus (BVD) types I & II, Parainfluenza virus (PI3), and Bovine Respiratory Syncytial Virus (BRSV) (Merck & CO, Madison, NJ), vaccinated with a killed bacterin-toxoid vaccine for *Clostridium spss.* (Merck & CO, Madison, NJ), ear-tagged with lot and individual identification, administered a trenbolone acetate and estradiol implant (Merck & CO, Madison, NJ), and given an oral anthelminthic (Merck & Co, Madison, NJ). All cattle from both treatment groups returned to their combined home pen after post treatment measurements and processing.

During baseline measurement sampling and at the 5 d, 21 d, and 42 d time points, all cattle were removed from the home pen calmly and quietly in order to minimize stress on the animals. Aggressive handling techniques were applied only to the AH treatment group at the time of processing.

Physiological Measurements and Blood Assays

Heart rate and respiratory rate were measured by a veterinarian at baseline and post-treatment. Heart rate (HR) was determined by auscultation of the left thorax, and respiratory rate (RR) was measured by flank visualization. The number of heartbeats and respirations were measured for 30 s and multiplied by 2 to convert to beats per min and respirations per min, respectively. Rectal temperatures were measured in degrees Fahrenheit using a digital thermometer (Eco-Fast Digital Thermometer, Agri-Pro Enterprises, Iowa Falls, IA) at baseline, and post treatment time points. Body weights were captured via a certified scale (Tru-test S3, Datamars Livestock, Temple, TX) on the chute at baseline, 5 d, 21 d, and 42 d.

Blood samples for stress analytes were collected at baseline and post-treatment via jugular venipuncture using a 60ml syringe with a 16 gauge x 1 1/2" needle. Blood was immediately transferred into 10 ml clotting and sodium-heparin tubes (Becton; Dickinson and Company, Franklin Lakes, NJ). Before centrifugation, blood from sodium-heparin tubes collected at baseline and post treatment was assayed for pH, lactate, total bicarbonate, partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2), base excess, total carbon dioxide (TCO_2), and saturated oxygen (sO_2) using CG4+ cartridges with the iSTAT Clinical Analyzer System (Abaxis, Inc., Union City, CA). Blood in sodium-heparin and clotting tubes were then refrigerated for transportation back to the laboratory for centrifugation. Sodium heparin and clotting tubes were centrifuged 1500 x g for 15 minutes at room temperature. Clotting tubes were allowed to sit for at least 35 minutes to allow clot formation before centrifugation. Supernatants were transferred into cryovials immediately after harvest and placed in -80°C storage until shipment to a reference laboratory for analysis (South Dakota State University, Brookings, SD; Catholic University of the Sacred Heart, Piacenza, Italy).

Plasma harvested from sodium-heparin tubes was assayed for cortisol, epinephrine, and norepinephrine concentrations at baseline and post treatment time points. Additionally, plasma samples were assayed for immunological measurements via a multianalyte panel that included; glucose, creatine kinase (CK), potassium, lactate, haptoglobin, ceruloplasmin, paraoxonase, derivatives of reactive oxygen metabolites (dROMs), myeloperoxidase, ferric reducing antioxidant power (FRAP), interleukin 6 (IL-6), interleukin 1 (IL-1), and serum amyloid A (SAA) for baseline, post-treatment, and 5 d. A clinical auto-analyzer (ILAB-650, Instrumentation Laboratory, Bedford, MA) was used to determine the concentration of glucose, CK, potassium, lactate, haptoglobin, ceruloplasmin, paraoxonase, dROMs, myeloperoxidase and FRAP in accordance with Mezzetti et al. (2019). The CK (CK-MB, Cat. 0014557200) was also detected with the same auto-analyzer. The SAA, IL-1 and IL-6 were detected with a multi-detection microplate reader (Synergy 2, BioTek Instruments, Winooski, VT), using commercial kits for the ELISA method, as previously described in Mezzetti et al. (2019).

Serum samples from clotting tubes taken at baseline, post treatment, and 5 d were assayed for TNF-α concentration. Additional serum samples were taken at baseline, 21 d and 42 d for serum neutralization assays for BVD types I & II, IBR, BRSV, and PI3. Serum samples were sent to a reference laboratory for analysis (South Dakota State University, Brookings, SD). The serum neutralization method utilized was previously described by Rosenbaum et al. (1970), and results were reported in titers. Titers were reported as the reciprocal of the greatest dilution of serum to provide complete protection of cells. The least dilution tested was 1:4 for IBR, BRSV, and PI3, and the least dilution tested for BVD types I & II was 1:8. Serum that did not provide protection at the 1:4 level for IBR, BRSV, and PI3 or did not provide protection for BVD types I & II at the 1:8 level were considered negative for seroconversion, similar to methods described by Richeson et al. (2009).

Statistical Analysis

Data were analyzed using SAS version 9.3 (SAS Inst. Inc., Cary, NC). Preliminary analyses for physiologic and immune parameters such as CK, L-lactate, TNF-α, SAA, IL-1, and IL-6 showed non-normal distributions of the data. To account for the distribution of the data, as well as the unequally spaced time points, analysis of variance were performed on the mean changes between time points, post treatment-baseline, 5d – baseline, and 5d-post treatment. Changes in the means were analyzed for normal distributions and reported for results. Continuous variable comparisons between LSH and AH cattle were analyzed using the GLIMMIX procedure with individual animal considered the experimental unit. The statistical model included the fixed effect of treatment, the random effect of date of enrollment, and the Kenward-Roger approximation to calculate degrees of freedom. Statistical significance was determined at $P \leq 0.05$ and tendencies when $0.05 \leq P \leq 0.10$.

For BW analysis, repeated measures models were used in order to account for the repeated measures taken at unequally spaced time points both within treatment groups and the groups processed during different days. A spatial power covariance structure sp (pow) was included in the model used for analysis. Comparisons between least squares means of factor levels utilized the PDIFF option of the LSMEANS statement. Statistical significance was determined at $P \leq 0.05$ and tendencies when $0.05 \leq P \leq 0.10$.

Preliminary serum neutralization analysis was performed utilizing the cut point of 1:4 for IBR, PI3, and BRSV, and the cut point of 1:8 for BVD I & II. Titer values above these cut points determined samples to be positive for seroconversion, and were analyzed as discrete variables. However, all samples at d 21 and d 42 were positive at greater titer values than the cut point, and thus statistical modeling would not satisfy convergence criteria. Therefore, the distributions of titer results for each time point can be found in tables 2-4, 2-5, and 2-6. Histograms of these results can be found in Appendix A (Figures, A-1, A-2, and A-3).

Results

LSH cattle maintained a consistently heavier mean body weight at all time points, including baseline (Figure 1). For this reason, baseline body weight was included as a covariate and LSH cattle tended to have heavier mean body weights compared to AH cattle ($P= 0.06$, Figure 1).

Physiological Measurements

At post treatment, AH cattle had a marked increase in respiratory rate compared to LSH cattle ($P<0.0001$, Table 2-1). LSH cattle had a reduced mean heart rate immediately post treatment compared to a greater increase in AH cattle heart rate ($P=0.0001$, Table 2-1). LSH and AH cattle had increased epinephrine and norepinephrine post-treatment; however, no differences were detected ($P>0.10$, Table 2-1). Plasma cortisol levels decreased in LSH and AH cattle post-treatment, with no difference observed between AH and LSH cattle ($P=0.93$, Table 2-1). AH cattle tended to experience a decrease in blood pH compared to an increase in blood pH in LSH cattle ($P=0.09$, Table 2-1). Oxygen saturation (sO_2) increased in LSH cattle post treatment, whereas sO_2 decreased in AH cattle ($P=0.05$, Table 2-1). No differences were observed between LSH and AH cattle for changes in bicarbonate, tCO_2, pCO_2, pO_2, or base excess ($P>0.10$, Table 2-1).

Additional stress measurements were taken as part of the analysis of immunological measures and were taken at baseline, post-treatment, and 5 d. LSH cattle tended to experience an increase in plasma CK concentrations from baseline to post treatment, while AH cattle experienced a decrease in plasma CK ($P=0.06$, Table 2-2). Glucose increased in both LSH and AH cattle post treatment, and AH cattle experienced a greater increase ($P=0.03$, Table 2-2). Glucose was reduced in both LSH and AH cattle 5 d post treatment, and AH cattle experienced the greater reduction ($P=0.0001$, Table 2-2). Plasma L-lactate concentrations increased from baseline to post treatment in both treatments, and AH cattle tended to have a larger increase compared to LSH cattle ($P=0.08$, Table 2-2). Five d post treatment, LSH and AH cattle experienced decreased L-lactate concentrations, with the larger reduction occurring in AH cattle ($P<0.01$, Table 2-2).

Immunological Measurements

AH and LSH cattle experienced a decrease in TNF-α concentrations from baseline to post treatment; however, the changes observed in TNF-α between baseline to post treatment and to 5 d post time points did not differ between LSH and AH cattle ($P>0.10$, Table 2-3). LSH and AH cattle had reductions in haptoglobin concentrations immediately post treatment, and increased haptoglobin concentrations at 5 d, but the differences between LSH and AH cattle were not significant ($P>0.10$, Table 2-3). SAA concentrations markedly decreased in AH cattle compared to LSH cattle immediately post treatment, but SAA increases observed in both LSH and AH cattle 5 d post did not differ between treatment groups ($P>0.58$, Table 2-3). IL-6 concentrations 5 d post treatment tended to increase in AH cattle compared to a reduction in IL-6 in LSH cattle ($P=0.06$, Table 2-3). Paraoxonase decreased from baseline to 5 d in LSH and AH cattle, as AH cattle tended to experience a greater decrease ($P=0.08$, Table 2-3). No differences were observed in the changes of ceruloplasmin, dROMs, myeloperoxidase, or FRAP ($P>0.10$, Table 2-3).

Serum Neutralizations

The results of serum neutralizations for BVD I & II, IBR, PI3, and BRSV are presented by sampling day 0 (Table 2-4), d 21 (Table 2-5), and d 42 (Table 2-6). The majority of cattle sampled at the baseline had antibodies for BVD I & II at baseline for both LSH and AH cattle (38/40 for LSH cattle and 38/40 for AH cattle, Table 2-4). Thirteen cattle had undetectable antibodies for IBR (8 LSH and 5 AH, Table 2-4), and 11 cattle had undetectable antibodies for BRSV (6 LSH and 5 AH, Table 2-4). All cattle had detectable antibodies ≥ 1:8 for all viruses measured on d 21 and d 42 (Table 2-5, Table 2-5, respectively) regardless of treatment. Clustered histograms for each time point are presented in Appendix A (Figures A-1, A-2, and A-3).

Discussion

The welfare of cattle at arrival to the feedlot has been a long-standing concern as it contributes to a multi-factorial problem in the control of bovine respiratory disease (Duff and Galyean, 2007). According to Noffsinger et al., the arrival period into the feedlot is an opportunity to increase processing product response and reduce stress (2015). While there are a number of studies that have been done regarding stress of transport to the feedlot, few studies have been done regarding the stress of processing. To our knowledge, this is the first study of its kind, and thus the comparisons of our results are to studies of transportation and receiving stress. Bristow and Holmes found a link between cortisol and anxiety-related behavior as cattle with higher cortisol levels spent less time ruminating (2007).

This study has provided evidence that handling intensity plays a role in the stress that cattle experience at processing; however, greater efforts to separate replicates can be made in future studies to clearly evaluate experimental units. In the present study, that was not possible due to the facility constraints of the contract feedlot. These conditions were more representative of what is typically observed in feedlot processing. Furthermore, Bristow and Holmes concluded that the order of entry into the chute did not affect cortisol measurement (2007). However, Bristow and Holmes used a smaller cohort of cattle, and there is the possibility that increased time spent waiting in the processing facilities may have played a role in the variability in some of the measurements in the present study. There were increases in the standard error of the mean observed for post-handling measurements of epinephrine and norepinephrine, and it is possible that some animals waited longer than others, thus contributing to the variability. Furthermore, the decreases in cortisol experienced by LSH and AH cattle in the present study were not expected, and the delay in sampling post-treatment may have created additional confounding in the results. Nevertheless, the ability to identify differences in cattle behavior is an ongoing challenge that is prone to confounders, and more research is needed in this area to obtain a more robust understanding of the relationship between processing and cattle stress.

Additionally, chute scoring for temperament was not included in this study to maintain a dataset that was primarily quantitative for analysis. Van Egan and Coetzee argue that temperament is a difficult confounding factor regardless of handling intensity (2018).

While LSH cattle tended to have heavier weights than AH cattle at all sampling points, it is not appropriate to conclude that LSH cattle performed better in terms of average daily gain or feed conversion since LSH cattle had higher average weights at the baseline measurement. This is a possible unique effect of the systematic allocation used in this study, and future studies may require additional blocking factors by weight if larger sample sizes are used. For this study, in order to block the cattle by weight, the animals would have entered into the processing facility an additional time before measuring the handling intensity, and the investigators were concerned that this extra time through the handling facility might confound any values gathered based on the animals becoming acclimated to the facility.

Hagenmaier et al. utilized a similar method of blood analysis on cattle prior to shipment to an abattoir and found that high-stress handled cattle had greater lactate, epinephrine, norepinephrine, cortisol and glucose concentrations after handling (2017). Our results showed marked increases in respiratory rate and blood glucose, tendencies of increased lactate and CK, and a tendency of reduced blood pH of AH cattle consistent with their results. However, the plasma cortisol results in the present study decreased in both treatment groups from baseline to post handling. Additionally, the present study did not observe a treatment effect of handling intensity on epinephrine and norepinephrine, which is not consistent with their results, (Hagenmaier et al., 2017). However, it is worth noting that cattle in the mentioned study were handled over a 1600 m course, whereas cattle in the present study were moved 100 m, suggesting a more clearly recognized connection between physiological stress and epinephrine and norepinephrine concentrations in cattle moved a greater distance. Results of the present study are consistent with Warner et al., where they found cattle handled with electric prods had higher blood plasma concentrations of lactate at slaughter (2007). Their study utilized an electric prod 6 times over five minutes, whereas the present study utilized 2 x 1-second impulses total. This suggests that lower total time of electric prod impulses may induce changes in lactate. Interestingly, the plasma cortisol concentrations in the present study were markedly elevated at the baseline measurement (data not shown). When compared to a simulated stress model in early-lactation dairy cows, Trevisi et al. found markedly lower values of baseline cortisol (2013). In that study, the baseline plasma cortisol concentrations were less than half of the values seen in the present study (Trevisi et al., 2013). While there are different management styles between newly arrived feedlot heifers and early-lactation dairy cows, the increased baseline cortisol concentrations seen in the present study (data not shown) suggest that these cattle already experienced stress prior to the initiation of this study, most likely from transportation. The reduction in cortisol concentrations after the baseline handling is consistent with Francisco et al., where steers acclimated to the processing facilities had decreased temperament scores and lower cortisol concentrations (2012). It was the objective of this study to determine the difference in handling intensity at processing, but both treatment groups saw a reduction in cortisol after the baseline measurement. This suggests the initial acclimation to the processing facility that occurred during baseline measurement collection potentially reduced the stress of subsequent handling, regardless of handling intensity at treatment allocation.

While the objective of this study was to determine the difference in handling intensity at processing, the role of transportation stress cannot be ignored. Even though the cattle used in this study were given a 3 d resting period prior to baseline measurement and treatment allocation, the baseline values in this study indicate that cattle in both treatment groups were in the process of experiencing an inflammatory response. Trevisi and Minuti developed a series of threshold values that suggest dairy cows are at greater risk for disease during the transition period using similar analyses in the present study (2017). Their work suggests that cows with IL1-β concentrations above 140 pg/mL, IL6 concentrations above 450 pg/mL, ceruloplasmin concentrations above 2.7 mcmol/L, and dROMs greater than 11.5 mg H_2O_2/100ml were associated with a higher prevalence of disease (Trevisi and Minuti, 2017). The baseline measurements of those parameters in the present study exceeded these thresholds (data not shown), suggesting that both treatment groups were undergoing physiological stress and inflammatory responses. Future studies evaluating the specific outcome of handling intensity of processing on physiological and inflammatory responses may require longer resting periods before treatment allocation to determine the difference between transportation or other stressors different from the stress of processing. Moreover, the information from this study may suggest that longer resting periods for newly arrived cattle before initial processing may be beneficial.

The results of this study suggest that stress induced by aggressive handling, compounded with other factors such as transport stress, triggered a hypothalamic response that led to an increase in corticotropin-releasing hormone. While handling intensity did not impact the increases of epinephrine and norepinephrine in the present study, the differences in heart rate and respiratory rate observed suggest handling intensity affected the clinical parameters that indicate an active hypothalamic response. Increased changes in blood glucose concentration experienced by AH cattle in the present study suggest a stronger hypothalamic response as cortisol stimulates gluconeogenesis and increases blood glucose.

This hypothalamic response has been well documented, and the increase in corticotropin-releasing hormone causes an increase in pro-inflammatory cytokines IL-1, IL-6, and TNF-α (Van Engen and Coetzee, 2018; Cooke and Bohnert, 2011; Carroll and Forsberg, 2007). The increase in pro-inflammatory cytokines triggers the acute phase protein response, thus increasing concentrations of haptoglobin, ceruloplasmin, and SAA (Carroll and Forsberg, 2007). Results of this study show the expected increases in haptoglobin, SAA, and IL-1 5 days post treatment for both AH and LSH treatment groups, but handling intensity did not appear to influence these changes. However, the change in IL-6 concentrations 5 d post treatment, specifically the decrease in LSH cattle compared to the observed increase in AH cattle, suggests handling intensity increased variation in the IL-6 response. This may be explained by greater variability of the LSH and AH cattle post-handling, or the possibility that LSH cattle mounted a more controlled immune response that extended to 5 d post treatment. When evaluating the change in the immunological measurements over time, the data in this study suggest that both treatment groups experience similar changes of similar intensity over time: an increase in haptoglobin, SAA, and ROM in conjunction with a reduction of TNF-α and paraoxonase. This indicates a strong acute phase protein reaction in all animals from both treatment groups, likely supported by the stress that occurred during transport.

Berry et al. found haptoglobin concentrations to be greater in calves one-week post treatment for BRD, but later decreased on day 14 (2004). This is consistent with our findings on day 5; however, as haptoglobin was not measured after day 5 in the present study, the trend in haptoglobin is not entirely clear, and thus, more work in this area is needed. In the same study, Berry et al. found higher haptoglobin concentrations in animals that received multiple treatments for BRD (2004). While treatment records collected after closeout (data not shown) indicate that this was not the case in the present study, the higher concentrations of haptoglobin in AH at post-treatment and 5 days post-treatment suggest that AH cattle may have an increased inflammatory condition, but not to the point in which morbidity was affected. There is not sufficient evidence in the present study to conclude any effect on morbidity or mortality, and additional work is needed to investigate a causal link.

As for vaccination and titer measurements, both AH and LSH cattle had increased 21 d and 42 d titers compared to the baseline. Most cattle in both LSH and AH groups had antibodies to all viruses measured, suggesting prior exposure to wild-type or previous vaccination. It is worth noting both treatment groups were commingled in the same pen after post-treatment measurements for the remainder of the 42 d study. While this does not have an effect on baseline and post-treatment measurements, pen-level interactions could play a role in the vaccine response seen in this study. Vaccine response is highly variable and complex in analysis, and although it was an objective of interest, it was not the primary objective of this study.

In conclusion, aggressive handling at processing may contribute to the overload of stresses on the animal at arrival to the feedlot. Low stress handling techniques may reduce some of changes in the physiologic indicators of stress including heart rate and respiratory rate. Future studies are needed in order to have a greater understanding of the complex relationship between handling intensity and the immunological response. The authors of the present study suggest that future work should be focused on either larger sample sizes or potentially the use of immunologically naïve calves.

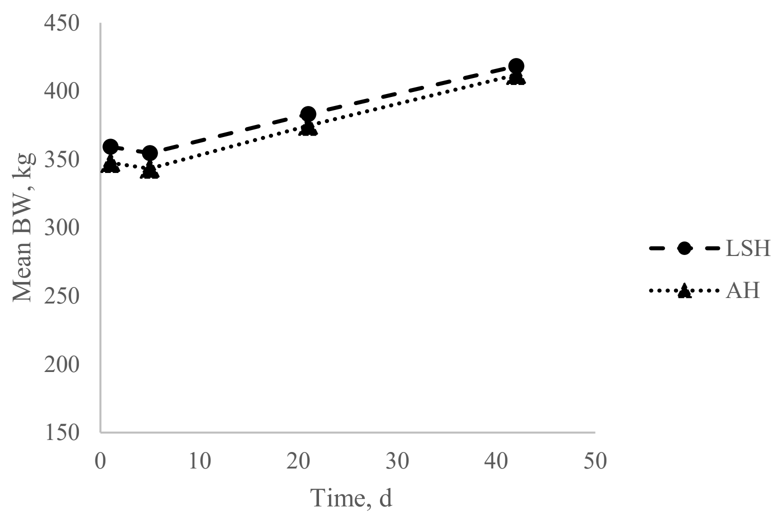

Figure 2-1. Effect of handling intensity on BW over time[1,2]

[1]Treatment P=0.06

[2]Time for the trial, 42 d

Table 2-1. Effect of handling intensity on the change in physiologic stress markers from baseline to post treatment

Item	LSH	AH	SEM[1]	P-Value
Respiratory Rate, rpm	0.60	14.0	2.87	<0.0001
Heart Rate, bpm	-6.40	17.2	5.7	0.0001
Rectal Temperature, °C	0.16	0.33	0.089	0.17
Epinephrine, pg/ml	312.2	398.6	40.4	0.12
Norepinephrine, pg/ml	443.0	536.8	69.7	0.34
Cortisol, ug/dL	-0.87	-0.90	0.31	0.93
pH	0.004	-0.019	0.015	0.09
Lactate, mmol/L	1.05	2.34	1.16	0.06
Bicarbonate, mmol/L	-0.95	-2.16	0.85	0.15
sO2, %	0.53	-4.12	3.06	0.05
tCO2, mmol/L	-0.96	-2.24	0.87	0.14
pCO2, mmHg	-1.98	-1.61	0.99	0.79
pO2, mmHg	0.17	-1.31	1.18	0.15
Base Excess, mmol/L	-0.88	-2.43	1.06	0.11

[1]The highest value of SEM was reported

Table 2-2. Effect of handling intensity on the change in CK, glucose, lactate, and potassium metabolites

	Post Treatment - Baseline				5 d - Baseline				5 d – Post Treatment			
Item	LSH	AH	SEM[1]	P-Value	LSH	AH	SEM	P-Value	LSH	AH	SEM	P-Value
CK, U/L	576.4	-53.8	237.2	0.06[1]	40.0	525.1	785.2	0.66	-577.3	619.8	772.8	0.28
Glucose, mmol/L	0.38	0.96	0.31	0.03	0.21	-0.24	0.36	0.10	-0.17	-1.19	0.17	0.0001
D-Lactate, mg/L	2.88	7.91	5.57	0.69	-3.94	-7.50	4.92	0.55	-6.82	-15.40	1.81	0.0003
L-Lactate, mg/L	64.0	146.1	149.9	0.08	-71.5	-177.6	119.4	0.01	-146.9	-312.3	50.3	0.0002
Potassium, mmol/L	0.21	0.38	0.18	0.12	-0.20	-0.17	0.47	0.78	-0.40	-0.56	0.24	0.18

[1]The highest value of SEM was reported

Table 2-3. Effect of handling intensity on change in immune response

	Post Treatment - Baseline				5 d - Baseline				5 d –Post Treatment			
Item	LSH	AH	SEM[1]	P-Value	LSH	AH	SEM	P-Value	LSH	AH	SEM	P-Value
TNF-α, pg/mL	-18.4	-16.3	1.8	0.40	-16.8	-14.6	4.9	0.61	-0.51	0.57	3.76	0.74
Haptoglobin, g/L	-0.05	-0.10	0.09	0.52	0.67	0.59	0.15	0.70	0.67	0.78	0.14	0.56
Ceruloplasmin, mcmol/L	0.037	-0.088	0.072	0.22	0.047	0.017	0.099	0.79	0.0005	0.109	0.119	0.47
dROMs, mg H2O2/100mL	0.31	0.67	0.22	0.25	1.48	1.78	0.39	0.58	1.18	1.09	0.33	0.85
Myeloperoxidase, U/L	-12.7	13.6	55.3	0.69	-59.4	18.0	47.0	0.17	-51.3	-0.11	84.5	0.36
FRAP, mcmol/L	-9.87	0.28	12.97	0.58	-31.1	-29.7	11.0	0.88	-22.2	-28.1	15.0	0.78
SAA, mcg/mL	-3.98	-60.0	23.7	0.05	158.6	162.1	59.0	0.97	152.6	112.0	51.6	0.58
IL-1, pg/mL	-22.5	-2.80	26.2	0.57	-57.0	-33.3	46.2	0.68	-27.6	-38.6	14.7	0.59
IL-6, pg/mL	58.0	-56.1	57.8	0.16	-10.8	115.6	106.1	0.25	-65.6	183.2	130.4	0.08
Paraoxonase, U/mL	2.22	1.68	1.60	0.57	-18.2	-22.5	3.95	0.08	-20.5	-24.2	5.42	0.15

[1]The highest value of SEM was reported

Table 2-4. Distribution of baseline serum neutralizations of LSH and AH cattle

Virus	BVD I		BVD II		IBR		PI3		BRSV	
Titer	LSH	AH	LSH	AH	LSH	AH	LSH	AH	LSH	AH
<1:8	2	2	2	2	8	5	0	0	6	5
1:8	0	0	0	1	4	7	0	0	8	8
1:16	0	1	1	0	2	5	1	0	11	11
1:32	0	0	2	0	9	6	2	0	10	4
1:64	3	1	0	1	11	5	3	4	1	6
1:128	0	0	1	1	1	8	14	10	2	3
1:256	4	4	2	3	5	4	6	14	2	3
>1:512	31	32	32	32	0	0	14	12	0	0

Table 2-5. Distribution of day 21 serum neutralizations of LSH and AH cattle

Virus	BVD I		BVD II		IBR		PI3		BRSV	
Titer	LSH	AH	LSH	AH	LSH	AH	LSH	AH	LSH	AH
<1:8	0	0	0	0	0	0	0	0	0	0
1:8	0	0	0	0	0	1	0	0	0	0
1:16	0	0	1	0	0	1	0	0	0	0
1:32	2	0	1	1	2	0	0	0	1	1
1:64	1	0	2	0	9	4	1	0	1	4
1:128	1	0	0	2	9	11	1	1	3	5
1:256	2	1	4	0	19	23	4	5	0	0
>1:512	34	39	32	37	1	0	34	34	35	30

Table 2-6. Distribution of day 42 serum neutralizations of LSH and AH cattle

Virus	**BVD I**		**BVD II**		**IBR**		**PI3**		**BRSV**	
Titer	LSH	AH	LSH	AH	LSH	AH	LSH	AH	LSH	AH
<1:8	0	0	0	0	0	0	0	0	0	0
1:8	0	0	0	0	0	1	0	0	1	2
1:16	0	0	0	0	2	2	0	0	0	2
1:32	0	0	0	0	2	4	0	1	1	6
1:64	1	0	1	0	7	9	0	0	4	2
1:128	3	0	6	1	11	7	6	5	10	7
1:256	5	2	2	3	18	17	13	9	0	0
>1:512	31	38	31	36	0	0	21	25	24	21

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Chapter 3 - Effects of feed additives on performance, carcass characteristics, and the control liver abscesses and coccidiosis the last 60 days on feed in cattle fed in a commercial Western Kansas feedlot.

Abstract

Crossbred steers (n = 4,849 hd; BW = 590 ± 19.7 Kg) were used in a randomized complete block design experiment in a commercial feedlot in Western Kansas to determine the effects of feed additives delivered the last 60 days on feed on performance outcomes, the control of liver abscesses, and the control of *Eimeria spp* in finishing cattle. All steers received the same base finishing diet and were randomly allocated to 1 of 4 feed additive treatments 60 days prior to their projected finish date: 1) Negative control (CON) fed without feed additives; 2)Positive control (MT) 75mg/hd/day tylosin (Tylan,® Elanco Animal Health, Greenfield, IN) with 15g/ton with targeted intake of 130 mg/hd/daymonensin (Rumensin,® Elanco Animal Health, Greenfield, IN); 3) Decoquinate (DEC) fed 275mg/hd/day (Deccox,® formerly Zoetis, Phibro Animal Health, Teaneck, NJ); or 4) *Yucca schidigera* (YS) fed at 3g/hd/day (Micro-Aid,® DPI Global, Porterville, CA). There was a total of 3 blocks and 13 replicates of the treatments (52 pens) with pen being the experimental unit. Feed additive treatments were fed to cattle in their diets during the last 60 days of the feeding period prior to shipment to an abattoir. Feed samples were taken from the bunk and evaluated to assure feed additive concentrations matched inclusion rate formulation. Qualitative fecal flotations were performed on freshly voided fecal samples collected on day 50 from ten calves per pen to assess the presence of *Eimeria spp* via the modified Wisconsin technique. Performance parameters from cattle on trial were captured on the feedlot's accounting system for daily dry matter intake (DMI), average daily gain (ADG), and gain efficiency (G:F). Trained personnel at a commercial abattoir observed and recorded liver abscess scores and carcass data. Cattle fed MT and YS gained 0.09 kg/day and 0.08 kg/day more, respectively, compared to cattle fed CON (P=0.008). Cattle fed MT had improved gain efficiency compared to CON cattle (5.7%, P=0.03) Cattle fed MT had a significantly lower total liver abscess prevalence compared to cattle fed CON (P<0.05), but did not differ from DEC or YS fed cattle (P>0.10). Cattle fed CON diet had a higher A+ liver abscesses compared to cattle fed MT (P<0.05), and MT fed cattle tended to have lower A+ liver abscess prevalence compared to cattle fed YS (P<0.10). Cattle fed CON had significantly more select grading carcasses than cattle fed DEC (P<0.05). *Eimeria spp* prevalence ranged from 0-5.0% on a pen level basis. However, no fecal samples tested had *Eimeria spp* concentrations high enough to be considered pathogenic regardless of treatment assigned to cattle in which samples were obtained. Cattle fed MT in the last 60 d had heavier final weights, heavier carcass weights, increased ADG, and improved gain efficiency relative to CON cattle. Cattle fed MT had lower prevalence and severity of liver abscesses compared to CON cattle. Cattle fed YS had similar final weights, carcass weights, ADG, and gain efficiency relative to MT. Cattle fed DEC and YS had similar total liver abscess prevalence and severity relative to cattle fed MT. However, cattle fed DEC and YS did not exhibit differences in liver abscess prevalence or severity compared to CON cattle. All things considered, monensin and tylosin improve performance and disease control the last 60 d on feed.

Keywords: Beef; Feedlot; Feed Additives, Liver Abscesses

Introduction

Implementation of the U.S. Food & Drug Administration's (FDA) Guidance for Industry number 213 and the establishment of the Veterinary Feed Directive (FDA GFI 213, 2013) along with growing consumer interest in antibiotic usage in the beef supply chain have led to a need to evaluate the use of feed grade antimicrobials used in cattle feeding. Prior to implementation of GFI 213, Samuelson et. al (2016) found the most common uses of direct-fed antimicrobials in finishing cattle are the control of liver abscesses, and improvement of foot health. Samuelson et al (2016) cited 83.4% of nutritionists' clients used medicated feed additives to control liver abscesses. Liver abscesses are a commonly found liver pathology found in feedlot cattle at slaughter (Nagaraja & Lechtenberg, 2007; Reinhardt & Hubbert, 2015; Amachawadi & Nagaraja, 2016). Liver abscesses result secondary to acidosis and rumenitis, often due to high concentrate feeds and aggressive feeding practices in feeder cattle (Nagaraja & Chengappa, 1998). Brown & Lawrence (2010) found liver abnormalities in 19.5% of cattle slaughtered, including abscesses (13.7%), cirrhosis (0.1%), liver flukes (5.4%), and telangiectasis (0.3%). Liver abscess prevalence has ranged from 1-95%, and several reports demonstrate the economic and production losses associated with liver abscesses (Nagaraja & Chengappa, 1998; Brown & Lawrence, 2010; Rezac et al., 2014).

Tylosin, a macrolide antimicrobial (Tylan®, Elanco Animal Health Greenfield, IN) has been used successfully for the reduction of liver abscesses in feedlot diets (Brown et al. 1975; Nagaraja & Lechtenberg 2007). Brown et al. (1975) saw a 66.9% reduction in liver abscesses in cattle fed tylosin compared to control cattle. Several subsequent studies show a 60-70% reduction in liver abscess incidence when tylosin is fed to cattle at 11 g/ton (Pendlum et al., 1978; Potter et al., 1985; Vogel & Laudert, 1994). The proposed mechanism of action of tylosin in liver abscess control comes from its inhibitory effect on *Fusobacterium necrophorum* (Nagaraja & Lechtenberg 2007). *F. necrophorum* inhibition by tylosin occurs primarily in the rumen (Nagaraja et al., 1999). Furthermore, the antimicrobial effects of tylosin act on the rumen microflora to moderate fermentation rates and reduce ruminal acidosis (Nagaraja et al. 1999; Nagaraja & Lechtenberg 2007). The World Health Organization considers macrolide antimicrobials such as Tylosin among the highest priority of critically important antimicrobials for human use (World Health Organization 2018).

Ionophores such as monensin (Rumensin, Elanco Animal Health) are widely used for increased feed efficiency, intake regulation, and the control of coccidiosis in feedlot cattle (Richardson et al. 1976; Russell & Strobel, 1989; Callaway et al. 2003; Ensley, 2016). Monensin inhibits lactate-producing bacteria, decreases methane production, and decreases ruminal amino acid degradation thus preventing ruminal acidosis and improving feed efficiency (Russell & Strobel, 1989). Additionally, monensin causes a dose-dependent decrease in feed intake, resulting in consistent feed intake without negative effects on ADG (Goodrich et al. 1984). Ionophores are used extensively for the treatment of coccidiosis in poultry and cattle, and monensin is specifically labeled for the treatment and control of coccidiosis in cattle (Fox, 1986; Elanco Animal Health). Coccidiosis in cattle is a parasitic disease caused by *Eimeria bovis*, & *Eimeria zuernii* that can cause production losses, digestive morbidity, and neurologic disease in growing cattle from 6-12 months of age (Radostits & Stockdale, 1980). Production losses caused by coccidiosis in cattle occur when the second generation schizonts and gamonts damage luminal epithelium of the cecum and colon, causing malabsorption (Radostits & Stockdale, 1980). This process creates subclinical disease that decreases weight gain and feed efficiency (Fox, 1986).

As consumer preferences continue to change, there is a need to evaluate alternatives to antimicrobial use in finishing cattle. A recent review of consumer perception studies by Barrett et al. found that 77.1% of consumer studies show concern over antibiotics in meat production (2021). With increased regulatory and consumer pressures, alternative feeding strategies without antimicrobials warrant exploration in the beef supply chain. Alternatives to monensin or monensin and tylosin combinations in feedlot cattle must maintain production benefits, liver abscess, and coccidiosis control.

Sousa et al. (2019) and Rett et al. (2020) explored dried extracts from *Yucca schidigera* as a non-antimicrobial alternative for improved feed efficiency. Sousa et al. (2019) found an 8% increase in ADG compared to control when *Yucca schidigera* was fed at 2g/hd/day, whereas Rett et al. (2020) found a 40% increase in ADG with *Y. schidigera* fed at 4g/hd/day. *Yucca schidigera* extracts are rich in saponins which shift VFA production from butyrate to propionate and increase microbial nitrogen outflow (Sousa et al. 2019; McMurphy et al. 2014). The proposed mechanism of action for *Y. schidigera* is a reduction in rumen protozoa as well as inhibitory effects on *Streptococcus bovis* (Hristov et al. 1999; Wallace et al. 1994).

Monensin is typically fed continuously to cattle for the prevention of coccidiosis. If monensin is removed from the diet, there is the potential for reinfection, subclinical disease, and performance loss from *Eimeria spp.* Decoquinate (Zoetis, Parsippany, NJ) is a non-antimicrobial alternative used for the prevention of coccidiosis in feeder cattle (Miner & Jensen, 1976; Fitzgerald & Mansfield, 1986). The effects of decoquinate on cattle performance beyond coccidiosis prevention are unclear. Harmon et al. (1987) found no difference in performance in steers fed decoquinate compared to controls or steers fed monensin and tylosin. Fox (1986) found that cattle fed decoquinate gained on average 0.23 kg per head per day compared to cattle not fed any feed additives.

Bohrer et al. (2016) found no difference in the presence of liver abscesses in cattle at slaughter administered, or not, with monensin and tylosin in their finishing diet for the last 35 days on feed. Therefore, the objectives of this study were to evaluate differences in feeding performance, carcass characteristics, liver abscess prevalence, and *Eimeria spp* prevalence in cattle fed combinations of monensin, tylosin, Y*ucca schidigera* extract, and decoquinate compared to cattle fed no feed additives in their diets during the last 60 days prior to slaughter.

Materials & Methods

Procedures involving live animals in this study were approved and performed in compliance with the Institutional Animal Care and Use Committee (IACUC) at Kansas State University protocol #4302.

Experimental design

Yearling steers, predominantly black hided (n = 4,849 hd; BW = 590 ± 19.7 Kg British and British X continental), were utilized in a feeding trial from May through December 2019. Steers selected from a larger population of crossbred cattle housed at a commercial cattle feeding facility located in the High Plains region of Kansas. A completely randomized block design utilized 4 treatments, three blocks and 13 replicates per treatment (52 pens total, 92.1 ± 0.94 head per pen). The first block (5 replicates; 20 pens) were enrolled in May 2019, the second block (5 replicates; 20 pens) were enrolled in July and August of 2019, and the last block (3 replicates; 12 pens) were enrolled in October of 2019. Blocks of replicates were managed identically prior to, and during, the study with the only difference being starting and slaughter dates.

Animal management and treatment enrollment

Before trial enrollment, all cattle underwent the same receiving protocol and were placed in approximately 200 hd pens (n=186.5 ± 13.3). At initial processing, all cattle received a modified live viral vaccine (Pyramid 5 Boehringer Ingelheim Animal Health USA, St. Joseph, MO), a progesterone and estradiol implant (Synovex S, Zoetis, Parsippany, NJ), an oral anthelmintic (Safe-Guard, Merck Animal Health, Kenilworth, NJ), and poured with ivermectin (Bimectin, Bimeda, Oak Terrace, IL). All cattle were fed a receiving diet and then transitioned to a finish ration over a 35-day period. All cattle remained on the same finish ration until trial enrollment, at approximately 60 days on feed. Starter, transition, and finish rations during the initial 60 days, including the 35-day transition, were formulated to contain 75mg/hd/day tylosin (Tylan, ® Elanco Animal Health, Greenfield, IN) with 15 g/ton monensin (Rumensin, ® Elanco Animal Health, Greenfield, IN).

At approximately 60 days on feed, two pens of cattle were selected to be used as a block for the study. Cattle were randomized to 1 of 4 pens of approximately 100 hd by gate sorting groups 5 hd of cattle at a time. If head counts were not exactly 100 hd per pen, the final gate sorts were made so that the number of animals per treatment group was within one head of each other. Once the 4- 100 hd pens (1 replicate of each treatment) were sorted, the cattle were weighed by pen, a 4% pencil shrink was applied, and the pens of cattle were randomly assigned to 1 of 4 treatments: 1) Negative control (CON) fed without feed additives; 2)Positive control (MT) 75mg/hd/day tylosin (Tylan,® Elanco Animal Health, Greenfield, IN) with 15g/ton with targeted intake of 130 mg/hd/day monensin (Rumensin,® Elanco Animal Health, Greenfield, IN); 3)

Decoquinate (DEC) fed 275mg/hd/day (Deccox,® Zoetis, Parsippany, NJ); or 4) 3g/hd/day *Yucca schidigera* (YS) (Micro-Aid,® DPI Global, Porterville, CA).

At the time of allotment, all cattle received a new, unique individual animal identification tag specific to the trial, an estradiol and progesterone implant (Synovex S, Zoetis, Parsippany, NJ) and poured with ivermectin (Bimectin, Bimeda, Oak Terrace, IL). Caretakers and processing staff were blinded to treatment. Animal housing consisted of dirt floor pens approximately 30m by 60m, providing 30 cm of linear bunk space per hd, and approximately 2.5 cm of linear water tank space per hd.

Diet Preparation

Cattle were adapted to increasing levels of energy in the diet by using a continuous transition system before initiation of study. Starter and transition diet consisted of (DM basis) 44.3% triticale silage, 37.8% wet distillers grains, 11.2% steam flaked corn, 4.7% mixed hay, 1.7% supplement, and 0.20% corn oil. Finishing diet consisted of 27.0% steam flaked corn, 27.5% high moisture corn, 29.6% wet distillers grains, 11.1% triticale silage, 4.1% liquid supplement, and 0.7% corn oil (Table 3-1). All treatment groups received the same base ration (Table 3-1) that was balanced to provide 14% crude protein DM, 2.25MJ/kg NE_m, and 1.55 MJ/kg NE_g (Table 3-1). Truck mounted horizontal rotary feed mixer with box-mounted scale (Roto-Mix, Inc., Dodge City, KS) prepared and delivered total mixed rations. Treatment rations were delivered twice daily (0800 and 1300) on separate trucks to prevent cross contamination of treatment rations. The computer feeding system employed by the feedlot (Animal Health International, Loveland, CO) recorded daily feed amounts delivered. Cattle were fed to ad libitum, and feed yard personnel adjusted the amount of feed issued as needed, taking into consideration feedbunk condition at approximately 0600, 1100, 1600, and 2300 hours each day.

Fecal Sample Collection and Diagnostics

Freshly voided fecal samples (n=10 per pen) were collected 50 d after treatment initiation for fecal flotation to determine the presence of *Eimeria spp*. Fecal samples were collected from 10 freshly voided fecal pats on the pen floor. Samples were collected in plastic bags (Whirl-pak, Madison, WI) and shipped on ice to the Kansas State University Veterinary Diagnostic Lab (Manhattan, KS) within 48 h of collection. Qualitative fecal floatation was performed using the Modified Wisconsin Technique double centrifugation fecal flotation using Sheather's sugar solution as described by Zejac & Conboy (2012). Qualitative fecal flotation was selected due to cost and for greater diagnostic detection of the presence of *Eimeria spp* (<50 oocysts/gram). Qualitative fecal flotation measurements were measured on a scale of 1+ to 5+ with 1+ having <10 oocysts per slide, 3+ samples having 50-100 oocysts per slide, and 5+ having >500 oocysts/slide. This technique is considered semi-quantitative, with 3+ samples equivalent to approximately 50 oocysts/gram (KSU VDL, personal communication). Due to shipping errors, fecal samples from 4 pens in one block and 8 pens from a second block were not analyzed.

Performance Data

Feedlot closeout reports after cattle shipment provided cattle final body weight, and dry matter intake. Prior to shipment to abattoir, cattle were weighed by pen on a certified scale had a 6 % pencil shrink applied to account for transportation and derive the final pen average BW. Daily dry matter intakes recorded via bunk management personnel and entered into the computerized bunk management system (Animal Health International, Greely, CO) comprised intake data. ADG was calculated on a pen basis using the equation (Final average BW – Initial average BW/ DOF). The equation (ADG/DMI) determined gain efficiency.

Liver Abscess & Carcass Data

All pens of cattle shipped at 60 ± 4 d to the same abattoir (National Beef, Liberal, KS). Complete blocks were shipped at the same time. Hot carcass weight was collected from the plant via scale on carcass rail. USDA-trained professionals inspected liver abscesses at slaughter, and third-party trained professionals (CattleTrail, Inc. Dodge City, KS) scored and recorded liver abscess prevalence and severity data. Assessors used the liver scoring system previously described by Brown et al. (1975): 0 = no abscesses, A- = 2-4 abscesses under 1 inch in diameter, A = 1-2 abscesses greater than 1 inch in diameter and A+ = abscesses greater than 2 inches in diameter, ruptured abscess, or adhesions to body wall. A third party (CattleTrail, Inc. Dodge City, KS) collected yield grade and quality grade data. Liver abscess and carcass data were not collected from 1 pen from the first block.

Statistical Analysis

Continuous variables were analyzed using PROC Glimmix (SAS 9.4, SAS Inst. Inc., Cary, NC). Pen was the experimental unit, and models contained treatment as a fixed effect, block as a random effect. The blocking factor was the source pen that the treatment replicates were originally sorted from. Least squares means comparisons used the PDIFF function of SAS and the Tukey-Kramer adjustment for multiple comparisons. Statistical significance was determined at $P<0.05$ with tendencies at $0.06 > P < 0.10$. Pairwise comparisons were evaluated using Tukey's test for variables whose overall treatment effect (F-test $P \leq 0.10$). Pairwise comparisons were not performed if the overall treatment effect was not significant. Pairwise differences were considered statistically significant when $P \leq 0.05$; tendencies were declared for comparisons where $0.05 < P \leq 0.10$.

Liver abscess scores, yield grade, and quality grade were converted to pen level frequencies by dividing the total number of sub-category (A+,A, or A- liver scores, and so on) by the total number of cattle in each pen at slaughter and analyzed as discrete variables. Discrete variables were analyzed with a generalized linear mixed model using a binomial distribution and a logit link function in PROC GLIMMIX. The classification of fixed and random effects and the handling of interactions and pairwise comparisons were performed in a similar manner as the continuous variables.

Observed prevalence of *Eimeria spp.* was low in the study and no samples reached a level of concentration deemed pathogenic as coccidiosis. Therefore, outcomes of fecal samples testing have been listed in Table 3.

Results and Discussion

Cattle Performance

The mean trial DOF for all treatment groups was 60.2 days (P=1.0, Table 3-2). Average headcount per pen did not differ between treatment groups (P=0.94, Table 3-2). There was a significant difference in initial body weight in cattle assigned to the different treatments (P=0.04, Table 3-2). To adjust for difference in initial BW, final BW, ADG, DMI, G:F, and HCW were modeled using initial BW as a covariate. Cattle fed MT and YS diets had significantly heavier final weights compared to cattle fed the CON diet (P<0.05, Table 3-2). These results differ from Mackey et al. where they found no difference in final body weight in cattle fed with or without monensin and tylosin, or with or without *Y.schidigera* extract, for 113 to 136 d (2023). Cattle fed YS and MT had a higher ADG than the CON (P=0.008, Table 3-2), but not higher than DEC treatment groups (P>0.05, Table 3-2). No treatment effect was observed for DMI in the present study (P=0.14, Table 3-2). Cattle fed MT had improved efficiency compared to cattle fed CON (P=0.03, Table 3-2), but did not differ in gain efficiency from DEC or YS fed cattle (P>0.10,

Table 3-2). These results are consistent with Sousa et al. (2019) in which the authors found that supplementing *Y. shidigera* extract in finish rations increased cattle ADG compared to cattle receiving no *Y. schidigera*. Rett et al. (2020) found a linear increase in ADG in heifers fed 1, 2, and 4g/hd/day (as fed) of *Y. schidigera* extract over a 28 d period in cannulated heifers. This increased ADG was explained as a result of increased propionate production caused by YS supplementation (Rett et al. 2020). Mackey et al. found no difference in ADG between cattle fed *Y. schidigera* with or without monensin and tylosin but did observe higher DMI in cattle fed without monensin and tylosin, which was not observed in the present study (2023). Depenbusch et al. (2008) reported no difference in DMI, ADG, or G:F in cattle fed diets with monensin, monensin and tylosin, or no additives. No difference in ADG, DMI, or G:F for cattle fed DEC compared to cattle fed MT or CON in this study is consistent with Harmon et al. (1987) in which no effect was seen when comparing Holstein steers fed decoquinate to Holstein steers fed monensin with tylosin over a 147 d feeding period.

Carcass Characteristics

A treatment effect for HCW was observed ($P=0.007$, Table 3-2), with CON fed cattle having lower HCW compared to cattle fed MT or YS ($P<0.05$, Table 3-2). Dressing percent was significantly higher for cattle fed MT compared to YS ($P<0.05$, Table 3-2) but did not differ from CON or DEC fed cattle ($P>0.10$, Table 3-2). Treatment effects were also observed for yield grade, as CON fed cattle had a higher percentage of YG 1 carcasses compared to MT and DEC, as well as a tendency for more YG 1 carcasses compared to YS fed cattle ($P=0.009$, Table 3-2). The percentage of select carcasses also differed between treatments, as CON fed cattle had a higher percentage compared to cattle fed DEC ($P=0.02$, Table 3-2) Results of the present contradict several studies evaluating the use monensin and tylosin compared to controls on carcass yield, yield grades, and quality grades. Muller et al. (2018) found marbling scores were lower in cattle continuously fed tylosin compared to cattle fed tylosin intermittently; however, this did not affect the overall carcass quality. Depenbusch et al. (2008) also did not see any effects of monensin and tylosin fed over a 150-d period on carcass weights, dressing yield, yield grade, or quality grades. When monensin and tylosin were removed for the last 35 d of feeding, Sides et al. (2009) did not observe any effects on carcass quality or cattle performance compared to continuous monensin and tylosin administration. Nichols et al. (2011) found no differences in carcass weight, yield grade or dressing yield in cattle supplemented with *Y.schidigera* (Ruma Just, Lallemand Animal Nutrition, Inc.) compared to controls. It is worth noting that in the present study no effects of treatment were observed for YG2-5, prime, choice, or standard quality grades (P>0.23, Table 3-2).

Liver Scores & Eimeria Prevalence

Treatment had a significant effect on the total prevalence of liver abscesses (P= 0.003, Table 3-2). Cattle fed MT had lower total prevalence of liver abscesses compared to cattle fed CON (P<0.05, Table 3-2) but did not differ compared to cattle fed DEC or YS (P > 0.05, Table 3-2). A+ liver prevalence was significantly affected by treatment (P=0.002, Table 3-2), with cattle fed MT having fewer A+ livers than CON and a tendency (P<0.10, Table 3-2) to have fewer A+ livers than YS supplemented cattle. These results are consistent with several studies that indicate tylosin administration reduced the number of A+ liver abscesses found at slaughter (Brown et al., 1975; Pendlum et al., 1978; Vogel and Laudert, 1994; Nagaraja & Chengappa, 1998). In more recent literature, other strategies have been explored to reduce the use of monensin and tylosin while still maintaining lower liver abscess prevalence. Bohrer et al. saw no differences in the prevalence of liver abscesses in cattle fed with monensin and tylosin compared to cattle fed without in the last 48 d of feeding (2016). A similar effect was seen by Montgomery et al. (2009), where monensin and tylosin were removed from the diet 35 d prior to slaughter with a minor reduction in liver abscess prevalence compared to the treatment group where continuous monensin and tylosin administration occurred. Müller et al. (2018) saw no effect between intermittent tylosin administration and continuous tylosin administration on the reduction of liver abscesses, but both treatment groups had significantly lower liver abscess prevalence compared to the negative control. The explanation proposed by Müller et al. (2018) indicated that prolonged inhibition of regrowth of gram-negative bacteria such as *Fusobacterium necrophorum* after initial exposure to the macrolide, a hypothesis derived from Mathers et al. (2011). In the aforementioned studies, cattle were fed less days than the present study, and thus the inhibition *F. necrophorum* may only occur for a shorter period. It is also worth noting that tylosin is labeled to be fed continuously, and intermittent administration of tylosin at this time would be an extra-label drug use, prohibited by FDA GFI 213 (2013).

Meyer et al. found equivalent results to the present study when they explored the use of essential oils with or without tylosin to reduce liver abscess prevalence and saw lower prevalence of liver abscesses in cattle fed monensin and tylosin compared to cattle fed with essential oils or no additives (2009). It is interesting to note that no difference was observed in total or A+ liver abscess prevalence between DEC and MT fed cattle in the present study. The relationship between decoquinate and liver health is not well understood, and future studies may point to another option for the reduction in liver abscesses.

There were no treatment effects evaluated for the difference in *Eimeria spp* incidence between treatment groups. The highest total prevalence was observed in cattle assigned to the decoquinate treatment, with 5.0% of samples positive for at least 1+ *Eimeria* (Table 3-3). Within pen samples, prevalence was as high as 30% positive samples for *Eimeria* (data not shown). However, none of the positive samples achieved any more than 3+ on the qualitative scale, which if converted to quantitative fecal counts, would be equivalent to 50 oocysts/gram (KSU VDL, personal communication). This amount is not considered pathogenic, as coccidiosis clinical signs occur with infections as high as 100,000 oocysts/gram (Constable, 2015). These results are to be expected, as coccidiosis most commonly occurs in cattle under 12 months of age (Radostits & Stockdale, 1980; Constable, 2015), and these cattle had previously received monensin as a coccidiostat prior to the start of the trial and were housed in a confinement operation.

Implications

Based on the results of this study, monensin and tylosin are effective at improving performance and reducing liver abscess prevalence compared to feeding without additives in the last 60 days of finishing. We did not identify consistent differences between cattle fed decoquinate or *Yucca schidigera* compared to cattle not fed additives, but more research is needed to better understand the relationship and impact of these additives on cattle performance and health at various times during the feeding period. *Eimeria spp* prevalence was very low at the end of the cattle finishing period.

Table 3-1. Composition of diets containing tylosin phosphate and monensin, no tylosin phosphate or monensin, decoquinate alone, or *Yucca schidigera*.

Item	
Ingredients (% DM)	
Corn oil	0.7
High moisture corn	27.5
Liquid starter	4.1
Triticale silage	11.1
Steam-flaked corn	27.0
Wet distillers grains	27.5
Nutrient Composition (DM basis)	
Ingredients (% DM)	
CP	13.94
Roughage	6.12
NE_m, Mcal/kg	2.25
NE_g, Mcal/kg	1.55
Salt	0.31
Calcium	0.63
Phosphorous	0.40
Magnesium	0.31
Potassium	0.97
Sulfur	0.23

Table 3-2. Effect of feed additives on cattle performance, carcass performance, and liver abscess prevalence

Item	Treatment CON	MT	DEC	YS	SEM	P-value
Descriptive						
Hd per pen, n	92.3	91.7	91.7	91.6	1.4	0.94
DOF, d	60.2	60.2	60.2	60.2	1.4	1.0
Cattle performance						
Initial BW, kg	588.4^{x}	591.9^{y}	592.1^{y}	592.1^{y}	5.6	0.04
Final BW, kg[5]	676.3^{a}	681.8^{b}	$678.6^{a,b}$	681.0^{b}	3.3	0.007
ADG, kg/d[3,5]	1.42^{a}	1.51^{b}	$1.46^{a,b}$	1.50^{b}	0.03	0.008
DMI, kg[5]	11.8	11.9	11.9	12.0	0.25	0.14
G:F[4,5]	0.121^{a}	0.128^{b}	$0.123^{a,b}$	$0.125^{a,b}$	0.004	0.03
Carcass performance						
HCW, kg[5]	432.8^{a}	436.4^{b}	$434.3^{a,b}$	435.8^{b}	2.1	0.007
Dressing percent, %	$64.1^{a,b}$	64.25^{a}	$64.1^{a,b}$	64.0^{b}	2.1	0.02
YG1,%	$10.1^{a,x}$	7.1^{b}	6.5^{b}	$7.4^{b,y}$	1.5	0.009
YG2, %	29.7	32.0	33.0	32.1	2.5	0.38
YG3,%	42.7	40.7	40.9	40.7	2.7	0.72
YG4,%	14.4	16.2	16.4	16.3	2.1	0.49
YG5, %	1.0	1.9	1.2	1.4	0.6	0.24
Prime, %	1.5	2.2	2.5	1.9	0.4	0.42
Choice,%	80.8	81.5	84.0	82.1	2.0	0.23
Select,%	15.8^{a}	$14.6^{a,b}$	11.4^{b}	$14.1^{a,b}$	1.8	0.02
Standard,%	1.5	1.2	1.9	1.3	0.6	0.53
Liver scores						
Total liver abscess, %	34.5^{a}	26.8^{b}	$30.3^{a,b}$	$31.6^{a,b,}$	3.0	0.003
A+, %[6]	22.4^{a}	$15.6^{b,x}$	$18.8^{a,b}$	$19.2^{a,y}$	2.4	0.002
A, %	5.1	3.6	4.0	4.5	0.85	0.30
A-,%	6.6	7.4	7.2	7.6	0.93	0.78

[1]Differing superscripts a,b,c indicate P<0.05
[2]Differing superscripts x,y,z indicate P<0.10
[3]Calculated by the equation (Final average BW – Initial average BW/ DOF)
[4]Calculated by the equation (ADG/DMI)
[5]Because of significance of Initial BW, it was included as a covariate for the analysis
[6]Scoring system as described in Brown et al., 1975: 0 = no abscesses, A- = 2-4 abscesses under 1 inch in diameter, A = 1-2 abscesses greater than 1 inch in diameter and A+ = abscesses greater than 2 inches in diameter, ruptured abscess, or adhesions to body wall.

Table 3-3. Effect of feed additive on prevalence of *Eimeria spp*

	Treatment			
Item	CON	MT	DEC	YS
Samples, n[1]	100	100	100	100
0,%[2]	97	100	95	100
1, %	2	0	3	0
2, %	1	0	1	0
3+, %	0	0	1	0

[1]Samples n=120 were not received at the laboratory

[2]Qualitive fecal flotation, expressed on a scale of 0 to >50 oocysts/g (3+)

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Chapter 4 - Effects of feed additives on performance, carcass characteristics, and the control of liver abscesses the last 120 days on feed in cattle fed in a commercial Western Kansas feedlot.

Abstract

Crossbred steers (n= 6,802; BW = 388±22.9 kg) in a commercial High Plains feedlot were used in a randomized complete block design study to determine the impact of three feed additive regimens fed during the last 120 days on feed to control liver abscesses and improve cattle performance. All steers were consuming the same base finishing diet prior to and at the time of trial initiation. Steers within previous feeding pen were randomly allocated to 1 of 3 treatments: 1)No feed additives (CON); 2) 15 g/ton with targeted intake of 130 mg/hd/day monensin (Rumensin,® Elanco Animal Health, Greenfield, IN) and 75mg/hd/day tylosin (Tylan,® Elanco Animal Health, Greenfield, IN) (MT); or 3) 275mg/hd/day decoquinate (Deccox,® formerly Zoetis, Phibro Animal Health, Teaneck, NJ) and 3g/hd/day *Yucca schidigera* (Micro-Aid,® DPI Global, Porterville, CA) (DY). There was a total of 18 replicates per treatment (54 pens, n=126±1 per pen) with pen being the experimental unit. Cattle were fed treatment diets during the last 120 days of the feeding period prior to shipment to an abattoir. Cattle fed DY consumed 0.1 kg more feed per day than CON fed cattle and 0.2 kg more per day than cattle fed the MT diet (P=0.05). There were no other differences in cattle performance due to feed additive treatment. Total liver abscess prevalence was reduced in cattle fed MT compared to CON and DY fed cattle (P<0.001). Cattle fed DY had a lower prevalence of A+ liver abscesses and tended to have lower total liver abscess prevalence compared to cattle fed CON (P<0.001, P<0.10, respectively). More cattle graded choice or prime when fed CON compared to cattle fed DY

(P=0.02). The results of this study suggest that feeding monensin and tylosin improved liver health of feedlot cattle but had minimal effects on cattle performance compared to feeding decoquinate and *Yucca schidigera* or no feed additive during the last 120 days on feed.

Keywords: Beef; Feedlot; Feed Additives, Liver Abscesses

Introduction

Feedlot finishing of cattle often includes high concentrate diets (NAHMS 2011). These diets can predispose cattle to acidosis and rumenitis, which has been shown as a predisposing factor to liver abscesses in feedlot cattle (Nagaraja & Chengappa, 1998). Liver abscesses affect the overall animal performance through decreased feed utilization, decreased carcass yield and cause additional carcass trim at slaughter. Lawrence estimated that the economic loss from liver abscesses ranges from $8 to $189 per animal (2022). Liver abscess prevalence has ranged from 1-95% (Nagaraja & Chengappa 1998), and the 2022 National Beef Quality Audit showed the prevalence of liver abscesses in cattle slaughtered in the US is 16.5% (Borders et al., 2024). High concentrate diets often include feed additives, including antimicrobials such as tylosin for the reduction of liver abscesses. Tylosin, a macrolide antimicrobial (Tylan®, Elanco Animal Health Greenfield, IN) has been used successfully for the reduction of liver abscesses in feedlot diets (Brown et al. 1975; Nagaraja & Lechtenberg 2007). Tylosin inhibits *Fusobacterium necrophorum* primarily in the rumen, in the liver through gut absorption, or both (Nagaraja and Lechtenberg, 2007). The effect of tylosin is well documented, with several studies show a 60-70% reduction in liver abscess incidence when fed to cattle at 8 to 10 g/ton or 60 to 90 mg/hd/d g/ton (Brown et al.,1975; Pendlum et al., 1978; Potter et al., 1985; Vogel & Laudert, 1994). Ionophores, such as monensin (Rumensin©, Elanco Animal Health), are commonly used in feedlot cattle to enhance feed efficiency, regulate intake, and control coccidiosis (Richardson et al., 1976; Russell & Strobel, 1989; Callaway et al., 2003; Ensley, 2016). Monensin has several mechanisms of action, shifting volatile fatty acid production from acetate to propionate, reducing methane production, and limiting ruminal amino acid degradation, which helps prevent ruminal acidosis and improves feed efficiency (Richardson et al., 1976; Schelling, 1984; Russell and Strobel, 1989). Additionally, monensin leads to a dose-dependent reduction in feed intake, promoting consistent consumption without negatively impacting average daily gain (ADG) (Goodrich et al., 1984).

Increased regulation of direct-fed antimicrobials, such as the implementation of the U.S. Food & Drug Administration's (FDA) Guidance for Industry number 213 and the establishment of the Veterinary Feed Directive (FDA GFI 213, 2013) has led to a need to evaluate the use of feed-grade antimicrobials used in cattle feeding. Furthermore, there is a growing population of cattle fed without antimicrobials in the US, and alternatives for direct-fed antimicrobials for maintained or enhanced cattle performance or the reduction of liver abscesses warrant exploration. Decoquinate (Deccox©, formerly Zoetis, Phibro Animal Health, Teaneck, NJ) is a non-antimicrobial alternative labeled for the prevention of coccidiosis in calves and cattle (Miner & Jensen, 1976; Fitzgerald & Mansfield, 1986). The effects of decoquinate on cattle performance beyond coccidiosis prevention are unclear. Harmon et al. (1987) found no difference in performance in steers fed decoquinate compared to controls or steers fed monensin and tylosin. Fox (1986) found that cattle fed decoquinate gained on average 0.23 kg/hd/dday greater compared to cattle not fed any feed additives.

Yucca schidigera extracts (Micro-Aid©, DPI Global, Porterville, CA) have also been evaluated for performance benefits in feedlot cattle. *Yucca schidigera* extracts are rich in saponins, which shift VFA production from butyrate to propionate, increase microbial nitrogen outflow, reduce rumen protozoa, and inhibit the growth of *Streptococcus bovis* (Sousa et al. 2019; McMurphy et al. 2014; Hristov et al. 1999; Wallace et al. 1994). Sousa et al. (2019) and Rett et al. (2020) explored dried extracts from *Yucca schidigera* as a non-antimicrobial alternative for improved feed efficiency. Sousa et al. (2019) found an 8% increase in ADG compared to control when *Yucca schidigera* was fed at 2g/hd/day, whereas Rett et al. (2020) found a 40% increase in ADG with *Y. schidigera* fed at 4g/hd/day.

A previous study analyzed the effects of feeding no additives, monensin and tylosin, decoquinate, and *Y. schidigera* extract during the last 60 days of feeding prior to slaughter and found cattle fed monensin and tylosin did not differ in the total prevalence of liver abscesses from cattle fed decoquinate or *Y.schidigera* extract (Bourek et al., 2020). Furthermore, Bourek et al. showed increased ADG and DMI in cattle fed *Y.schidigera* extract compared to cattle fed without additives (2020). Therefore, the objectives of this study were to examine the effects of direct-fed antimicrobials, monensin and tylosin, compared to feeding no additives, and the combination of non-antimicrobial, direct-fed additives decoquinate and *Y.schidigera* have on overall performance, liver abscess prevalence at slaughter, and carcass quality over the entire feeding period of yearling steers during the last 120 days of the feeding period.

Materials & Methods

Procedures involving live animals in this study were approved and performed in compliance with the Institutional Animal Care and Use Committee (IACUC) at Kansas State University protocol #4302.

Experimental Design

Predominantly black hided British and British X continental yearling steers (n= 6,802; BW 388 ± 22.9 kg) were utilized in the feeding trial from July 2020 through April 2021. Steers were selected from a larger population at a commercial cattle feeding facility located in the High Plains region of Kansas. A randomized complete block design utilized 3 treatments and 18 replicates per treatment (54 pens total, n=126±1 hd per pen). Complete replicates were enrolled weekly based on incoming cattle flow, starting in July of 2020 with the last replicate enrolled in November of 2020. Groups were managed identically, with the only difference being starting dates and slaughter dates.

Animal Management and Treatment Enrollment

Prior to initial processing and trial initiation (-34d), 6 pens of approximately 60 hd were selected from newly arrived steers to be used as a block for the study. Cattle were randomized to 1of 3 pens of approximately 120 hd by gate sorting groups 4 hd at a time. If head counts were not exactly 120 hd per pen, the final gate sorts were made so that the number of animals per treatment group were within one hd of each other. Once cattle were randomized to complete a replicate of pens, the pens of cattle were then randomly assigned to 1 of 3 treatments to be initiated at day 1: 1) No feed additives (CON); 2) 15 g/ton with targeted intake of 130 mg/hd/day monensin (Rumensin,® Elanco Animal Health, Greenfield, IN) and 75mg/hd/day tylosin (Tylan,® Elanco Animal Health, Greenfield, IN) (MT); or 3) 275mg/hd/day decoquinate (Deccox,® formerly Zoetis, Phibro Animal Health, Teaneck, NJ) and 3g/hd/day *Yucca schidigera* (Micro-Aid,® DPI Global, Porterville, CA) (DY). All pens of cattle were processed and given a modified live viral vaccine (Pyramid 5, Boehringer Ingelheim Animal Health USA, St. Joseph, MO), a progesterone/estradiol implant (Synovex S, Zoetis, Parsippany, NJ), and poured with ivermectin (Bimectin, Bimeda, Oak Terrace, IL), and given a new unique individual identification tag specific to the trial. At 35 d on feed, (trial d 1), pens of cattle were weighed by pen to for initial body weight, and a 4% shrink was applied. Cattle were additionally reimplanted with a progesterone/estradiol implant (Synovex S, Zoetis, Parisppany, NJ) at approximately 100 d prior to slaughter. All pens within replicate were processed and re-implanted on the same day. Caretakers and processing staff were blinded to treatment. Animal housing consisted of dirt floor pens approximately 33 m by 90 m, providing 26 cm of linear bunk space per hd and approximately 2.5 cm of linear water tank space per hd.

Diet Preparation

Cattle were adapted to increasing levels of energy in the diet by using a continuous transition system before initiation of the study (-34d to 0d). All cattle remained on the same starter and transition rations until trial initiation, at approximately 35 days on feed (trial day 1). Starter and transition rations until day 1 of the trial were formulated to contain 75mg/hd/day tylosin (Tylan, ® Elanco Animal Health, Greenfield, IN) with 15 g/ton monensin (Rumensin, ® Elanco Animal Health, Greenfield, IN). Starter and transition diets consisted of (DM basis) 67.3% corn silage, 11.0% steam flaked corn, 13.4% wet distillers grains, 7.1% mixed hay, and 1.1% supplement. At trial initiation (d 1), all cattle received the same base finishing diet which consisted of 24.0% steam flaked corn, 11.7% high moisture corn, 31.1% wet distillers grains, 27.8% corn silage, 1.2% mixed hay, 3.6% liquid supplement, and 0.6% corn oil (Table 4-1). The base finishing ration was balanced to provide 12.94% crude protein DM, 2.20 MJ/kg NE_m, and 1.51 MJ/kg NE_g (Table 4-1). Truck-mounted horizontal rotary feed mixer with box-mounted scale (Roto-Mix, Inc., Dodge City, KS) prepared and delivered total mixed rations. Treatment rations were delivered twice daily (0800 and 1300) on separate trucks to prevent cross-contamination of treatment rations. The computer feeding system employed by the feedlot (Animal Health International, Loveland, CO) recorded daily feed amounts delivered. Cattle were fed to ad libitum, and feed yard personnel adjusted the amount of feed issued as needed, taking into consideration feed bunk condition at approximately 0600, 1100, 1600, and 2300 hours each day.

Data Collection

Performance Data

Feedlot closeout reports after cattle shipment provided cattle final body weight and dry matter intake. Prior to shipment to the abattoir, cattle were weighed by pen on a certified scale and had a 6% pencil shrink applied to account for transportation and derive the final pen average BW. Daily dry matter intakes recorded via bunk management personnel and entered into the computerized bunk management system (Animal Health International, Greely, CO) comprised intake data. ADG was calculated on a pen basis using the equation (Final body weight – Initial body weight/ days on feed). The equation (total weight gained divided by the average daily dry matter intake) determined feed conversion.

Liver Abscess & Carcass Data

Complete replicates of pens were shipped at the same time, and all pens of cattle shipped at 120 ± 4 d to the same abattoir (National Beef, Liberal, KS). Hot carcass weight was collected from the plant via scale on carcass rail. USDA-trained professionals assessed liver abscess scores, and third-party trained professionals (CattleTrail, Inc. Dodge City, KS) recorded and collected liver abscess data. Assessors used the liver scoring system previously described by Brown et al. (1975): 0 = no abscesses, A- = 2-4 abscesses under 1 inch in diameter, A = 1-2 abscesses greater than 1 inch in diameter and A+ = abscesses greater than 2 inches in diameter, ruptured abscess, or adhesions to body wall. A third party (CattleTrail, Inc. Dodge City, KS) collected carcass yield grade and quality grade data.

Statistical Analysis

Continuous variables were analyzed using PROC Glimmix (SAS 9.4, SAS Inst. Inc., Cary, NC). Pen was the experimental unit, and models contained treatment as a fixed effect, replicate as a random effect. Least squares means comparisons used the PDIFF function of SAS and the Tukey-Kramer adjustment for multiple comparisons. Statistical significance was determined at $P<0.05$ with tendencies at $0.06 > P < 0.10$. Pairwise comparisons were evaluated using Tukey's for variables whose overall treatment effect (F-test $P \leq 0.10$). Pairwise comparisons were not performed if the overall treatment effect was not significant. Pairwise differences were considered statistically significant when $P \leq 0.05$; tendencies were declared for comparisons where $0.05 < P \leq 0.10$.

Liver abscess scores, yield grades, and quality grades were converted to pen level frequencies by dividing the total number of sub-category (A+, A, or A- liver scores, and so on) by the total number of cattle in each pen and analyzed as discrete variables. Discrete variables were analyzed with a generalized linear mixed model using a binomial distribution and a logit link function in PROC GLIMMIX. The classification of fixed and random effects and the handling of interactions and pairwise comparisons were performed in a similar manner to the continuous variables.

Results and Discussion

Cattle Performance

The mean total DOF for cattle in all treatment groups was 155.4 ($P=1.0$, Table 4-2). There were no significant differences in the number of animals per pen nor in initial BW ($P= 0.78$, Table 4-2). There was no treatment effect observed in the final body weight in cattle ($P= 0.67$, Table 4-2). Dry matter intake was higher in cattle fed DY diet compared to cattle fed MT, but did not differ from cattle fed CON (P=0.05, Table 4-2). These results are consistent with Mackey et al. (2023) where they found no significant difference in dry matter intake in cattle supplemented with *Y.schidigera* extract compared to negative control. Mackey et al. (2023) observed decreased DMI in cattle fed monensin and tylosin compared to negative control cattle, which was not observed in the present study. There were no treatment effects on cattle ADG or G:F (P=0.31, P=0.30, respectively, Table 4-2). The results of the present study are not consistent with Sousa et al. (2019), who found increased ADG in cattle supplemented with 2g/d *Y.schidigera* compared to cattle fed no additives during a 60-d receiving period. Rett et al. (2020) observed a linear increase in ADG with increasing levels from 1-4g/d in cannulated heifers. Decoquinate supplementation compared to monensin and tylosin was evaluated by Harmon et al. (1987), in which no differences in cattle performance were observed when comparing Holstein steers fed over a 147-d feeding period. When comparing the results of cattle fed MT to cattle fed CON in the present study, the results are consistent with Depenbusch et al. (2008) where they reported no difference in ADG, DMI, or G:F in cattle fed diets with no additives, monensin, or monensin and tylosin. Meyer et al. (2009) observed a 0.7 kg/d decrease in DMI and a 7.5% increase in G:F in steers fed monensin and tylosin the entire feeding period compared to steers fed no additives during the entire feeding period.

Carcass Characteristics

There were no treatment effects observed in HCW or dressing percent between cattle of assigned to any of the treatment groups (P=0.67, P=0.85, respectively, Table 4-2). These results are consistent with Mackey et al. (2023), where they did not observe changes in HCW or dressing percent in cattle fed *Y.schidigera* with or without monensin and tylosin. Cattle fed DY had a higher percentage of yield grade 2 carcasses compared to cattle fed CON (P=0.03, Table 4-2) but did not differ from cattle fed MT (P>0.10, Table 4-2). Cattle fed MT tended to have a higher percentage yield grade 2 carcasses compared to cattle fed the CON diet (P=0.10, Table 4-2). Cattle fed CON had more yield grade 3 carcasses compared to cattle fed MT (P=0.03, Table 4-2) but did not differ from cattle fed DY (P>0.10, Table 4-2). Results of the present study differ from Meyer et al. (2009), where they did not observe a difference in yield grade between steers fed no additives and steers fed monensin and tylosin during the entire feeding period. Cattle fed CON diet had a higher percentage of prime and choice carcasses compared to cattle fed DY (P=0.03, Table 4-2) and tended to have a higher percentage of prime and choice carcasses compared to cattle fed MT (P=0.08, Table 4-2). Cattle fed CON had significantly fewer select carcasses compared to cattle fed DY (P=0.03, Table 4-2) but did not differ from cattle fed MT (P>0.10, Table 4-2). These results are not consistent with Nichols et al. (2011), where they observed increased marbling in cattle supplemented with *Y. schidigera* compared to control fed cattle. Meyer et al. (2009) did not observe a difference in marbling score between cattle fed no additives and cattle fed monensin and tylosin during the entire feeding period. Mackey et al. 2023 found no treatment effects in percentage of prime and choice carcasses in cattle supplemented with *Y.schidigera* compared to cattle fed with or without monensin and tylosin.

Liver Scores

Cattle supplemented with MT had fewer total liver abscesses compared to cattle fed no additives or cattle fed DY (P<0.01, Table 4-2). Cattle fed DY tended to have fewer total liver abscesses compared to cattle fed CON (P=0.09, Table 4-2). MT fed cattle had significantly lower A+ livers compared to CON and DY fed cattle (P<0.001, Table 4-2). Cattle fed DY had significantly lower liver abscess prevalence compared to cattle fed the negative control. Cattle fed MT tended to have fewer A- liver abscesses compared to cattle fed DY (P=0.06, Table 4-2) but did not differ from cattle fed the CON (P>0.10, Table 4-2). These results are consistent with several studies that indicate tylosin administration reduced the number of total and A+ liver abscesses found at slaughter (Brown et al., 1975; Pendlum et al., 1978; Vogel and Laudert, 1994; Meyer et al., 2009). Results for liver abscess prevalence between cattle fed MT compared to cattle fed DY found in the present study are not consistent with Mackey et al., where they found no significant difference in liver abscess prevalence in cattle supplemented with *Y.schidigera* with or without monensin and tylosin (2023).

Implications

The results of this study suggest that feeding cattle a combination of Y. *schidigera* extract and decoquinate, or a combination of monensin and tylosin the last 120 days of the feeding period had minimal impacts on performance or carcass characteristics compared to cattle not fed any feed additives. This study shows that monensin and tylosin supplementation is an effective tool for the control of liver abscesses in cattle compared to cattle fed a combination of *Y. schidigera* and deoquinate or in cattle not fed and feed additives the last 120 days on feed

Table 4-1. Composition of diets containing no additives, tylosin and monensin, or decoquinate with *Yucca schidigera* extract

Item	
Ingredient (% DM)	
Corn oil	0.6
High moisture corn	11.7
Liquid starter	3.6
Corn silage	27.8
Dry ground hay	1.2
Steam-flaked corn	24.0
Wet distillers grains	31.1
Nutrient Composition (%DM)	
CP	14.26
Roughage	8.41
NE_m, MJ/kg	2.20
NE_g, MJ/kg	1.51
Salt	0.33
Calcium	0.69
Phosphorous	0.41
Magnesium	0.33
Potassium	1.00
Sulfur	0.23

Table 4-2. Effect of feed additive on cattle performance, carcass performance, and liver abscess prevalence and severity

Item	Treatment			SEM	P-value
	CON	MT	DY		
Descriptive					
Hd Count, #	126.1	126.0	125.8	0.14	0.55
DOF, d	155.4	155.4	155.4	1.9	1.0
Cattle Performance					
Initial BW, kg	387.0	387.5	386.9	7.0	0.78
Final BW, kg	678.9	677.2	678.9	8.1	0.67
ADG, kg[3]	1.88	1.87	1.88	0.05	0.31
DMI, kg	$11.9^{a,b}$	11.8^{a}	12.0^{b}	0.24	0.05
G:F, kg[4]	0.158	0.159	0.157	0.02	0.30
Carcass Performance					
HCW, kg	434.5	433.4	434.5	5.2	0.67
Dressing percent, %	64.1	63.8	64.0	0.4	0.85
YG1,%	6.0	5.3	5.1	1.4	0.35
YG2, %	$26.4^{a,x}$	29.3^{y}	30.0^{b}	2.2	0.03
YG3,%	44.0^{a}	40.0^{b}	42.9^{a}	2.0	0.03
YG4,%	18.3	16.6	15.9	2.4	0.11
YG5, %	2.4	1.7	1.6	0.4	0.10
Prime & choice, %	$88.0^{a,x}$	85.8^{y}	85.3^{b}	1.8	0.02
Select,%	10.5^{a}	$12.0^{a,b}$	12.9^{b}	1.7	0.05
Standard,%	0.8	1.1	0.9	0.7	0.14
Liver abscess prevalence					
Total liver abscess, %	$32.2^{a,x}$	22.0^{b}	$29.2^{a,y}$	1.5	<0.001
A+, %[5]	22.0^{a}	12.9^{b}	17.8^{c}	1.5	<0.001
A, %	2.9	2.2	2.6	0.4	0.32
A-,%	$6.9^{x,y}$	6.6^{y}	8.4^{x}	0.8	0.05

[1]Differing superscripts a,b,c indicate p<0.05
[2]Differing superscripts x,y,z indicate p<0.10
[3]Calculated by the equation (Final average BW – Initial average BW/ DOF)
[4]Calculated by the equation (ADG/DMI)
[5]Scoring system as described in Brown et al., 1975: 0 = no abscesses, A- = 2-4 abscesses under 1 inch in diameter, A = 1-2 abscesses greater than 1 inch in diameter and A+ = abscesses greater than 2 inches in diameter, ruptured abscess, or adhesions to body wall.

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Chapter 5 - Integrated Discussion

Introduction

The objectives of this research were to address specific stressors in cattle production: 1) stress due to the human-animal interactions during processing, which could lead to increased bovine respiratory disease in feeder cattle, and 2) stress from digestive upset that could result in liver abscesses in feeder cattle, which are observed at slaughter. In the first study presented, human-animal interactions and the intensity of those interactions affected markers of physiological stress, principally heart rate, respiratory rate, and lactate, and minor effects were observed in inflammatory and immune system markers such as IL-6. However, these changes ultimately did not affect the immune response or the morbidity or mortality outcomes of the cattle in this study.

In the feed additive studies, digestive stress was present in the cattle studied, evidenced by the prevalence of liver abscesses found in all pens of cattle at slaughter. Cattle fed the combination of monensin and tylosin had lower prevalence in total and A+ liver abscesses compared to feeding no additives, which have the most significant impact on performance and profitability. Alternative feed additives such as decoquinate and *Y.schidigera* extract showed minor differences in performance and liver abscess prevalence compared to cattle fed no additives during the last 60 d of the feeding period, but these effects were not observed when fed the last 120 d. This discussion will evaluate the results of these studies, review the limitations of these studies, and highlight the opportunities for future experiments.

Cattle handling intensity and the study of physiologic, inflammatory, and immune responses

For physiologic markers of stress, the results of the presented study concluded AH cattle had increased changes in heart rate, respiratory rate and tended to have a reduction in blood pH compared to LSH cattle. This suggests the intensity of cattle handling directly influences the hypothalamic-pituitary-adrenal (HPA) axis. This means ACTH should be stimulating the adrenal medulla and increasing cortisol concentrations in the bloodstream. However, cortisol levels were lower post-treatment compared to the baseline in both LSH and AH cattle in the presented study. This is not what the authors expected and warrants further explanation. One possible explanation is that the sampling time affected and potentially confounded the observed cortisol concentrations. Cattle were not sampled in the same order between baseline and post-treatment time points, so the moment a cortisol sample was taken could have been at a much different point in the animal's HPA axis response, creating more variation in the blood cortisol levels observed. This explanation can be extended to the observations of epinephrine, norepinephrine, and blood gas parameters. If the time between baseline and post-treatment differs from animal to animal, the physiologic functions will be at various response points, and there is too much confounding variation to detect a difference. Future studies evaluating the physiologic response in cattle at processing may benefit from standardizing the time between baseline and post-treatment sampling.

For inflammatory and immune measurements, there was significant variation in the changes between the differing time points. For example, the changes in TNF-α concentrations between LSH and AH cattle were numerically different, with decreasing TNF-α concentrations in LSH cattle and increasing concentrations in AH cattle at 5 d. However, the variation (i.e., standard error) was so large that a difference was not detected. One possible explanation for the large variation is that cattle experienced different stressors at different times. Due to technical issues and facility constraints on the initial day of enrollment and treatment application, the first 40 hd (20 per treatment group) were enrolled approximately 18h before the last 40 hd. Yet, all samples taken on day 5 were collected on the same day, and thus, half of the cattle observed were at a different point of response to the stimuli, both in handling intensity and the response to the applied vaccine. The likely conclusion is that each animal was at a different point in the inflammatory response, both in response to handling intensity and vaccination, not to mention response to environmental factors. This variation made detection of differences, if any, difficult to detect. Sampling at time points that are not evenly spaced and sampling at time points 5 days apart contribute to the variation in these results. Future studies should have more uniform time differences for post-treatment time points and increased sampling intervals, less than 5 days, to expand on the changes in the inflammatory and immune measurements observed in the presented study. Future studies would also benefit from additional sampling times before the initiation of treatments to further understand the variation in physiological and immune markers between animals.

Furthermore, there were limitations to the study design in the presented study. Firstly, systematic allocation to treatments did not adequately account for the variation in body weight, and LSH cattle were heavier than AH cattle at baseline sampling. While weight gain and performance parameters were not direct objectives of this study, this confounding created difficulty in the analysis and interpretation of performance results. Future studies should be designed to properly randomize animals to treatments and control for confounding factors such as variation in body weight, breed, and sex by blocking. Future studies would also benefit from the randomization of the order in which cattle or experimental units of cattle undergo treatment. One experimental design to consider involves small groups of cattle that could be blocked by the aforementioned confounders, randomly assigned to treatments, and randomly allocated to baseline sampling order. Post-treatment order could also be randomized, but this may create confounding as not all cattle would be sampled at the same length of time post-treatment, and the physiologic and inflammatory systems would be at varying degrees of response. Secondly, case definitions in the presented study were not explicitly outlined, leaving room for confounding. For example, the AH cattle experienced yelling by handlers and novel sounds by radio, but the specific decibel level of noise in the facility was not recorded and was subject to confounding and variation. Additionally, the approximate 100 m distance cattle traveled to the processing barn may not have reflected realistic conditions observed in typical feedlots. Receiving pens for new cattle entering feedlots are typically a short distance from processing facilities. However, in the case of additional processing events, such as re-implant, cattle are moved over great distances in commercial feedlots, sometimes several hundred to thousands of meters. To understand the physiologic stress induced during that time, a course similar to the one described in Hagenmaier et al. (2017) would allow for consistent application across treatment groups and satisfy realistic conditions observed in feedlots.

Ultimately, more research is warranted to understand the effects of handling intensity at processing on inflammatory and immune function. Interestingly, baseline concentrations of inflammatory markers such as IL-1, ceruloplasmin, and dRoms in the presented study were higher than Trevisi and Minuti (2018) found utilizing similar methods to evaluate disease risk in dairy cows during the transition period. To the author's knowledge, this was the first study conducted using these methods to evaluate handling intensity in beef cattle. More research is needed in this area to understand the values of these parameters concerning feeder cattle and the role of these parameters in immune function. Understanding the variation of immune response within breed, sex, weaning status, transportation distance, etc., would give better insight into the severity of stress that cattle experience at arrival to the feedlot.

The effects of feed additives on cattle performance, carcass quality, and liver abscess prevalence

The objective of this research was to evaluate the effect of feed additives on reducing dietary stress and disease that ultimately result in liver abscesses at slaughter. The results of the presented studies indicated that cattle, regardless of feed additives, experienced dietary stress and presented with liver abscesses at slaughter. The methods used by cattle feeders to maximize performance and carcass quality, namely high concentrate feeding and rapid acclimation to high grain diets, are at odds with the prevention of metabolic disease that subsequently causes performance losses and liver abscesses. Feed additives, specifically monensin and tylosin, effectively improved performance, maintained carcass quality, and reduced liver abscess prevalence compared to cattle not fed feed additives. *Yucca schidigera* extract improved performance compared to cattle fed no additives in the last 60 days of finishing, but this was not maintained during the last 120 days of finishing. Decoquinate showed minor effects on carcass quality but did not affect performance or liver abscess prevalence compared to cattle fed without additives. Cattle fed the combination of decoquinate and *Y. schidigera* had lower A+ liver abscess prevalence but only tended to have lower total liver abscess prevalence compared to cattle fed no additives and higher total and A+ liver abscess prevalence compared to cattle fed monensin and tylosin for the last 120 days of finishing. In practical application of this information, monensin and tylosin are effective feed additives for managing the dietary stress feedlot cattle experience, improving performance and reducing liver abscess prevalence.

There are limitations to the results and interpretations of the presented studies. Firstly, monensin was fed at low levels during the transition phase and in the treatment groups. Before treatment initiation, all cattle in both studies were fed 7.5 g/ton of monensin, and the treatment diets in both studies included 15g/ton monensin. The suggested inclusion ranges from 5 to 40g/ton; however, industry inclusion rates are typically 25-40 g/ton, nearly three times the amount in the transition diets of the presented studies and double the amount in the treatment diets. Secondly, tylosin was fed at 75mg/hd/d in the middle of the 60-90 mg/hd/d label dosage range. Liver abscess prevalence in the presented studies was higher than the national average found by Borders et al. (2024). This could be explained by the low levels of tylosin and monensin fed to cattle during the starting and transition periods. The transition period is critical for the adaptation of rumen microbes, and the risk of rumenitis and colonization of the rumen wall by *Fusobacterium necrophorum* is greatest during that time. Had monensin and tylosin been fed at higher levels in treatment diets in the presented studies, it is likely the performance effects would have been greater, and liver abscess prevalence would have been lower than the results observed. Future studies evaluating feed additives should include monensin and tylosin closer to industry-utilized levels. Furthermore, no beta-agonists were used in either of the presented studies. Beta-agonists are commonly used for increased muscle deposition, improved performance, and increased yield at the end of the finishing period. Several studies have evaluated the effects of beta agonists, with or without monensin and tylosin (Bohrer et al., 2016). Future studies would benefit from evaluating the effects of decoquinate and *Y. schidigera* on performance, carcass quality, and liver abscess prevalence in combination with or without beta-agonists. Finally, the differences observed in initial body weight in the 60 day study made analysis and interpretation of performance metrics challenging. Future studies should utilize blocking by initial body weight to prevent confounding of performance metrics.

Ultimately, feeding monensin and tylosin are considered industry standards, and the results of the presented studies support the continued use of these additives to mitigate the digestive stressors that cattle experience during the finishing phase. More research is needed to further understand the role of decoquinate and *Y. schidigera* and the potential use of these products in finishing cattle.

Conclusion

Overall, the research in this dissertation showed that stress causes physiological and clinical effects on cattle during the feedlot phase of beef supply chain. Stress due to cattle handling intensity at processing affected the physiological stress response, suggesting human-animal interactions may impact inflammatory and immune functions in feedlot cattle. Future studies are needed to understand the variation and changes in inflammatory and immune functions, with special attention paid to study design, sample collection timing, and increased frequency of baseline and subsequent sample collection. Stress from digestive upset occurred, resulting in liver abscesses observed in the presented studies on feed additives. The combination of monensin and tylosin fed to cattle in the last 60 or 120 days of finishing was an effective strategy to improve performance and reduce the prevalence of liver abscesses. Additional research is needed to understand the potential roles of decoquinate and *Y. schidigera* in finishing cattle.

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Appendix A - Additional Figures from Chapter 2

Figure A-1. Distribution of baseline titers of LSH and AH Cattle

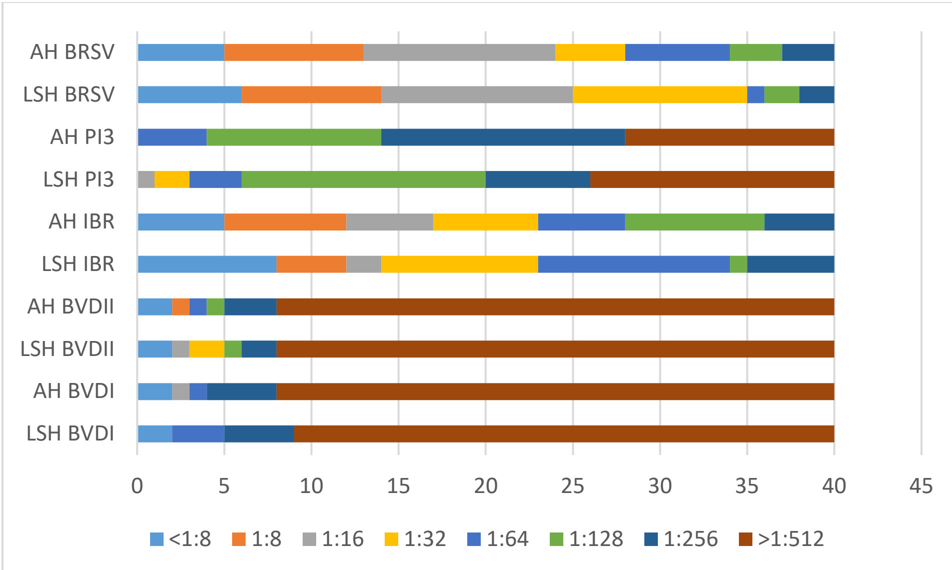

Figure A-2. Distribution of day 21 titers of LSH and AH Cattle

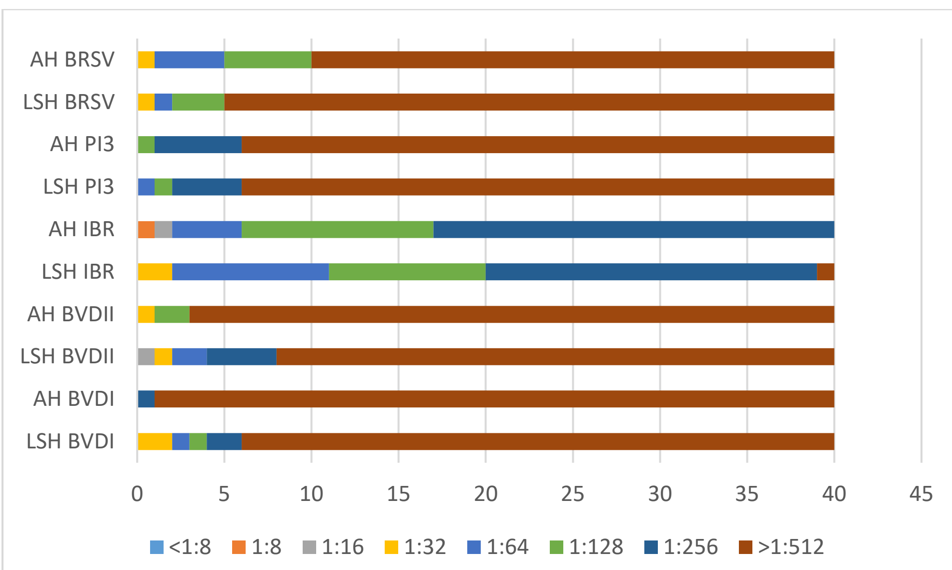

Figure A-3. Distribution of day 42 titers of LSH and AH cattle