Mechanistic Analysis of Variability in Subacute Rumen Acidosis in Ruminants: Postprint

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Abstract

Subacute ruminal acidosis (SARA) is a common nutritional metabolic disease in high-producing ruminants resulting from excessive consumption of high-starch, readily fermentable carbohydrate diets, which impairs rumen health and thereby reduces feed conversion efficiency. Under the same treatment conditions, different individuals exhibit considerable differences in tolerance to SARA; therefore, investigating the mechanisms of inter-individual variation in SARA among ruminants represents an important scientific question. This paper respectively elucidates the potential mechanisms underlying inter-individual variation in SARA from three aspects: feeding behavior, rumen epithelial absorption function, and microbial flora, providing references and theoretical basis for ruminant health and efficient production.

Full Text

Mechanism Analysis of Variation in Subacute Ruminal Acidosis in Ruminants

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Abstract

Subacute ruminal acidosis (SARA) is a common nutritional metabolic disease in high-producing ruminants caused by excessive consumption of high-starch, readily fermentable carbohydrate diets. SARA impairs rumen health and reduces feed conversion efficiency. Under identical management conditions, individual animals exhibit substantial differences in SARA tolerance, making the investigation of inter-individual variation mechanisms a critical scientific question. This review analyzes potential factors contributing to SARA variability from three perspectives: feeding behavior, rumen epithelial absorption function, and microbial community structure, providing theoretical foundations for healthy and efficient ruminant production.

Keywords: ruminant; subacute ruminal acidosis; variability; underlying mechanism

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High-energy, high-starch diets have become typical nutritional strategies during lactation in dairy cows and fattening phases in beef ruminants [1-3]. While these approaches enhance animal performance, they also disrupt rumen homeostasis, leading to various rumen health issues dominated by subacute ruminal acidosis (SARA). Malekkhahi et al. [4] demonstrated that SARA induced by high-grain diets in dairy cows severely negatively impacts dry matter intake, milk yield, rumen microbial community, and blood metabolites. The detrimental effects of SARA on animal health and production performance represent a prominent challenge in modern ruminant production [5-6].

Numerous studies have shown that excessive consumption of high-energy, high-starch diets by ruminants [7] causes prolonged depression of rumen fluid pH below normal physiological ranges, representing the primary pathogenic pathway [8] and nutritional factor [9-10] for SARA. Research indicates that even under consistent feeding management, significant inter-individual variation exists in rumen fluid pH and SARA risk among dairy cows [11], beef cattle [12], and sheep [13] receiving identical diets. This variability complicates ruminant production management and SARA prevention [11], affecting nutritional supply strategies, precision feeding implementation, group housing decisions, and herd-level rumen health assessment. However, the physiological basis for inter-individual SARA variation, particularly intrinsic animal factors, remains poorly documented. Differences in nutritional and physiological pathways leading to individual SARA susceptibility variation and alterations in rumen microbial diversity are still unclear. Therefore, investigating the sources and mechanisms of inter-individual SARA variability represents an important scientific question. This review synthesizes current knowledge on potential nutritional and physiological factors affecting SARA susceptibility from three aspects—feeding behavior, rumen epithelial absorption function, and microbial community—aiming to provide a scientific basis for related research.

1.1 Research Necessity

Phase- and group-feeding are primary nutritional management approaches for achieving precision feeding in ruminant production [14]. These methods assume similar nutritional requirements within animal groups at specific production stages or with expected production potentials. However, this nutritional supply strategy fails to adequately account for inter-individual differences in SARA tolerance within high-producing groups. In scientific research, heterogeneity among experimental animals in genetics and life history represents a significant source of variation in results [15]. From a biostatistical perspective, this variation is considered random error. Although increasing animal numbers and strict selection criteria can reduce this error, inter-individual variation in SARA susceptibility is ubiquitous in practical ruminant production, making appropriate feeding management crucial in intensive, large-scale operations.

Currently, rumenocentesis based on random sampling has been applied to assess herd-level SARA risk [5,16-17], but this method cannot effectively detect individual differences in SARA susceptibility. This means that even when dietary strategies are modified for high-SARA-risk herds (by reducing readily fermentable carbohydrate content or increasing forage proportion) to decrease overall SARA risk, the maximal production performance of SARA-tolerant individuals is simultaneously compromised. Therefore, reducing or eliminating inter-individual differences in SARA susceptibility is key to ensuring efficient and healthy herd production. Future ruminant production could consider individual SARA tolerance as a basis for group housing, combined with targeted nutritional strategies for specific production stages and expected potentials, to safeguard rumen health and efficient production while refining precision feeding approaches.

1.2 Evidence of Variability

Various nutritional regulation and management practices are employed to prevent SARA in production settings, including maintaining appropriate dietary ratios of physically effective neutral detergent fiber (peNDF) to starch, group feeding [18-19], reducing heat stress [20], and increasing feeding frequency [21]. Studies have found substantial inter-individual variation in SARA risk among cattle and sheep consuming identical diets [11,13]. Macmillan et al. [21] reported that among lactating Holstein cows (n=16) fed a 70:30 concentrate-to-forage ratio, seven cows developed SARA symptoms (rumen fluid pH $<$ 5.8 for 535 min/day vs. 18.4 min/day). Castillo-Lopez et al. [22] demonstrated that in feedlot steers (n=28) fed a high-grain diet (81.2% barley grain) during late fattening, an average of 37.8% of individuals developed SARA (rumen fluid pH $<$ 5.5 for $>$180 min/day), with individual SARA occurrence probability ranging from 0% to 96.9%. Nasrollahi et al. [11] similarly found that among lactating dairy cows (n=78) fed a 65:35 concentrate-to-forage ratio, 31 cows exhibited SARA symptoms (rumen fluid pH $<$ 5.8 for $>$330 min/day). Comparable results have been reported in dairy goats [23-24]. Furthermore, severe variation in rumen acidosis severity exists among individual lactating cows postpartum, independent of feed intake, diet composition, and rumen volatile fatty acid (VFA) concentration and profile [25]. These studies confirm that under identical dietary conditions, significant inter-individual differences in SARA risk exist, likely regulated by intrinsic physiological factors rather than nutrient supply.

2.1 Feeding Behavior

Rumen buffering capacity primarily originates from saliva produced during chewing, bicarbonate secreted by rumen epithelium, and ammonia generated from dietary degradation in the rumen [26]. These buffers are crucial for stabilizing rumen fluid pH and supporting microbial growth and nutrient digestion. Saliva represents the primary source of rumen buffers, with phosphate and bicarbonate buffer systems in high-producing dairy cows neutralizing approximately 37% of hydrogen ions in the rumen [27]. Saliva secretion in ruminants depends mainly on chewing time (sum of eating and ruminating time). Research indicates substantial inter-individual variation in feeding behavior among ruminants, including eating rate, rumination activity, and feed sorting behavior [28-29].

Giger-Reverdin et al. [24] reported that dairy goats fed a 60:40 concentrate-to-forage diet had an average chewing index (chewing time/dry matter intake) of 4.05 h/kg, but individual values ranged from 1.83 to 6.30 h/kg. In another study with dairy goats (n=12) fed a 65:35 concentrate-to-forage diet, fast-eating individuals showed rumen fluid pH fluctuations of 5.25–6.25 at 13 hours post-feeding, while slow-eating individuals maintained pH between 6.25–6.50, demonstrating that rapid eating increased SARA risk despite identical diet composition [30]. Feed sorting is an inevitable issue in ruminant feeding management. Long-term sorting behavior leads to unbalanced nutrient intake, digestive metabolic disorders, and nutritional metabolic diseases such as diarrhea, laminitis, and liver abscesses [31], causing substantial losses to the livestock industry. Consequently, studies have attempted to reduce or eliminate sorting behavior through dietary structure modifications and feeding strategies [32].

Muhammad et al. [33] found that weaned calves (n=28) exhibited significantly greater sorting behavior for long-particle alfalfa hay compared to short-particle hay. Macmillan et al. [21] reported that feeding lactating Holstein cows (n=8) three times daily versus once daily was more effective at reducing sorting behavior and decreased SARA risk in high-producing cows. These studies demonstrate significant inter-individual variation in feeding behavior among animals consuming identical diets. Since feeding behavior affects saliva secretion (via chewing time), nutrient entry rate into the rumen (via eating rate), and nutrient composition (via sorting behavior), these behavioral differences influence rumen fluid pH [Figure 1: see original paper] [34], suggesting that feeding behavior may contribute to inter-individual differences in SARA susceptibility, though definitive conclusions require further investigation.

2.2 Rumen Epithelial Transport Function

Rumen fluid pH fluctuation results from the combined effects of organic acid (VFA and lactate) production, absorption, efflux, and buffer neutralization in the rumen [Figure 1: see original paper]. VFA removal primarily occurs through rumen epithelial absorption, accounting for 50–85% of total VFA production [26]. During adaptation to high-grain diets, ruminants undergo morphological and functional changes in rumen epithelium, including altered cellular proliferation and differentiation, absorption and transport functions, and metabolic capacity [35], characterized by reduced thickness of basal, spinous, and granular layers [36-37], increased epithelial permeability [38], and elevated endotoxin levels [39].

Penner et al. [40] found that increasing dietary concentrate levels enhanced rumen epithelial absorption rates of propionate and butyrate in dairy cows by 65.7% (0.35 vs. 0.58 mol/h) and 77.8% (0.18 vs. 0.32 mol/h), respectively. Both in vitro and in vivo studies have demonstrated that increased VFA concentrations and decreased pH affect VFA absorption by rumen epithelial cells [41-42] and expression of genes related to intracellular pH regulation and proton transport [43-44]. Yan et al. [42] reported that moderately increasing dietary concentrate (10% vs. 35%) upregulated expression of genes involved in VFA transport and intracellular pH regulation in goat rumen epithelium, including monocarboxylate transporters (MCT1 and MCT4), anion transporters [DRA, PAT1, and anion exchanger 2 (AE2)], and Na+/H+ exchangers (NHE1, NHE2, and NHE3), thereby promoting VFA absorption. Similarly, Liu et al. [45] found that high-grain diets (65:35) significantly increased MCT1 and Na+/K+-ATPase expression while decreasing MCT4 expression. These results indicate that rumen VFA absorption capacity is regulated by epithelial transporters, with increasing dietary concentrate proportion upregulating expression of NHE1, NHE2, NHE3, and Na+/K+-ATPase, potentially enhancing VFA absorption capacity [46].

Consistent with these findings, Penner et al. [13] induced SARA in sheep through single-dose glucose infusion and observed that SARA-resistant (AR) sheep exhibited more rapid absorption of acetate and butyrate compared to SARA-susceptible (AS) animals, accelerating acid removal from the rumen and increasing rumen fluid pH. Additionally, Schlau et al. [12] reported that differences in rumen fluid pH between AR and AS beef cattle (6.05 vs. 5.59) were primarily associated with rumen VFA concentration (122 vs. 164 mmol/L), but also found significantly higher NHE3 expression in AR animals, while other VFA absorption-related genes (MCT1 and DRA) showed no significant differences. These results suggest that inter-individual variation exists in rumen epithelial transporter gene expression during adaptation to high-concentrate diets. Since transporter expression is simultaneously regulated by rumen fluid pH, VFA composition, and concentration, these differences in gene expression lead to substantial variation in VFA absorption capacity among individuals under identical treatments, representing a potential physiological factor underlying differential SARA susceptibility. Future research should systematically evaluate the mechanisms of SARA variability by integrating rumen fluid pH, organic acid composition, and epithelial transporter expression.

3 Rumen Microbiota and Metabolites in SARA Susceptibility

High-concentrate diets induce SARA and alter rumen microbial community structure. Pyrosequencing analysis revealed that SARA-susceptible groups exhibited significantly lower rumen bacterial richness indices (Chao1 and Ace) and diversity indices (Shannon) compared to resistant groups [47], with bacterial populations showing increased starch-utilizing, lactate-producing, and lactate-utilizing bacteria and decreased fiber-degrading bacteria [48-50]. Rumen protozoa populations also decreased [51]. Since rumen fluid pH environments differ between SARA-susceptible and resistant individuals, and pH directly affects microbial growth and proliferation, we hypothesize that variation in SARA susceptibility influences rumen microbial community structure and fermentation products.

PCR-DGGE-based studies have demonstrated distinct differences in rumen microbial diversity between AR (mean rumen pH = 6.02) and AS (mean rumen pH = 5.55) beef cattle, with AS individuals exhibiting a propionate fermentation tendency [52]. Zhang [47] reported that high-grain-induced SARA significantly decreased relative abundances of Bacteroidetes and Proteobacteria while increasing Firmicutes and Actinobacteria at the phylum level. At the genus level, SARA cows showed significantly reduced relative abundances of *Prevotella*, *Treponema*, *Anaeroplasma*, *Acinetobacter*, and *Papillibacter*, but increased *Ruminococcus*, *Atopobium*, *Bifidobacteria*, and unclassified Clostridiales.

The relationship between rumen metabolites and SARA susceptibility remains unclear. However, metabolomics studies have revealed that individual dairy cows fed identical high-concentrate diets (45:55 concentrate-to-forage ratio) exhibited 2- to 4-fold differences in concentrations of certain rumen metabolites, including acetoacetate, maltose, and formic acid [53], indicating inter-individual variation in rumen metabolites under uniform dietary conditions. Metagenomics and metabolomics technologies have been widely applied to explore rumen microbial information, including species diversity, community structure, metabolic patterns, and functional activity. Mao et al. [50] used 454 pyrosequencing and metabolomics in a goat model to reveal relationships between SARA-associated rumen microbial diversity and metabolome profiles. However, whether differential SARA susceptibility induces changes at the genus and species levels remains unclear, necessitating investigation from microbial genomic and metabolomic perspectives to elucidate variability mechanisms.

Rumen microbial system establishment and stability depend on nutritional and physiological factors affecting the rumen environment. Feeding behavior and rumen epithelial function determine rumen buffering capacity and VFA removal rate, respectively, jointly influencing rumen internal environment parameters such as pH, osmotic pressure, and redox potential. These parameters are both critical factors affecting rumen microbial community structure and primary indicators for diagnosing SARA occurrence and severity. Therefore, clarifying the relationships among feeding behavior, rumen epithelial function, and microbial community is essential for revealing mechanisms underlying inter-individual variation in SARA susceptibility.

4 Summary

Inter-individual differences exist in SARA susceptibility among ruminants, primarily regulated by intrinsic physiological factors. Variation in feeding behavior and rumen epithelial absorption capacity may represent the main nutritional and physiological factors causing differential SARA susceptibility. Future production and research should identify sources and mechanisms of inter-individual SARA susceptibility variation and implement targeted nutritional interventions for different individuals to ensure efficient production and rumen health.

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Note: Figure translations are in progress. See original paper for figures.