

Subacute ruminal acidosis and ruminal lactic acidosis: a review

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Abstract

Subacute ruminal acidosis (SARA) is a digestive disorder associated with systemic inflammation that affects both dairy and beef cattle. The effects of grain-induced SARA have been extensively studied in dairy and beef cattle, but information on diagnosing SARA in beef cattle is limited. Beef cattle on soluble carbohydrate diets experience SARA and have higher morbidity for bovine respiratory disease, despite extensive preventive measures. Monitoring for SARA is important for developing strategies to prevent its related morbidities in both beef and dairy cattle.

Key words: cattle, rumen, acidosis, SARA

Résumé

L'acidose ruminale subaiguë est un trouble digestif associé à une inflammation systémique qui affecte autant les bovins laitiers que les bovins de boucherie. L'acidose ruminale subaiguë induite par la consommation de grains a été amplement étudiée chez les bovins laitiers et de boucherie. Toutefois, il y a peu d'information sur le diagnostic de cette condition chez les bovins de boucherie. Cette acidose s'observe chez les bovins de boucherie avec un régime alimentaire contenant des glucides solubles. En dépit de mesures préventives considérables, ces bovins de boucherie ont aussi une plus grande morbidité associée au complexe respiratoire bovin. La surveillance de l'acidose ruminale subaiguë est importante afin de développer des stratégies pour prévenir les maladies qui y sont associées chez les bovins laitiers et les bovins de boucherie.

Introduction

The digestive system of cattle is adapted to unselective plant cell wall (roughage) fermentation in the forestomach.²⁶

The economics of feedlot beef production dictate that cattle should gain weight at their maximum efficient potential rate; this usually involves feeding a diet containing concentrates with grains.⁵⁸ In addition, consumers in some countries, including the United States and Canada, are more familiar with beef produced from feeding both grain and grass than for beef produced from feeding grass only.⁴² Similarly, dairy cattle frequently are fed diets containing highly fermentable carbohydrates to meet their energy demands and to increase milk production.⁵²

Unfortunately, consumption of soluble carbohydrate diets can be associated with increased morbidities and decreased production.⁵⁸ An important consideration at the herd level is subacute ruminal acidosis (SARA). This article reviews the impact and prevention of SARA in dairy and beef production. The pathophysiology and manifestation of SARA is extensively compared and contrasted to ruminal lactic acidosis (RLA). Gaps in knowledge are also discussed.

Ruminal Acidosis Syndromes

Definitions

Ruminal acidosis is a digestive disorder of ruminants that occurs following overconsumption of highly fermentable carbohydrates.⁷¹ There are 2 forms of the condition: a life-threatening, acute disease culled ruminal lactic acidosis (RLA; also called lactic acidosis, ruminal overload, grain overload, grain engorgement, acute ruminal impaction, acid indigestion, D-lactic acidosis or toxic indigestion), and an insidious condition with less obvious clinical signs referred to as subacute ruminal acidosis (SARA).^{10,49,51} Ruminal lactic acidosis is characterized by ruminal fluid pH values less than 5.2, whereas SARA is characterized by a ruminal fluid pH range of 5.2 to 5.5 for at least 3 hours per day.^{21,33,55} Besides ruminal pH, there are other physiologic, systemic, and pathologic characteristics and sequelae of the 2 conditions which are discussed extensively under the following head-

ings. Elam¹³ outlined scenarios that predispose feedlot cattle to RLA, including weather changes, breakdown of equipment or personnel errors, introduction to concentrate feed, short adaptation period, and long-term feeding of high-concentrate diets. Ruminal lactic acidosis can be induced by a wide variety of traditional feedstuffs, including wheat, barley, rye, oats, and corn.⁷¹ Feeding other non-traditional feedstuffs, such as sugar beets and potatoes, can also result in RLA.⁵⁵

Ruminal Bacteria Changes

Until recently, the specific microbial changes in SARA were unknown.^{20,46} Although limited, recent molecular studies appear to support the earlier culture-based experiments that demonstrated shifts from cellulolytic bacteria, such as *Ruminococcus* spp, to such lactate-utilizing bacteria as *Megasphaera elsdenii* and *Selemonas ruminantium* when cattle were transitioned from forage-based diets to grain diets.^{16,30,67} In contrast, microbial changes in RLA have been extensively studied.^{13,27,46} In the normal anaerobic ruminal environment of grass-fed cattle, the pH is above 6.5 and there is a microbial population of protozoa and predominantly gram-negative bacteria.²⁷ Consumption of excessive amounts of fermentable carbohydrates results in increased fermentation and volatile fatty acid (VFA) production, resulting in moderately acidic ruminal fluid pH with values ranging from 5 to 5.5.⁴⁶ The ruminal fluid pH further decreases to levels below 5.0 because of the production of lactic acid by *Streptococcus bovis*.⁴⁶ At pH levels below 5, most gram-negative, lactate-utilizing bacteria, including *Megasphaera elsdenii* and *Selomonas ruminantium*, die off.¹¹ The death of other substrate-competing bacteria and the increasing acidity of the fluid results in proliferation of another lactate-producing bacteria, *Lactobacillus* spp.¹¹ Even the *S. bovis* that initiated the lactic acid production is inhibited below pH 4.5, leaving *Lactobacillus* spp — the most acid-resistant species — to generate more lactic acid.¹¹

Rumen Physiological Changes

Consumption of excessive amounts of fermentable carbohydrates results in increased fermentation and VFA production.¹³ Both the increasing concentrations of VFA and accumulating lactate are responsible for the increase in ruminal osmolality.¹¹ In a normal animal, ruminal osmolality is maintained at approximately 280 mOsm/L, but may double in some cases of RLA.¹¹ The increased osmolality draws fluid from the extracellular space into the rumen, resulting in increased ruminal fluid volume.¹¹ Lactate is not readily absorbed into circulation because of the hypertonicity of the ruminal fluid, but the detection of high levels of D- lactate in circulation provides evidence of significant absorption nonetheless.¹¹ Ruminal acidosis also causes an increase in the concentration of endotoxin in the ruminal fluid because of increased proliferation or death of gram-negative bacteria.³¹ Other substances, such as biogenic amines and ethanol, also increase in the ruminal fluid.⁷³ Biogenic amines are formed from decarboxylation of amino acids by the ruminal mi-

crobes. Normally, amino acids are deaminated by the ruminal microbes, but they are decarboxylated when there is excess fermentable carbohydrates.⁷³

Although lactate plays a significant role in the pathogenesis of acute ruminal acidosis, its levels are generally not increased in SARA because of the concomitant increase in lactate utilizers.²⁰ Therefore, the decrease in ruminal fluid pH observed in acute ruminal acidosis is a combination of increased VFA concentrations and lactate accumulation, whereas the decrease in pH observed in SARA is a result of increased VFA concentration only.¹⁹ There is a shift in the proportion of VFA in the ruminal fluid of cattle with SARA. The molar proportions of butyrate and propionate increase while acetate decreases in cases of SARA.^{19,25,39} Increasing proportions of butyrate and propionate by ruminal bacteria stimulate proliferation of rumen papillae.⁶³ An exaggeration of this process results in parakeratosis of the ruminal papillae, which predisposes it to trauma and also prevents absorption of VFA, which results in further decreases in pH.⁶³

Pathologic and Systemic Physiological Changes

Low ruminal pH may favor proliferation of fungus that can result in mycotic rumenitis.¹² Ruminal acidosis also causes proliferation of thiaminase-producing bacteria and H₂S-producing bacteria, and death of thiamine-producing bacteria.¹¹ Thiamine deficiency and H₂S toxicity lead to neuronal edema, likely because of disturbances of ATP production pathways.^{4,6,17,57} Laminitis, the other sequelae of ruminal acidosis, is covered under the “effects of SARA on animal welfare” heading.

Lactic acid produced in RLA is corrosive to the ruminal mucosa and can result in toxic rumenitis.¹⁹ Feeding soluble carbohydrates has been associated with parakeratosis and hyperkeratosis of the rumen wall.⁷⁴ In addition, ruminal acidosis and SARA have been associated with other structural and molecular changes to the stratified squamous epithelium.⁷⁴ The damaged mucosa then facilitates translocation of bacteria and endotoxin into the systemic circulation.¹⁹ The various mechanisms of these changes, including possible interactions with ruminal microbes, have been extensively studied and reviewed.⁷⁴ The translocated bacteria can be seeded in other body organs including the liver, where they can potentially result in liver abscesses.⁶² Liver abscesses can erode through the caudal vena cava, resulting in formation of thrombi.^{25,59,62} Septic emboli detach from the thrombus and metastasize to the lungs through the pulmonary arterial system.⁵⁹ Smaller emboli lodge in the arterioles, where they cause thromboembolism, arteritis, endarteritis, and pulmonary abscesses.²⁴ Arteritis and endarteritis, in combination with pulmonary hypertension, result in the formation of aneurysms. In some cases, a perivascular abscess may erode both an arterial wall and a bronchial wall and cause rupture of the aneurysm, thereby channeling blood into the bronchus which results in hemoptysis.²⁴ Occasionally, large emboli may block lobar or larger arteries, causing an acute hypoxic state

and death.²⁴ The entire condition has been called caudal vena caval thrombosis, pulmonary thromboembolism, embolic pulmonary aneurysm and hemoptysis, or simply caudal vena caval thrombosis syndrome.^{3,24}

The liver responds to grain-induced SARA by producing acute-phase proteins that can modify immune function and generate a systemic inflammatory response. The most recognized bovine acute-phase proteins are serum amyloid A, haptoglobin, LPS-binding protein, and α -1 acid glycoprotein.⁷⁴ Acute phase proteins stimulate tissue repair, remove harmful compounds, isolate infectious agents, and prevent further damage,⁷⁴ and are therefore potential targets for markers of SARA; however, they are non-specific because they result from inflammation caused by any insult. The non-specificity of acute-phase proteins limits their use as diagnostic markers for SARA.

Clinical Signs

Ruminal lactic acidosis affects cattle of any age, breed or sex.²⁹ Morbidity within a herd can range from 2 to 50%, while mortality can range from 30 to 40% in treated animals and can be as high as 90% in untreated animals.²⁹ Clinical signs of acute ruminal acidosis depend on the type and amount of feed consumed, and the time at which the animal is examined relative to the time of consumption.⁷² Endotoxin is considered to be a major factor in the development of clinical signs, but this assertion has not been definitely proven.⁷² Initially, cattle are thirsty and exhibit abdominal distension. There is ruminal atony and fluid is detected on abdominal ballottement and succussion.⁷² Diarrhea occurs in the later stages as a result of the hyperosmolar intraluminal environment in the intestines. Hypovolemia develops when fluid continues to accumulate in the rumen secondary to the osmotic gradient produced by accumulating acids. Other clinical signs include anorexia, depression, ataxia, and recumbency. Laminitis and polioencephalomalacia are possible complications.⁷²

Clinical signs of SARA are nonspecific and include fluctuating dry matter intake, low body condition scores in dairy cattle, diarrhea or manure containing undigested feed, unexplained high cull rates due to vague health problems in dairy cows, low milk fat, and lower milk production in second and higher lactation cows compared to first-lactation cows.^{8,53} Dry matter intake also decreases in experimentally induced SARA in dairy cattle.⁵ Some veterinarians recommend estimating the percentage of cows chewing their cud, and fewer than 70% cud chewing can be a warning sign for SARA.⁹ Clinical signs of SARA in beef cattle are nonspecific, and the disease often goes unrecognized.¹³

Diagnosis

Diagnosis of RLA is based on the history of intake of highly digestible carbohydrates, clinical signs, and is confirmed by ruminal pH of less than 5.2.⁵⁸ The differential diagnoses of RLA include simple indigestion, parturient hypocalcemia, coliform mastitis, diffuse peritonitis, and pyloric outflow failure.⁵⁸

In dairy cattle, SARA should be diagnosed and prevented at the herd level rather than in individual animals.⁵³ Strategies for monitoring SARA have been developed for lactating dairy cows. When SARA is strongly suspected in the herd, a representative sample should be tested by measuring ruminal fluid pH via rumenocentesis. The cutoff pH value for SARA diagnosis is 5.5 or less.⁵³ A ruminal fluid pH value of less than 5.2 indicates RLA. For most dairy herds, a sample of 12 cows is usually appropriate. The critical value for the proportion of cows with SARA should be less than 3 out of 12 (25%).⁵³ If the proportion is close to the critical value, retesting is recommended. The strategy of sampling 12 animals in a herd with a prevalence of 5% gives a confidence of 75%.⁵³ This strategy works for herds with prevalence of greater than 25% or less than 15%.⁵³ There are questions about the accuracy of this strategy when considering that the duration of acidosis is not determined, and ruminal pH may not be the only factor that is important in SARA.³² Ruminal acidosis induced by feeding alfalfa resulted in increased ruminal endotoxin, but there was no systemic inflammation, suggesting other factors in addition to pH play a role in the pathophysiology of SARA.³² Testing is only recommended when there are indications of a SARA problem in the herd, and rumenocentesis is still considered useful; there are no reported studies to disprove the utility of rumenocentesis for the diagnosis of SARA. The use of radio transmission pH measurement systems for continuous monitoring of ruminal pH in cows might be more accurate compared to a single rumenocentesis.⁶¹ A radio transmission system utilizes a pH sensor that is administered orally and settles in the reticulorumen, and sends signals to a detector or receiver. Measurements are usually taken every 15 minutes. Ruminal pH depressions of 5.5 or less for more than 3 hours are considered indicative of SARA. SARA diagnosis is always at herd level, regardless of the method of diagnosis.

The insidious nature of SARA makes its diagnosis very difficult in feedlot cattle.⁴⁶ Monitoring intake and feeding behaviors is necessary to detect irregularities in intake patterns because decreased feed intake may be the only sign of the problem.¹³ The practice of averaging intake per pen may mask the daily intakes of individual animals, particularly as the number of animals in the pen increases.^{46,64} Rumenocentesis is not used for monitoring SARA in feedlots because there are no reports that evaluate the overall impact of SARA on production in feedlot animals. Ruminal lactic acidosis is monitored because it has specific clinical signs, but diagnosis of SARA is usually retrospective at postmortem when liver abscesses are noticed. A way of monitoring SARA antemortem is needed so that prevention strategies can be evaluated or refined.

Subacute Ruminal Acidosis and Bovine Respiratory Disease

The incidence of bovine respiratory disease (BRD) continues to be high in feedlot cattle despite the use of vaccines

and other management and husbandry practices.⁴⁸ In 1999, most feedlots (97.4%) within 12 states reported an overall BRD incidence of 14.4%, nearly 5 times the percentage of the next most commonly reported disease, acute interstitial pneumonia.⁴⁸ The efficacy of vaccines for decreasing BRD morbidity and mortality is variable.^{36,44,56} The variability is likely due to multiple factors such as prior vaccination and stress of commingling, transportation, environment, timing, and inconsistent diets.⁷⁰ High-grain diets provided to backgrounding and feedlot cattle potentially play a role in increasing BRD morbidity and mortality.⁴⁰ Beef cattle fed soluble carbohydrate receiving diets had higher morbidity due to BRD compared to cattle fed forage-based diets.^{40,45} It was speculated that high-grain diets were causing immunosuppression resulting in animals being more susceptible to BRD pathogens, but the mechanisms of immunosuppression were not investigated. It is possible that the immunosuppression is due to endotoxin tolerance, a condition where cells exposed to low concentrations of endotoxin enter into a transient unresponsive state and are unable to respond to further challenges with endotoxin in the same magnitude.⁴¹ The concept of endotoxin tolerance needs to be investigated in ruminants because it has only been studied in rodents and humans. The association between BRD and SARA has not been documented in dairy cattle.

Economic Losses Associated with SARA

Economic costs associated with SARA in dairy cattle were estimated to be \$500 million to \$1 billion annually in the United States.¹⁴ These estimates were provided in the late 1990s, suggesting current costs may be higher. Losses are associated with reduced milk production, decreased efficiency of milk production, premature culling, and increased deaths. In beef calves, losses of \$10 to \$13/animal were attributed to reduced growth alone, while condemned livers in feedlot cattle accounted for \$3/animal;⁶⁵ livers were condemned because of abscesses. In addition, SARA is associated with conditions that cause both direct and indirect losses, including death, reduced feed efficiency, laminitis, ruminal tympany, abomasal displacement, abomasal ulcers, and reproductive losses. The economic effects of SARA in dairy cows remain an active area of research. In contrast, little is known about its effects in beef cattle. Further studies are required to provide information about direct and indirect costs, including the effectiveness of the current prevention strategies.

Effects of SARA on Animal Welfare and Public Health

Animal Welfare Concerns

One of the major animal welfare concerns in SARA-affected cattle is laminitis. The association between SARA and subclinical laminitis has been described in previous studies.^{18,23} The pathophysiology of laminitis is complex and not fully understood in cattle. Subacute ruminal acidosis is

thought to cause release of endotoxin and bioactive messengers such as biogenic amines that affect the dermis of the claws.^{18,23} Endotoxin and bioactive messengers are thought to be vasoactive molecules that can alter the vasculature of the dermis of the claw.²³ Endotoxin and bioactive messengers are believed to trigger production of inflammatory cytokines, which activate matrix metalloproteinases.²³ Matrix metalloproteinases disrupt connective tissues, including the suspensory apparatus of the claws.²³ Although cattle with subclinical laminitis may not exhibit overt signs, it causes lesions that result in discomfort and pain to the animal. Examples of lesions caused by subclinical laminitis include white line disease, hemorrhages of the sole, sole ulcers, and disintegration of the heel bulbs.²³ Laminitis was successfully induced in heifers using an overdose of alimentary oligofructose.⁶⁹ In the same study, laminitis was detected in 4 of 6 heifers administered an overdose of oligofructose. Hoof testing enabled pain detection in animals that were otherwise walking and eating, suggesting that inexperienced observers could have easily missed it. Laminitis was confirmed by histopathology, and the same investigators concluded that the term "subclinical" laminitis is probably a misnomer, because most of the subclinical cases are in fact clinical.²³

Public Health Concerns

Enterohemorrhagic *Escherichia coli* (EHEC) is an ubiquitous Shiga toxin-producing strain of *E. coli* that causes foodborne illness in humans.³⁷ Illness ranges from uncomplicated diarrhea to hemorrhagic colitis and hemolytic-uremic syndrome in humans.³⁷ The gastrointestinal tract of cattle is an important reservoir of EHEC.⁷ Ethanolamine, one of the biogenic amines produced in SARA, is utilized by EHEC for growth, and thus commensal bacteria are outgrown.² The use of ethanolamine also confers a marked growth advantage for *Salmonella enterica* serovar Typhimurium (*S. Typhimurium*) in the lumen of the inflamed intestine,⁶⁸ implying that SARA might be a risk factor for contamination of food with EHEC and *S. Typhimurium*.^{2,68}

Prevention of SARA

Subacute ruminal acidosis is linked to feeding conditions, and proper rations and/or good feed-bunk management can help prevent the problem.¹⁴ The critical time for acidosis in beef cattle is during the period of transition from high-roughage to high-grain diets, when cattle enter feedlots.⁴⁶ Traditionally, increased dietary concentrate is fed as incremental amounts of grain over a 3- to 4-week period to minimize the risk of acidosis, but the problem can still occur.⁴⁶ The type and amount of grain, type of grain processing, type and level of roughage, feed additives, pen cleaning, water availability, and prudent bunk management are important factors influencing SARA. Grains and processed grains vary in digestibility; the higher the starch digestibility, the greater the risk of causing acidosis.⁴⁶ SARA can thus be prevented by

blending grains that have higher rates of fermentation with those with lower starch digestibility.⁶⁶

Ionophores, such as monensin and lasalocid, are used to increase feed efficiency in US feedlot cattle by reducing hydrogen and formic acid producers and increasing propionate production.⁶⁰ Ionophores also reduce lactate-producing bacteria.²⁸ Monensin was successfully used to increase ruminal pH in beef cattle fed high-grain diets and in transition dairy cows.^{22,47} However, monensin was not efficacious in raising ruminal pH in SARA-induced dairy cows in other studies.^{15,54,55} The inconsistency of monensin as a substance that increases ruminal pH could be due to differences in concentrations of ruminal lactic acid in the studies.³⁵ Ruminal lactic acid concentration was reported to be above 5mM in most studies that reported the efficacy of monensin in increasing ruminal pH, whereas a concentration of less than 1mM was reported in studies that reported monensin not efficacious.^{54,55} These studies suggest that monensin is likely efficacious against acute ruminal acidosis, but its efficacy for prevention of SARA may be equivocal.

Adding feed-grade alkalinizers to the ration, such as magnesium oxide, sodium bicarbonate, calcium carbonate, and potassium carbonate, resulted in increased ruminal pH and decreased SARA.²⁸ Sodium bicarbonate fed at 110-225g/day was reported most effective.²⁸

The use of direct-fed microbes (DFM) has also been associated with increased ruminal pH.⁵⁰ *Enterococcus faecium*, *Lactobacillus plantarum*, and *Saccharomyces cerevisiae* are some of the microbes that have been evaluated. In addition, *Megasphaera elsdenii* (NCIMB 41125) may offer benefits as a DFM. In a study of the effect of drenching *M. elsdenii* on health and performance of feedlot steers, average daily gain was improved in the immediate post-adaptation phase.³⁸ In another study in high-risk cattle from Oklahoma and Texas, average daily gain did not differ among calves receiving DFM versus no DFM; however, calves receiving DFM during their first antimicrobial treatment for clinical BRD were less likely to be treated a second time within the following 96 hours.³⁴ In addition, the number of calves treated twice for clinical BRD tended to be lower for calves administered DFM, compared with calves not receiving DFM. These findings suggest that DFM have potential to decrease morbidity due to clinical BRD, and possibly improve performance in feedlot cattle.

Prevention of SARA in dairy cattle is largely dependent on dietary management. In general, neutral detergent fiber (NDF) should be 25% (dry matter basis) when dairy cows are fed dry corn as the predominant starch source in total mixed rations (TMR).⁵² Twenty percent of the NDF in such diets should be forage-based in order to provide enough physically-effective fiber (peNDF), which is defined as the proportion of DM retained by a 1.18 mm screen multiplied by NDF.⁴³ Particle size also needs to be appropriate.⁵² Similar to feedlot cattle, the amount of grain should be gradually increased to allow for adaptation over a 4- to 6-week period. Other strategies employed to prevent SARA in dairy cattle

include formulating separate TMRs for early lactation cows and for mid-late lactation cows, instead of just 1 TMR for lactating cows and 1 TMR for dry cows.^{1,41} Buffers could also be added to diets, particularly in critical situations when SARA has been determined to be a major problem. However, buffers should not be used to offset the problems of inappropriate dietary formulations.

Conclusion

Use of molecular techniques during the past few years has significantly improved our understanding of the pathophysiology of ruminal acidosis. While prevention is the best strategy, monitoring and detection strategies for SARA are limited, especially for beef cattle. The practice of performing rumenocentesis to diagnose SARA at the herd level in dairy cows has been shown to be useful, although some questions exist about accuracy due to the inability to measure the duration of pH depression. Telemetric methods of monitoring ruminal pH might be helpful for both dairy and feedlot cattle if they can be optimized to function consistently and are economical on a commercial scale. Prevention and monitoring is key for producers to maximize production while maintaining animal welfare standards. Most of the preventive strategies involve formulating appropriate diets, as well as implementation of appropriate feeding and management protocols.

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