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Effect of Prebiotic and Spirulina on Blood Gas Parameters and Acute Phase Proteins in Dairy Cattle with Sub-Acute Ruminal Acidosis

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ABSTRACT

Feeding on a diet that supports high calories maximized milk production in the dairy cattle industry. However, it also decreases rumen pH, leading to widespread sub-acute rumen acidosis (SARA). In the present study, we investigated a novel treatment approach based on safe, non-chemical components and evaluated the anti-SARA efficacy of "2" novel candidates, prebiotics, and spirulina, to prevent unfavorable pH decline in the rumen and hence treatment of SARA. Detailed field diagnosis and rumenocentesis were applied to 210 dairy cows. Suspected cases of SARA were further subjected to biochemical analysis. Only 73 cows were regarded as SARA positive. Thirty days treatment protocol was followed using the addition of prebiotics either alone or in combination with spirulina to diets of SARA-affected cows. The results indicated that the rumen pH, the estimated blood gas parameters (PO2, PCO2, and HCO3-), the glucose level, hepatic enzymes (ALT and AST), lipid profile, and the acute phase reactants (SAA and CRP), were significantly improved in the treated cases, when compared with the non-treated ones ($P \leq 0.05$). Data of the present study have pointed to the beneficial use of prebiotics in combination with spirulina in SARA handling in the dairy cattle industry.

Key words: Sub-acute ruminal acidosis, Treatment, Cattle, Prebiotics, Spirulina.

INTRODUCTION

Sub-acute rumen acidosis (SARA) is considered one of the basic substantial metabolic diseases that affect the dairy industry worldwide. The main cause which is incriminated in outstanding this condition is feeding high concentrate diets, with high input of readily fermentable carbohydrates and low levels of digestible fibers (Brzozowska et al. 2013). However, feeding on diets that conserve high inclusion rates of grains was found to maximize milk production, but it also decreases rumen pH, leading to a widespread prevalence of SARA simultaneously (Brzozowska et al. 2013). The cut-off point which is accepted in SARA recognition is depression of ruminal pH below 5.6 at least 3h/day (Gozho et al. 2005).

As a generalized concept, traditional treatment of SARA condition was mainly relying on symptomatic approach that includes correction the case of acid-base imbalance, alkalizing agents (probably magnesium hydroxide) orally, transfaunation of fluid intravenously, antihistaminic and antibiotics such as Procaine penicillin G (22,000U/kg/day), in order to effectively control the lactate production, mainly by *S. bovis* and Lactobacillus species (Beauchemin et al. 2003). To date, feed additives are put up to control SARA disease as using ionophores like monensin or lasalocid (Garry and McConnel 2002). Recently, live yeast supplementation in the diet was proven to improve rumen fiber degradation in cattle grazing tropical pastures (Sousa et al. 2018). Interestingly, Kumprechtová et al. (2019) also reported positive effects of both live and killed dried yeast in reducing the severity of subacute ruminal acidosis irrespective of its viability and this may also reduce lipopolysaccharides (LPS) content in the rumen (Sun et al. 2021). Yeast cultures are additives composed of live microorganisms that potentiate animal productivity, promote the growth of lactic acid utilizing microorganisms and reduce lactic acid accumulation in the rumen through removing oxygen and increasing the total rumen microflora (Chaucheyras-Durand et al. 2016). Indeed, under field condition, usage of the available chemotherapeutics for Lean et al. (2000) mentioned that using of yeasts and Ionophore (monensin sodium) may

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results in incomplete treatment of such cases with expected recurrency of the condition in affected animals. Thus, administration of feed additives could be the optimal solution for counter in decreases in ruminal bacteria, particularly in animals with digestive disorders (Ma et al. 2020). Moreover, the effects of feed additives on animal nutrition and ruminal fermentation have been studied over the last years. Several studies have documented that supplying animal feed with certain additives points to enhance rumen fermentation traits and increases the DMI in feedlot cattle, received excessive amounts of concentrates (Mobiglia et al. 2021). In this regard, prebiotics are non-digestible carbohydrates that influence host beneficially (Patterson and Burkholder 2003). Lactolytic flora was implied as good enhancers for ruminal lactate-utilizing, through direct addition to feed such as, *Saccharomyces cerevisiae* (Poppy et al. 2012; Khan et al. 2022).

Spirulina is a microalga which is a highly nutritious and potent feed supplement for many agriculturally important animal species (Doreau et al. 2010; Korany et al. 2019; Gul et al. 2022). Also, spirulina has been shown to increase microbial crude protein production and to reduce its retention time within the rumen (Quigley et al. 2009). Moreover, Piovan et al. (2021) found that cows receiving dietary Spirulina had a 21% increase in their milk production. Furthermore, Šimkus et al. (2007) showed an increase in milk fat (between 17.6 and 25.0%), milk protein (up by 9.7%) and lactose (up by 11.7%).

In the current study, we targeted for the possible control of the rumen pH decline in SARA affected dairy cattle and for this, we evaluated the anti-SARA efficacy of two microbiota; Saccharomyces cerevisiae and spirulina, in the treatment strategy, on the expected changes of some selected biochemical parameters (Kulpys et al. 2009).

MATERIALS AND METHODS

All experiments performed in this study were approved by the Research Ethical Committee in the Faculty of Veterinary Medicine, Mansoura University, Egypt (Code No.: Ph.D. /55).

Animals' Data

A number of 210 dairy cows, belonged to 12 farms, were enrolled in this study. All cows were divided into two groups, of which, thirty apparently healthy cows were served as control group, besides 180 cows supposed to clinically suffer SARA condition. The investigated cows were aged (26±5) months old and weighed (560±20). The average values of cows' body condition scores (BCS) were (3.03±0.07) (Edmonson et al. (1989). All cows were studied during the first 60 days of lactation. Animals were fed according to National Research Council (NRC) (concentrate ration and corn silage). Fresh and clean drinking water was supplied ad-libitum.

Field Diagnosis of SARA

Thorough clinical examination of the studied cows was performed and used as a preliminary diagnosis for SARA conditions that were further confirmed by the biochemical diagnosis. Decreased dry matter intake, reduction in rumination, decreasing the daily milk yield, laminitis, diarrhea with general loss of body condition were taken in consideration during the field diagnosis (Patterson 2017). Ruminocentesis was performed for all of the examined cows for actual detection of the rumen pH media as methods described previously by Duffield et al. (2004). The analysis was set using a portable pH-meter (Horiba, B-213, Kyoto, Japan). Depending on the findings of the rumen fluid analysis pH, suspected cases with SARA disease, (pH<5.5) (Khafipour et al. 2009b), were included for further analytical investigation, while the other cases were excluded.

Blood Samples

Individual blood samples (10mL) were collected from all studied dairy cows from the jugular vein, where (7mL) of the collected blood were received in anticoagulant free tubes to get sera needed for the biochemical examination, while the other blood sample (3mL) was kept in sodium fluoride tubes for rapid glucose analysis. Additionally, (3mL) blood samples were collected from all investigated cows via the tail coccygeal artery using ventilated syringes with 23 G × 1 needle, containing freeze-dried lithium heparin for blood gas analysis. Samples were kept in ice box and rapidly sent to the laboratory for further analysis.

Biochemical Examination

All oxygenated blood samples were immediately analyzed in a calibrated blood gas analyzer (“Stat Profile pH Ox” blood gas analyzer, Nova Biomedical Corp., USA), set at the body temperature of the cow. The following parameters were determined; blood pH, partial pressure of Oxygen (PO2), partial pressure of carbon dioxide (PCO2), bicarbonate level (HCO3−), base excess (BE-B), and electrolytes; Sodium (Na) (mmol/L), Potassium (k) (mmol/L) and Calcium (Ca) (mmol/L). All measurements were calculated following the method descried by Gianesella et al. (2010).

Serum samples were separated by centrifugation at 3000 rpm for 10 minutes. The clear sera were received in dry sterile sample tube using sterilized pipettes, processed directly for assessing glucose concentration using the GOD/PAP test kit (Merit Choice Bioengineering Co., Ltd., Beijing, China) (Samanc et al. 2011) and the enzymatic activities of liver markers; alanine transaminase (ALT), and aspartate transaminase (AST) (Stojević et al. 2005). Furthermore, serum triglycerides (TG) and total cholesterol concentrations were measured following the kit instructions (Shensuo Unf Medical Diagnostic Article Co., Ltd., Shanghai, China (Kaneko et al. 2008). Additionally, the non-esterified fatty acid (NEFA) concentration was estimated using commercially available kit (Sekisui Medical Co., Ltd., Tokyo, Japan) (Duffield et al. 2009). The β-hydroxybutyrate (β-HBA) was quantified using the kit: (Jingyuan Medical Co., Ltd., Shanghai, China) (Ospina et al. 2010). The high density lipoprotein (HDL) was measured as previously described by Qiu et al. (2022). Finally, the acute phase proteins; albumin, haptoglobulin (Hp) and serum amyloid A (SAA) were measured using commercially available ELISA kits, Hp: ml002480; SAA: ml002466; Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China) as described by Gozho et al. (2005), meanwhile, the C-reactive protein (CRP) was determined using mispa-i2 according to Tietz (1995).

Treatment

Next generation prebiotics powder (Ecocell prebioticsR; Nile Vet Company, Egypt) containing derived cell wall of saccharomyces cerevisiae, with Mannan Oligosaccharides (MOS) enforced by extract of the root of chicory, β glucans and inulin (FOS), was used in a dose of 0.5kg/Ton in feed. Moreover, flash start- spirulina powder (Amoun Vet Company, Egypt, 250gm) was used in a dose rate of 1kg/Ton, added to feed for dairy cattle (Christaki et al. 2012).

Statistical Analysis

Statistical analysis was carried out by a commercial software program (SPSS for windows version 16, USA. For continuous data (biochemical and blood gas analysis) (One-way Analysis of Variance (ANOVA) with post- hock Duncan multiple comparison test was used. For all results $P \leq 0.005$ was considered significant.

RESULTS

In the present study, we investigated the presence of SARA in dairy cows in Egypt. Of 210 cows, only 73 cows were found to endure the typical criteria of SARA condition. In atrial to find the best control strategy for SARA in cows, treatment by prebiotics were used. Several biochemical variables were monitored in these cows including PO2, PCO2, HCO_3^-, BE-B, Na, k, Ca, AST, ALT, TG, cholesterol, NEFA, HDL, β-HBA, glucose, potassium, Hp, SAA, and CRP either pre- or post the treatment.

Data of the blood gas analysis revealed significant changes between healthy and SARA affected cows on the zero day, where significant decrease of rumen Ph and HCO3- were recorded in SARA affected cases with significant increase in PO2 ($P<0.05$) (Table 1). Of note, treatment with prebiotics alone or in conjugation with spirulina for 30 days normalized the levels of PH, and selected blood gas parameters including PO2, PCO2, and HCO_3^- (Table 1).

SARA affected cows exhibited significant increase ($P<0.05$) in the estimated glucose level and liver enzymes (ALT and AST), as compared with healthy cows ($P<0.05$) (Table 1). Similarly, diseased cows exhibited significant increase ($P<0.05$) in TG, cholesterol, and HDL levels in comparison with healthy cows ($P<0.05$) (Table 1). On contrary, NEFA, and β-HBA levels were significantly decreased ($P<0.05$) in cows with SARA in comparison with the healthy ones (Table 2). Treatment of cows with either probiotic alone or probiotic combined with spirulina normalized the levels of glucose, AST, ALT, and β-HBA (Table 2). Treatment with probiotic alone normalized the levels of TG, cholesterol, HDL, and NEFA (Table 2). In astonishing way, adding spirulina to the probiotic significantly decreased ($P<0.05$) these parameters (TG, cholesterol, HDL, and NEFA) in treated cows (Table 2).

For the acute phase reaction in cows with SARA, SARA leading to significant increase ($P<0.05$) in SAA, and CRP levels in comparison with the healthy cows (Table 3). Our obtained results revealed the non-significant effect ($P>0.05$) of SARA on HP levels in cows (Table 3). Notably, treatment with probiotic normalized the selected APPs parameters (Table 3). The obtained data highlighted the significant role of either probiotic alone or combined with spirulina in the treatment of SARA in cows.

DISCUSSION

Nowadays, high-yield lactating dairy cows are always fed with high proportion of rapidly fermentable non-fiber carbohydrates, which affect the ruminal pH stabilization (Wang et al. 2019). It is commonly known that, the best prevention of any fermentative disorder in the fore stomach has been brought with proper feeding management (Plaizier et al. 2008). In this study, (73) cows suffered SARA were diagnosed basing on the rumen pH depression between 5.2 and 5.6 for more than 180 min/d, laminitis, feed intake and milk production depression (Gozho et al. 2005). The recorded significant changes in the blood gas profile of SARA cases were matched with those mentioned by González et al. (2012).

As SARA has been viewed as a direct consequence from maximizing energy intake to reach the economic point of the high milk yield, the use of a promising novel feed resource should have high nutritive value and a good conversion efficiency as well (Poppi and McLennan 2010). A one proposition to make a good balance between the highly energized diet, needed for the efficient productivity, and the lowest resulted repercussions was to apply additives to cows' diets which are supposed to minimize the outcome changes in the ruminal pH value. For this, feed additives such as exogenous buffers, ionophores like monensin and lasalocid are implied to control SARA disease in dairy cattle industry (Garry and McConnel 2002). Our study evaluated a novel pattern for the treatment of SARA in cows using, Saccharomyces cerevisiae and spirulina. Usually, prebiotics are assumed to offer a selective effect on the host microbiota which leads to their improved health. When prebiotics are not well fermented, they often exert an osmotic response in the host GIT, whereas once they are effectively fermented by GIT flora shows higher metabolic gas production and exert its prebiotic effect (Yadav et al. 2022). Besides prebiotic and balanced amino acids source, algae derived compounds implied as therapeutics owing to comprising bioactive properties to elicit immunomodulatory, antioxidative, anticancerous, anticoagulant, hepato-protective, and antihypertensive responses (Burdick Sanchez et al. 2021).

Blood gas analysis is a valuable tool to diagnose acidemia in dairy cattle because it provides a good definite assessment for the acid-base imbalance situation of the body (Gianesella et al. 2010). Our results recorded significant variations in the blood pH, pCO2, pO2, and HCO3- levels, reflecting the effects of the body buffering systems, which represent one of the mechanisms to maintain the blood pH balance within a physiological range. Our data recorded a reduction in the estimated blood pH in cattle categorized to be SARA positive.

In fact, during SARA, as a first response to the lowered blood pH, there is a shift in the oxy-hemoglobin dissociation curve, where the red blood cells release oxygen to the tissues more readily to conserve the normal physiological functions of body cells. This would result in reduction of the (pO2) and an increase in (pCO2) in the blood circulation and subsequently, the HCO3- level (Jones 2010). At this point, the excess level of (pCO2) stimulates

Table 1: Determination of the effect of prebiotic and spirulina on blood gas analysis and electrolytes in cattle with sub-acute ruminal acidosis

	0 day		30 day	
Parameters	Healthy Cows	SARA	Prebiotic	Prebiotic+Spirulina
PH	7.54±0.67a	5.33±0.44b	7.49±0.03a	7.54±0.051a
PCO_2 (mmHg)	34 ±2.05a	39.14±1.29b	35.93±2.26a	32.87±2.51a
PO_2 (mmHg)	86.2±3.21a	161.48±3.27b	82.03±3.86a	81.22±3.11a
HCO_3^- (mmol/L)	27.5±1.3a	14.92±9.05b	26.06±2.15a	27.76±0.15a
BE (mmol/L)	3.07±1.77a	3.69±1.08 a	4.8±0.75 a	5.23±0.15 a
Na (mmol/L)	1.35±1.91a	1.37±5.07a	1.34±2.5a	1.38±0.57a
K (mmol/L)	3.98±0.39a	3.85±0.31a	4.27±0.06a	4.15±0.04a
iCa (mmol/L)	1.09±0.069a	1.19±0.23a	1.13±0.14a	1.06±0.02a

Values (mean±SD) with different letters in the same row differ significantly (P<0.05). Abbreviations: Oxygen (PO_2), partial pressure of carbon dioxide (PCO_2), bicarbonate level (HCO_3^-), the base excess (BE), in addition to some electrolytes including sodium (Na) (mmol/L), potassium (k) (mmol/L), ionized calcium (Ca) (mmol/L).

Table 2: Determination of the effect of prebiotic and spirulina on biochemical parameters in cattle with sub-acute ruminal acidosis

	0 day		30 day	
Parameters	Healthy Cows	SARA	Prebiotic	Prebiotic+Spirulina
Glucose (mg/dl)	1.21±0.14a	2.09±0.55b	1.25±0.31a	1.15±0.05a
ALT (U/L)	4.08±1.75a	9.39±3.45b	3.41±1. 90 a	2.57±0.50a
AST (U/L)	50.68±1.51a	87.72±1.28b	56.93±1.64a	49.79±9.63a
TG (mg/dl)	33.19±5.08b	43.44±5.13c	35.2±2.04b	21.89±3.48a
Cholesterol (mg/dl)	1.82±0.46b	2.93±0.67c	1.48±0.38b	0.67±0.21a
HDL (mg/dl)	4.38±0.24a	6.10 ±1.73b	4.24±0.54a	3.91±0.24a
NEFA (mmol/l)	90.26±1.57b	35.22±2.12c	80.75±1.59b	56.55±5.71a
β-HBA (mmol/l)	35.94±1.60a	11.37±3.38b	30.51±7.13a	23.96±7.25a

Values (mean±SD) with different letters in the same row differ significantly (P<0.05): The obtained values represent the mean±SD. Abbreviations: Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Triglycerides (TG), High- density lipoprotein (HDL), Non-esterified fatty acids (NEFA) and β-hydroxybutyrate (β-HBA).

Table 3: Determination the effect of prebiotic and spirulina on acute phase protein levels in cattle with sub-acute ruminal acidosis

	0 day		30 day	
Parameters	Healthy Cows	SARA	Prebiotic	Prebiotic+Spirulina
Albumin (g/ dl)	0.40±0.16a	0.33±0.62a,b	0.23±0.09a	0.18±0.06a
HP (g/L)	3.40±0.44a	3.80±0.10a	3.10±0.12a	3.10±0.25a
SAA (mg/L)	68.29±3.9a	85.6±1.39c	65.05±6.59b	45.5±1.12a
CRP (mg/L)	1.47±6.65a	2.07±2.53b	1.62±9.03a	1.50±2.11b

Values (mean±SD) with different letters in the same row differ significantly (P<0.05): The obtained values represent the mean±SD. Abbreviations: Serum Amyloid A (SAA), the haptoglobin (HP) and the C-reactive protein (CRP).

the respiratory center to start a buffering mechanism through hyperventilation to increase the (pO2) and to get rid of the excess (pCO2). Data of the current work showed a significant increase in (pO2), and an actual decrease in the (HCO3-) concentrations, which guide for trials of compensatory mechanism displayed by the respiratory system, that further supposed to be perfected by increasing the bicarbonate elimination through the kidney buffering system (Constable et al. 2017). These findings come to fit nicely to those reported by Bevans et al. (2005).

The obtained data revealed a reverse correction of the blood gas parameters in cows affected by SARA after the followed treatment regimen as compared with healthy ones. This results could be attributed to that, the cells of Saccharomyces cerevisiae provide growth factors for rumen microbiota including oligosaccharides, organic acids, B complex vitamins and amino acids, which potentiate the microbial growth in the rumen, thereby indirectly stabilize ruminal pH and thus inhibit lactic acid producing bacteria (Piñeiro et al. 2008). Furthermore, spirulina actively introduce a more alkalizing effect into the cows' feed (Marín et al. 2009).

The elevated level of blood glucose in the pre-treated cases may be a result of the considerable variations in dietary patterns and the stress related glucocorticoid effect. Additionally, the highest concentration of liver enzymes noticed with SARA cases might be attributed to liver damage due to fatty infiltration and microabscess formations in the liver cells (Kaneko et al. 2008). Continuing the improved profiles, blood glucose level and the tested liver enzymes showed a significant decrease in the treated cases. These findings could be due to the fact that prebiotics undergo a fermentation process by the beneficial microbial flora in the large intestine, providing new sources of energy for further microflora growth (Gibson et al. 2017). Moreover, the hepato-protective effect of spirulina may be due to it's chemical composition, which includes C-phycocyanin, β-carotene, and vitamin E content that elicits antioxidant and anti-inflammatory effects on the hepatocytes (Howe et al. 2006).

The lipid profile showed marked alterations before and after treatment either with prebiotic alone or both of them. During SARA, there was significant elevation of serum TG, cholesterol and HDL, while significant decreased values of NEFA and β-HBA levels were detected (Neubauer et al. 2018). This may be indicative for an altered energy status of the cattle reflecting a high level of carbohydrates supplying and also that could be resulted from the stress related glucocorticoid release (Puppel et al. 2019).

Hepatic insufficiency, accompanied with elevated serum liver enzymes, could be a cause for alterations of liver metabolism (Ospina et al. 2010). Moreover, the high level of blood glucose in SARA affected cases could have lowered the β-HBA concentration. These findings were in agreement with those mentioned by van Knegsel et al. (2005). On the other side, after treatment, our results revealed a significant decrease in serum TG, cholesterol and HDL levels in the cows' group received prebiotic only, whilst there was marked significant decrease in cows received prebiotic and Spirulina (Saadaoui et al. 2021). These outcomes might be attributed to the large quantities of antioxidants such as creatine, phycocyanin, unsaturated fatty acids, particularly linolenic acid, omega-3 and omega-6 fatty acids, and phenolic in spirulina which modify cholesterol level, glucose uptake and expand the antioxidant capacity as previously explained by Moura et al. (2011).

Concerning the serum protein profile, there was a mild hypoalbuminemia in SARA affected group. Such decrease might be attributed to the effect of endotoxins produced from the rumen on the performance of the liver of the affected cows (Sevinc et al. 2001).

For the APR in cows with SARA, the current work studied levels of the APPs that could ameliorate the inflammatory cascades in SARA affected cases. During low rumen pH, bacterial cells are lysed more rapidly, increasing the concentration of LPS in the rumen and cause massive disruption of the ruminal epithelial tight junctions (Khafipour et al. 2009a). When LPS are released in large quantities, they induce an acute phase response mediated by some inflammatory proteins. Additionally, Gruys et al. (2005) reported a positive acute phase response associated with a change in the metabolic pattern. In fact, stress also has a role in activating latent infections through the activation of the hypothalamic–pituitary–adrenal (HPA) axis augmenting hepatic acute phase protein synthesis and release into the bloodstream. Regarding this, we monitored a significant elevation in the SAA and C-RP levels in SARA affected cases that could reflect a case of positive acute phase proteins. These findings are similar to those reported before by Heegaard et al. (2000); Khafipour et al. (2009a) and Li et al. (2013). Also, there was an evidence that physical stress in cattle can induce acute phase response (APR) (Lomborg et al. 2008) through activation of the hypothalamic–pituitary–adrenal (HPA) axis augmenting the hepatic APP synthesis and release into the bloodstream (Murata et al. 2004). Into the bargain, this inflammation could be initiated by the dietary-induced damage of the gut mucosa and translocation of immunogenic compounds such as free LPS into circulation and lysis of gram-negative bacteria (Nagaraja and Titgemeyer 2007; Plaizier et al. 2008). A previous study showed that being fed with high concentrate diets is simultaneous with activation of a non-specific acute phase reaction (APR) in cows (Tana et al. 2018) triggering the activation of a systemic APR due to the translocation of LPS into the blood of systemic circulation stimulates the release of proinflammatory cytokines, such as IL-1, IL-6, and TNF-α by liver macrophages (Puppel et al. 2019).

In the present study, after treatment, the obtained results highlight that there was a significant decrease in these acute inflammatory reactants. These findings could be attributed to production of short chain fatty acids (SCFA), including butyrate, which may sluggish cytokine production within the intestinal mucosa (Sartor 2004).

Conclusion

Sub-acute rumen lactic acidosis continues to be one of the most impetrative metabolic conditions affecting dairy cattle industry worldwide. Big and continuous trials are still performed to build up strategies for the most effective control of the condition. In our study, for the first time, we tried to use prebiotics represented in Saccharomyces cerevisiae either alone or in combination with spirulina as potent modifiers for SARA disease under field condition. Data were summarized as; prebiotic and spirulina significantly affect the selected biochemical variables in cattle with SARA, where correction of the rumen pH, PO2, PCO2 and HCO3- levels, in addition to limitation of the concurrent acute phase response were detected, the matter that implies for further research work based on evaluating other microbial therapy instead of the routinely used chemical therapy alone.

Author Contributions

Conceptualization: SA, MAR. Data curation: SA, MAY, MAR. Formal analysis: SA, MAR. Funding acquisition: SA, MAR. Investigation: MAR. Methodology: SA, MAY, MAR. Project administration: MAR. Resources: SA, MAR, MME. Software: MAR. Supervision: EME, MAY, MAR. Validation SA, MAY, MAR. Visualization: MAY, MAR. Writing – original draft: SA, MAR. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest

REFERENCES

Beauchemin KA, Yang WZ, Morgavi DP, Ghorbani GR, Kautz W and Leedle JAZ, 2003. Effects of bacterial direct-fed microbials and yeast on site and extent of digestion, blood chemistry, and subclinical ruminal acidosis in feedlot cattle. Journal of Animal Science 81: 1628-1640. https://doi.org/10.2527/2003.8161628x

Bevans D, Beauchemin K, Schwartzkopf-Genswein K, McKinnon J and McAllister T, 2005. Effect of rapid or gradual grain adaptation on subacute acidosis and feed intake by feedlot cattle. Journal of Animal Science 83: 1116-1132. https://doi.org/10.2527/2005.8351116x

Brzozowska A, Sloniewski K, Oprzadek J, Sobiech P and Kowalski Z, 2013. Why are dairy cows not able to cope with the subacute ruminal acidosis? Polish Journal of Veterinary Sciences 16. https://doi.org/10.2478/pjvs-2013-0116

Burdick Sanchez NC, Broadway PR and Carroll JA, 2021. Influence of yeast products on modulating metabolism and immunity in cattle and swine. Animals 11: 371. https://doi.org/10.3390/ ani11020371

Chaucheyras-Durand F, Ameilbonne A, Bichat A, Mosoni P, Ossa F and Forano E, 2016. Live yeasts enhance fibre degradation in the cow rumen through an increase in plant substrate colonization by fibrolytic bacteria and fungi. Journal of Applied Microbiology 120: 560-570. https://doi.org/10.1111/jam.13005

Christaki E, Karatzia M, Bonos E, Florou-Pan P and Karatzias C, 2012. Effect of dietary *Spirulina platensis* on milk fatty acid profile of dairy cows. Asian Journal of Animal and Veterinary Advances 7: 597-604. https://doi.org/10.3923/ajava.2012.597.604

Constable PD, Hinchcliff KW, Done SH and Grünberg W, 2017. Veterinary medicine: a textbook of the diseases of cattle, horses, sheep, pigs, and goats. In: Constable PD, Hinchcliff KW, Done SH and Grünberg W (eds), Veterinary Medicine, 11th Ed. Elsevier Ltd, USA; pp: 2217–2219.

Doreau M, Bauchart D and Chilliard Y, 2010. Enhancing fatty acid composition of milk and meat through animal feeding. Animal Production Science 51: 19-29. https://doi.org/10.1071/AN10043

Duffield T, Plaizier JC, Fairfield A, Bagg R, Vessie G, Dick P, Wilson J, Aramini J and McBride B, 2004. Comparison of techniques for measurement of rumen pH in lactating dairy cows. Journal of Dairy Science 87: 59-66. https://doi.org/10.3168/jds.s0022-0302(04)73142-2

Duffield TF, Lissemore KD, McBride BW and Leslie KE, 2009. Impact of hyperketonemia in early lactation dairy cows on health and production. Journal of Dairy Science 92: 571-580. https://doi.org/10.3168/jds.2008-1507

Edmonson AJ, Lean IJ, Weaver LD, Farver T and Webster G, 1989. A body condition scoring chart for Holstein dairy cows. Journal of Dairy Science 72: 68-78. https://doi.org/10.3168/jds.s0022-0302(89)79081-0

Garry FB and McConnel C, 2002. Indigestion in Ruminants, In: Large Animal Internal Medicine, 3rd Ed. (ed. Smith BP), Mosby, Baltimore, USA; pp: 722–747.

Gianesella M, Morgante M, Stelletta C, Ravarotto L, Giudice E and Van Saun RJ, 2010. Evaluating the effects of rumenocentesis on health and performance in dairy cows. Acta Veterinaria Brno 79: 459-468. https://doi.org/10.2754/avb201079030459

Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, Scott K, Stanton C, Swanson KS, Cani PD, Verbeke K and Reid G, 2017. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nature Reviews Gastroenterology & Hepatology 14: 491-502. https://doi.org/10.1038/ nrgastro.2017.75

González LA, Manteca X, Calsamiglia S, Schwartzkopf-Genswein KS and Ferret A, 2012. Ruminal acidosis in feedlot cattle: Interplay between feed ingredients, rumen function and feeding behavior (a review). Animal Feed Science and Technology 172: 66-79. https://doi.org/10.1016/j.anifeedsci.2011.12.009

Gozho G, Plaizier J, Krause D, Kennedy A and Wittenberg K, 2005. Subacute ruminal acidosis induces ruminal lipopolysaccharide endotoxin release and triggers an inflammatory response. Journal of Dairy Science 88: 1399-1403. https://doi.org/10.3168/jds.S0022-0302(05)72807-1

Gruys E, Toussaint M, Niewold T and Koopmans S, 2005. Acute phase reaction and acute phase proteins. Journal of Zhejiang University Science B 6: 1045. https://doi.org/10.1631/jzus.2005.B1045

Gul ST, Mahmood S, Bilal M, Saleemi MK, Imran M and Zubair M, 2022. Acute phase proteins as biomarkers in perspective to animal diseases diagnosis. Agrobiological Records 9: 45-57. https://doi.org/10.47278/journal.abr/2022.013

Heegaard PM, Godson DL, Toussaint MJ, Tjørnehøj K, Larsen LE, Viuff B and Rønsholt L, 2000. The acute phase response of haptoglobin and serum amyloid A (SAA) in cattle undergoing experimental infection with bovine respiratory syncytial virus. Veterinary Immunology and Immunopathology 77: 151-159. https://doi.org/10.1016/s0165-2427(00)00226-9

Howe P, Meyer B, Record S and Baghurst K, 2006. Dietary intake of long-chain ω-3 polyunsaturated fatty acids: contribution of meat sources. Nutrition 22: 47-53. https://doi.org/10.1016/j.nut.2005.05.009

Jones MB, 2010. Basic interpretation of metabolic acidosis. Critical Care Nurse 30: 63-69. https://doi.org/10.4037/ccn2010521

Kaneko JJ, Harvey JW and Bruss ML, 2008. Preface: Clinical Biochemistry of Domestic Animals. Elsevier. https://doi.org/10.1016/b978-0-12-370491-7.00031-3

Khafipour E, Krause D and Plaizier J, 2009a. Alfalfa pellet-induced subacute ruminal acidosis in dairy cows increases bacterial endotoxin in the rumen without causing inflammation. Journal of Dairy Science. 92: 1712-1724. https://doi.org/10.3168/jds.2008-1656

Khafipour E, Krause DO and Plaizier JC, 2009b. Alfalfa pellet-induced subacute ruminal acidosis in dairy cows increases bacterial endotoxin in the rumen without causing inflammation. Journal of Dairy Science 92: 1712-1724. https://doi.org/10.3168/jds.2008-1656

Khan SZ, Khan I, Aimen UE, Ali A, Abidullah, Safiullah, Imdad S, Atta-ur-Rehman, Israr-ud-Din and Waseemullah, 2022. Effect of dietary supplementation of *Saccharomyces cerevisiae* on growth performance and cost of feeding in Damani goat kids. Agrobiological Records 8: 7-12. https://doi.org/10.47278/journal.abr/2022.002

Korany RMS, Ahmed KS, El Halawany HA and Ahmed KA, 2019. Pathological and immunohistochemical studies on the ameliorating effect of *Spirulina platensis* against arsenic induced reproductive toxicity in female albino rats. International Journal of Veterinary Science 8: 113-119.

Kulpys J, Paulauskas E, Pilipavicius V and Stankevicius R, 2009. Influence of cyanobacteria Arthrospira (Spirulina) platensis biomass additive towards the body condition of lactation cows and biochemical milk indexes. Agronomy Research 7: 823-835.

Kumprechtová D, Illek J, Julien C, Homolka P, Jančík F and Auclair E, 2019. Effect of live yeast (Saccharomyces cerevisiae) supplementation on rumen fermentation and metabolic profile of dairy cows in early lactation. Journal of Animal Physiology and Animal Nutrition 103: 447-455. http://doi.org/10.1111/jpn.13048

Lean I, Wade L, Curtis M and Porter J, 2000. New approaches to control of ruminal acidosis in dairy cattle. Asian Australasian Journal of Animal Sciences 13: 266-269

Li S, Danscher A and Plaizier J, 2013. Subactue Ruminal Acidosis (SARA) in dairy cattle: new developments in diagnostic aspects and feeding management. Can Journal Animal Science 94: 353-364. https://doi.org/10.1016/j.als.2016.11.006

Lomborg SR, Nielsen LR, Heegaard PMH and Jacobsen S, 2008. Acute phase proteins in cattle after exposure to complex stress. Veterinary Research Communications 32: 575-582. https://doi.org/10.1007/s11259-008-9057-7

Ma Zhen-Zhu, Cheng Yu-Yang, Wang Sheng-Qi, Ge Jian-Zhen, Shi Huai-Ping and Kou JC, 2020. Positive effects of dietary supplementation of three probiotics on milk yield, milk composition and intestinal flora in Sannan dairy goats varied in kind of probiotics. Journal of Animal Physiology and Animal Nutrition 104: 44-55. https://doi.org/10.1111/jpn.13226

Marín A, Casas-Valdez M, Carrillo S, Hernández H, Monroy A, Sanginés L and Pérez-Gil F, 2009. The marine algae Sargassum spp. (Sargassaceae) as feed for sheep in tropical and subtropical regions. Revista de Biología Tropical 57: 1271-1281. https://doi.org/10.15517/RBT.V57I4.5464

Mobiglia AM, Camilo FR, Couto VRM, Castro FGF, Drouillard JS, Gouvêa VN and Fernandes JJR, 2021. Effects of grain adaptation programs and antimicrobial feed additives on performance and nutrient digestibility of Bos indicus cattle fed whole shelled corn. Translational Animal Science 5: txab119. https://doi.org/10.1093/tas/txab119

Moura LP, Puga GM, Beck WR, Teixeira IP, Ghezzi AC, Silva GA and Mello MAR, 2011. Exercise and spirulina control non-alcoholic hepatic steatosis and lipid profile in diabetic Wistar rats. Lipids in Health and Disease 10: 77-77. https://doi.org/10.1186/1476-511X-10-77

Murata H, Shimada N and Yoshioka M, 2004. Current research on acute phase proteins in veterinary diagnosis: an overview. The Veterinary Journal 168: 28-40. http://doi.org/10.1016/S1090-0233(03)00119-9

Nagaraja TG and Titgemeyer EC, 2007. Ruminal acidosis in beef cattle: The current microbiological and nutritional outlook. Journal of Dairy Science 90: E17-E38. https://doi.org/10.3168/jds.2006-478

Neubauer V, Petri R, Humer E, Kröger I, Mann E, Reisinger N, Wagner M and Zebeli Q, 2018. High-grain diets supplemented with phytogenic compounds or autolyzed yeast modulate ruminal bacterial community and fermentation in dry cows. Journal of Dairy Science 101: 2335-2349. https://doi.org/10.3168/jds.2017-13565

Ospina PA, Nydam DV, Stokol T and Overton TR, 2010. Evaluation of nonesterified fatty acids and β-hydroxybutyrate in transition dairy cattle in the northeastern United States: Critical thresholds for prediction of clinical diseases. Journal of Dairy Science 93: 546-554. https://doi.org/10.3168/jds.2009-2277

Patterson C, 2017. Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. 11th Ed, Volume 2; pp: 1116.

Patterson JA and Burkholder KM, 2003. Application of prebiotics and probiotics in poultry production. Poultry Science 82: 627-631. https://doi.org/10.1093/ps/82.4.627

Piñeiro G, Perelman S, Guerschman JP and Paruelo JM, 2008. How to evaluate models: Observed vs. predicted or predicted vs. observed? Ecological Modelling 216: 316-322. https://doi.org/10.1016/j.ecolmodel.2008.05.006

Piovan A, Battaglia J, Filippini R, Dalla Costa V, Facci L, Argentini C, Pagetta A, Giusti P and Zusso M, 2021. Pre- and Early Post-treatment With *Arthrospira platensis* (Spirulina) extract impedes lipopolysaccharide-triggered neuroinflammation in microglia. Frontiers in Pharmacology 12: 724993. https://doi.org/10.3389/ fphar.2021.724993

Plaizier J, Krause D, Gozho G and McBride B, 2008. Subacute ruminal acidosis in dairy cows: the physiological causes, incidence and consequences. The Veterinary Journal 176: 21-31. https://doi.org/10.1016/j.tvjl.2007.12.016

Poppi DP and McLennan SR, 2010. Nutritional research to meet future challenges. Animal Production Science 50: 329. https://doi.org/10.1071/an09230

Poppy GD, Rabiee AR, Lean IJ, Sanchez WK, Dorton KL and Morley PS, 2012. A meta-analysis of the effects of feeding yeast culture produced by anaerobic fermentation of *Saccharomyces cerevisiae* on milk production of lactating dairy cows. Journal of Dairy Science 95: 6027-6041. https://doi.org/10.3168/jds.2012-5577

Puppel K, Gołębiewski M, Solarczyk P, Grodkowski G, Slósarz J, Kunowska-Slósarz M, Balcerak M, Przysucha T, Kalińska A and Kuczyńska B, 2019. The relationship between plasma β-hydroxybutyric acid and conjugated linoleic acid in milk as a biomarker for early diagnosis of ketosis in postpartum Polish Holstein-Friesian cows. BMC Veterinary Research, 15: 367. https://doi.org/10.1186/s12917-019-2131-2

Qiu X, Qin X, Chen L, Chen Z, Hao R, Zhang S, Yang S, Wang L, Cui Y, Li Y, Ma Y, Cao B and Su H, 2022. Serum biochemical parameters, rumen fermentation, and rumen bacterial communities are partly driven by the breed and sex of cattle when fed high-grain diet. Microorganisms10: 323. https://doi.org/10.3390/microorganisms10020323

Quigley S, Poppi D and McLennan S, 2009. Strategies to increase growth of weaned Bali calves. Project Report. Australian Centre for International Agricultural Research.

Saadaoui I, Rasheed R, Aguilar A, Cherif M, Al Jabri H, Sayadi S and Manning SR, 2021. Microalgal-based feed: promising alternative feedstocks for livestock and poultry production. Journal of Animal Science and Biotechnology 12: 76. https://doi.org/10.1186/s40104-021-00593-z

Samanc H, Kirovski D, Stojic V, Stojanovic D, Vujanac I, Prodanovic R and Bojkovic-Kovacevic S, 2011. Application of the metabolic profile test in the prediction and diagnosis of fatty liver in Holstein cows. Acta Veterinaria 61: 543-553. https://doi.org/10.2298/avb1106543s

Sartor RB, 2004. Therapeutic manipulation of the enteric microflora in inflammatory bowel diseases: antibiotics, probiotics and prebiotics. Gastroenterology 126: 1620-1633. https://doi.org/10.1053/j.gastro.2004.03.024

Sevinc M, Basoglu A, Birdane F and Boydak M, 2001. Liver function in dairy cows with fatty liver. Revue de Medecine Veterinaire (France): https://doi.org/10.1016/s0749-0720(15)31048-3

Šimkus A, Oberauskas V, Laugalis J, Želvytė R, Monkevičienė I, Sederevičius A, Šimkienė A and Pauliukas K, 2007. The effect of weed Spirulina platensis on the milk production in cows. Veterinarija ir Zootechnika 38: 74-77.

Sousa DO, Oliveira CA, Velasquez AV, Souza JM, Chevaux E, Mari LJ and Silva LFP, 2018. Live yeast supplementation improves rumen fibre degradation in cattle grazing tropical pastures throughout the year. Animal Feed Science and Technology 236: 149-158. https://doi.org/10.1016/j.anifeedsci.2017.12.015.

Stojević Z, Piršljin J, Milinković-Tur S, Zdelar-Tuk M and Ljubić BB, 2005. Activities of AST, ALT and GGT in clinically healthy dairy cows during lactation and in the dry period. Veterinarski Arhiv 75: 67-73.

Sun X, Yue W, Erdan W, Shu Z, Qianqian W, Yan Z, Yajing W, Zhijun C, Hongjian Y, Wei W and Shengli L, 2021. Effects of *Saccharomyces cerevisiae* culture on ruminal fermentation, blood metabolism, and performance of high-yield dairy cows. Animals 11: 2401. https://doi.org/10.3390/ani11082401

Tana S, Saraswati TR and Yuniwarti EY, 2018. Hematology and blood chemistry status of most frequently consumed ruminants in community. Biosaintifika: Journal of Biology & Biology Education 10: 341-347. https://doi.org/ 10.15294/biosaintifika.v10i2.12714

Tietz N, 1995. Clinical Guide to Laboratory Tests. 3rd Ed. WB Saunders Company, Philadelphia, pp: 22-23. https://doi.org/10.1111/j.1537-2995.1995.tb03571.x

Van Knegsel ATM, Van den Brand H, Dijkstra J, Tamminga S and Kemp B, 2005. Effect of dietary energy source on energy balance, production, metabolic disorders and reproduction in lactating dairy cattle. Reproduction Nutrition Development 45: 665-688. https://doi.org/10.1051/rnd:2005059

Wang H, Yang H, Hang L, Fei W, Qinghua Q, Wenjing N, Zhibiao G, Huawei S and Binghai C, 2019. Rumen fermentation, intramuscular fat fatty acid profiles and related rumen bacterial populations of Holstein bulls fed diets with different energy levels. Applied Microbiology and Biotechnology 103: 4931-4942. https://doi.org/10.1007/s00253-019-09839-3

Yadav MK, Indu K, Bijender S, Kant SK and Kumar TS, 2022. Probiotics, prebiotics and synbiotics: Safe options for next-generation therapeutics. Applied Microbiology and Biotechnology 106: 505-521. https://doi.org/10.1007/s00253-021-11646-8