Effects of supplementing *Saccharomyces cerevisiae* fermentation products to dairy cows from the day of dry-off through early lactation

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ABSTRACT

The scope of this experiment was to study the effects of *Saccharomyces cerevisiae* fermentation product (SCFP; NutriTek, Diamond V) on milk yield, milk composition, somatic cell count, rumination activity, and immunometabolic profile (inflammation) of dairy cows during the peripartum period. Postpartum inflammation severity was evaluated as the liver functionality index (LFI). The LFI is based on profiles of specific blood inflammatory markers in the first month of lactation. We hypothesized that SCFP could increase the rumination time in dairy cows. Treatments were control (CTR; no supplement, $n = 17$) or SCFP (19 g/d of NutriTek, $n = 17$) included into a pellet delivered at robotic milking unit. Treatments were fed from d -60 to 42 relative to parturition. Cows were fed the same basal rations formulated to pre- or postpartum requirements. Cows were voluntarily milked with robotic milking unit. Blood samples were collected at d -60 , -28 , -7 , 7, and 28 relative to parturition. To study the effect of the treatment and severity of inflammation during periparturient period on subsequent cow performance, cows were retrospectively divided into 2 groups based on their LFI score: low (LLFI) and high (HLFI). Thus, LFI grouping and supplementation treatment groups were as follows: LLFI-CTR, LLFI-SCFP, HLFI-CTR, HLFI-SCFP. Data were analyzed with ANOVA using a mixed model for repeated measures; the model included the effect of the diet, LFI group, time relative to parturition, and their interaction. The nonesterified fatty acids concentrations were greatest at d 7 of lactation for LLFI-CTR compared with other groups. No other differences in plasma metabolites were observed. The LLFI-CTR cows had a greater reduction of body condition score from d -7 until 28 relative to parturition compared with other groups. Somatic cell counts were not different among groups, with averages of 175,

169, 384, and $126 \times 1,000$ cells/mL for the HLFI-CTR, HLFI-SCFP, LLFI-CTR, and LLFI-SCFP group, respectively, regardless of day. However, the LLFI-CTR had greater somatic cell count on d 42 compared with other groups. During the week before parturition, the LLFI-CTR group had reduced rumination time of 46 min compared with the other 3 groups. However, the minutes of rumination per day was only different between LLFI-CTR and the LLFI-SCFP groups. Milk production of cows was different for LFI scores as follows: 50.2 versus 46.7 kg/d for HLFI and LLFI, respectively. Interestingly, there were no differences of milk production due to supplementation treatment of the HLFI cows. However, the LLFI-SCFP group produced 49.1 kg/d compared with 44.3 kg/d of the LLFI-CTR group during the first month of lactation. Milk composition did not differ throughout the experimental period for the 4 groups of cows. In conclusion, SCFP supplementation assisted cows experiencing low LFI to maintain milk production, somatic cell count, and plasma nonesterified fatty acid concentrations similar to cows with high LFI.

Key words: *Saccharomyces cerevisiae* fermentation products, inflammation, postpartum, liver functionality index

INTRODUCTION

Dairy cattle experience inflammation during the postpartum period (Humblet et al., 2006; Trevisi et al., 2012). Liver synthesis of inflammatory positive acute-phase proteins (+APP) increases in the days after parturition, even in cows not necessarily showing clinical signs of disease (Huzzey et al., 2009; Mullins et al., 2012; Akbar et al., 2015). Furthermore, +APP reduce the synthesis of other liver proteins, called negative acute-phase proteins (−APP; Gruys et al., 2005). Because the changes of −APP are prolonged compared with the increase of +APP, Trevisi et al. (2011) explained that −APP are more appropriate to evaluate the severity of inflammation in the transition period. Cows that had a prolonged reduction of −APP after

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parturition also had a greater incidence of health problems and a marked reduction in lactation performance (Bertoni et al., 2008; Trevisi et al., 2009). The severity of inflammation can be characterized with the liver functionality index (**LFI**; Bertoni et al., 2006; Bertoni and Trevisi, 2013; Trevisi and Minuti, 2018). The LFI is a composite index based on profiles of some –APP and other related molecules during the first month of lactation.

Multiple stressors during the periparturient period may contribute to this inflammation (Bradford et al., 2015). Specifically, dietary stressors around parturition include the shift from a high-forage, lower energy dry-cow diet to a high-grain and high-energy lactating cow diet, which can then result in an acute-phase response (Gott et al., 2015; Minuti et al., 2015). Similarly, fasting can cause an inflammatory response (Marques et al., 2012).

Saccharomyces cerevisiae fermentation products (**SCFP**) reduced the fluctuation in rumen pH during SARA (Li et al., 2016; Shi et al., 2019a), possibly via stabilizing feeding behavior (Olagaray et al., 2019). Furthermore, SCFP increased DMI in the first 10 wk after calving (Poppy et al., 2012). Milk production of cows fed SCFP were mostly positive, with significant increase of milk production in some studies (Zaworski et al., 2014; Acharya et al., 2017) as well as reviewed by Lopreiato et al. (2020), but other studies had only numerical increases (Schingoethe et al., 2004; Olagaray et al., 2019) associated with SCFP feeding. In a meta-analysis summarizing 36 separate studies with 69 comparisons, Poppy et al. (2012) reported that the SCFP supplementation increased milk production by 1.43 kg/d (95% CI = 0.89–1.96 kg/d) for early-lactation cows. Across studies, the variation of milk production responses to SCFP may be attributed to differences of dietary NDF concentration (Robinson and Erasmus, 2009), dietary starch concentration (Shi et al., 2019b), forage-to-concentrate ratio (Piva et al., 1993), DMI and initial milk production (Allen and Ying, 2012), or stage of lactation (Poppy et al., 2012). An additional factor to consider that has not been described fully would be the health status and severity of diseases to assess the severity of systemic inflammation and supplementation of SCFP interactions on milk production.

We hypothesized that feeding SCFP to dairy cows from the day of dry-off until 42 DIM would decrease the inflammatory response and increase the rumination time in dairy cows during postpartum period. The objectives of this study were to determine the effect of SCFP supplementation on the severity of postpartum inflammation in dairy cows as indicated by LFI, and the effect of SCFP supplementation on lactation performance.

MATERIALS AND METHODS

Farm, Animals, and Diets

This study was conducted on a commercial farm in accordance with Italian laws on animal experimentation (DL n. 26, 04/03/2014) and ethics (authorization of the Italian Ministry of Health n. 204/2020-PR). The farm consisted of 170 milking cows that averaged 40 kg/d of milk, and milk was used for the production of Parmigiano Reggiano cheese. During lactation, cows were housed in a freestall barn with cubicle resting areas, whereas for the dry period, cows were moved to a straw-bedded pen. Cows were milked using 4 free-flow stations of an automated milking system (**AMS**; Lely Astronaut A4, Lely Industries N.V.). Rumination was monitored via the AMS rumination monitoring system (Lely Qwes-HR collars, Lely Industries N.V.). Partial mixed ration (**PMR**) was delivered by robotic feeder (Lely Vector, Lely Industries N.V.) to nonlactating and lactating cows. Dry cows were fed with PMR and automatic feeders, and lactating cows were fed PMR and supplementation at AMS stations.

Thirty-four multiparous Holstein dairy cows without any clinical sign of disease were enrolled in the experiment at the time of dry-off. The number of cows and group size were chosen to ensure a type I error probability of 0.05 and a type II error probability of 0.20 (i.e., power of 0.8), considering variability of most relevant blood parameters, for the evaluation of inflammatory condition during the transition period (albumin, cholesterol, ceruloplasmin; Premi et al., 2021). Experimental cows were blocked by previous lactation milk production, milk composition, minutes of rumination, SCC in the last 2 mo of lactation, parity, calving interval, and BCS at dry-off, and randomly assigned to the treatment (SCFP) or control (**CTR**; Table 1). The allocation sequence was generated with the RAND function of Microsoft Excel (Microsoft Excel 2010, 14.0.7190.5000). Milk production, milk composition, SCC, and minutes of rumination were obtained from the daily average of the previous lactation as reported by the AMS computer system. Cows were enrolled into the study at the day ($\pm$ SD) of dry-off (63 ± 5 d before expected parturition date) and fed diets supplemented with SCFP (NutriTek, Diamond V; $n = 17$) or without supplementation (CTR; $n = 17$) until 42 DIM.

Cows in the dry group received a common mixed hay, ad libitum. The concentrate was supplemented via automatic feeders at rate of 2.5 kg/d during d –60 to –30 (far-off) and 5.2 kg/d during d –30 to parturition (close-up), as-fed basis (Table 2). Two delivery lines were used at the automatic feeders as follows: treatment dry line and common dry line. Cows assigned to

Table 1. Averages of previous lactation milk production, milk composition, minutes of rumination, SCC, parity, calving interval, and BCS at enrollment of experimental dairy cows¹

Item	CTR		SCFP	
	Mean	SD	Mean	SD
Milk production, kg/d	43.29	5.57	43.95	7.23
Milk fat, %	3.83	0.34	3.89	0.43
Milk protein, %	3.40	0.16	3.34	0.15
Rumination, min/d	421.95	50.77	414.35	51.99
SCC, × 1,000 cell/mL	187.11	212.82	183.10	138.92
Parity, no.	2.70	0.98	2.75	0.97
Calving interval, d	417.15	84.56	427.00	73.14
BCS	3.13	0.42	2.88	0.38

¹CTR = control diet, no *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation; SCFP = supplementation diet of *Saccharomyces cerevisiae* fermentation product. There were no significant differences between the means of CTR and SCFP.

SCFP received 300 g/d of concentrate with 19 g/d of SCFP, as-fed basis, via treatment dry-delivery line and the remaining concentrate from the common dry line. The 300 g/d of concentrate containing SCFP was evenly distributed throughout the day, and refusals were monitored for each cow independently to make sure the SCFP was consumed completely. The concentrate was formulated based on an expected DMI of 11.6 kg/d and 10.6 kg/d, respectively, for the far-off and close-up groups.

During lactation, cows received a common PMR and 5 kg/d (as-fed basis) of a milking robot concentrate formulated for a 650-kg cow producing 40 kg/d of milk at 3.8% fat and 3.2% protein and eating 26 kg/d of DM (Table 2). Cows with greater milk production were allowed additional milking robot concentrate up to a maximum of 2 kg/d for a maximum daily allowance of 7 kg/d concentrate, as-fed basis. To deliver the SCFP supplementation, 2 separate lines were used to deliver concentrates to the milking robots (treatment milk line and common milk line). Cows assigned to the SCFP supplementation group received 2.5 kg/d of concentrate with 19 g/d of SCFP from the treatment milk line, as-fed basis, and the remaining amount of 2.5 up to 4.5 kg/d, depending on milk production, from the common milk line. The 2.5 kg/d of concentrate containing SCFP were evenly distributed throughout the day, and refusals were checked for each cow independently to make sure the SCFP was consumed completely.

Three strategies were implemented with the mangers of the automatic feeders and robotic milking stations to reduce the risk of SCFP intake by control cows. First, the dispensing speed of concentrate was set to avoid any refusals remaining in the mangers. Second, the 34 experimental cows were housed with approximately 60 other nonexperimental cows, which reduced the op-

portunity for consumption of residual concentrate by control cows. Third, the mangers were cleaned twice a day by the farm personnel.

Diet ingredients were analyzed by near-infrared spectroscopy using the MAX System for Dairy (Cargill Inc.). Diets were formulated using MAX System for Dairy to meet the nutrients requirements of the cows in this study.

Sample Collection and Analysis

Blood samples were collected at 0900 h at d -60 (day of dry-off), -7, 7, and 28 relative to parturition date. To reduce animal distress, cows were head-locked by the herd manager, who collected blood samples as well throughout the all experimental period. Blood samples were collected in lithium heparin tubes (BD Vacutainer, BD Diagnostics) from jugular vein and centrifuged immediately after collection at $3,500 \times g$ (16 min, 6°C). Plasma was harvested and stored at -20°C until analysis. Plasma samples were analyzed as described in Mezzetti et al. (2019) for glucose, cholesterol, nonesterified fatty acids (NEFA), BHB, urea, creatinine, aspartate amino transferase-glutamate oxaloacetate transaminase, gamma-glutamyl transferase, total bilirubin, myeloperoxidase, haptoglobin, ceruloplasmin, globulin, zinc, albumin, paraoxonase, reactive oxygen metabolites, ferric-reducing ability of plasma, Ca, P, and Mg. The concentration of cholesterol, albumin and total bilirubin at 7 and 28 DIM were used to determine the LFI index (Bertoni et al., 2006; Trevisi et al., 2011).

Milk yield, milk composition, SCC, and minutes of rumination were recorded daily by the AMS computer system for all cows. Daily measurements were combined into a 7-d average. During the trial, the calibration of AMS on milk components was done on a weekly basis. Every week, a milk sample was analyzed in the laboratory for the following components: protein, fat, lactose, and SCC. The result of analysis was then used to calibrate the algorithm of the AMS. Furthermore, on a monthly basis, individual samples of milk of each animal were analyzed and used as well to calibrate the AMS.

The BCS were determined at dry-off, d -7, 7, and 28 relative to parturition. Body condition score was recorded independently by 3 individuals using a 5-point scale (Wildman et al., 1982). Representative samples of ingredients were taken for each field-lot of forages and for each batch of other ingredients, and sent to Cargill Laboratories (Fiorenzuola D'Arda, Italy). Feed ingredients were analyzed for moisture, CP, NDF, fat, and ash with near-infrared spectroscopy. Other nutrients were calculated.

Table 2. Ingredients (kg of DM) and chemical composition of experimental diets

Item	Far-off		Close-up		Postpartum	
	CTR ¹	SCFP ²	CTR	SCFP	CTR	SCFP
Alfalfa hay	—	—	—	—	5.4	5.4
Mixed hay ³	9.45	9.45	6.13	6.13	—	—
Grass hay	—	—	—	—	8.0	8.0
Corn fine ⁴	—	—	—	—	3.9	3.9
PMR concentrate ⁵	—	—	—	—	4.3	4.3
AMS concentrate SCFP ⁶	—	—	—	—	—	2.2
AMS concentrate CTR ⁷	—	—	—	—	4.4	2.2
Dry concentrate SCFP ⁸	—	0.27	—	0.27	—	—
Dry concentrate CTR ⁹	2.17	1.90	4.50	4.23	—	—
Total	11.62	11.62	10.63	10.63	26.00	26.00
Nutrient content						
DM, %	89.3	89.3	88.9	88.9	88.3	88.3
CP, % DM	12.5	12.5	14.4	14.4	17.1	17.1
NDF, % DM	47.9	47.9	41.7	41.7	29.6	29.6
Forage NDF, % DM	46.0	46.0	38.5	38.5	24.6	24.6
Starch, % DM	10.2	10.2	16	16	24.8	24.8
Ether extract, % DM	1.6	1.6	1.8	1.8	3.8	3.8
Ash, % DM	8.2	8.2	11.3	11.3	9.7	9.7
NE _L , Mcal/kg	1.37	1.37	1.50	1.50	1.67	1.67
NE _L allowable milk, kg/d	—	—	—	—	40.8	40.8
AA allowable milk, ¹⁰ kg/d	—	—	—	—	40.2	40.2

¹CTR = control diet, no *Saccharomyces cerevisiae* fermentation product (SCFP) supplementation.

²SCFP = supplementation diet of *Saccharomyces cerevisiae* fermentation product.

³Estimated intake as hay was fed ad libitum to the dry cows.

⁴Corn finely ground.

⁵Partial mixed ration (PMR) contained 43.8% corn, 50.4% soybean meal, and 5.8% mineral-vitamin mix, as fed.

⁶Automated milking system (AMS) concentrate contained 66.8% corn, 17.2% soybean meal, 6.1% soyhulls, 8.7% mineral-vitamin mix, and 0.8% SCFP, providing 19 g/d per cow of SCFP, as fed.

⁷Automated milking system concentrate contained 68.0% corn, 17.2% soybean meal, 6.1% soyhulls, 8.7% mineral-vitamin mix, and 0% SCFP, providing 0 g/d per cow of SCFP, as fed.

⁸Contained 58.5% corn, 34.5% soybean meal, 1.5% mineral-vitamin mix, and 5.5% SCFP providing 19 g/d per cow of SCFP, as fed.

⁹Contained 64.0% corn, 34.5% soybean meal, and 1.5% mineral-vitamin mix, providing 0 g/d per cow of SCFP, as fed.

¹⁰AA allowable milk represents the milk production when amino acids supply is limiting. The MAX System for Dairy (Cargill Inc.) bases animal requirements on amino acids.

Health Status

Health status was monitored daily by the personnel and veterinarian staff operating in the farm facilities. Diseases and detection dates were registered. Mastitis was diagnosed by visual evaluation of abnormal milk from each quarter and SCC analysis on suspicious cases. Retained placenta was diagnosed when the fetal membranes had not been completely expelled within 24 h after calving. Fever was diagnosed when rectal temperature was above 39.5°C. Displacement of the abomasum was diagnosed by veterinary diagnosis.

Animal Grouping and Statistical Analysis

Before analysis, the normality of distributions was verified for each parameter by reckoning the skewness and kurtosis according to the Shapiro test of SAS (re-

lease 8.0; SAS Institute Inc.). Nonnormally distributed parameters (plasma aspartate amino transferase-glutamate oxaloacetate transaminase, haptoglobin, creatinine, and milk SCC) were normalized through natural logarithms. Through the text, the data are presented in tables and graphs in the original scale (mean and SEM).

To evaluate the effect of the supplementation treatment and the severity of the inflammation during early lactation, the 32 cows (CTR = 17 cows and SCFP = 15 cows) were retrospectively divided into 2 groups based on their LFI index (Bertoni et al., 2006; Bertoni and Trevisi, 2013; Trevisi and Minuti, 2018); 16 cows with LFI less than 0 identified as the low (**LLFI**) group and 16 cows with LFI greater than 0 were identified as the high (**HLFI**) group. Data were analyzed with ANOVA using a mixed model for repeated measures (mixed procedure is SAS) in accordance with Littell et

Table 3. Liver functionality index (LFI) values and disease incidence for control cows (CTR) and cows supplemented with a *Saccharomyces cerevisiae* fermentation product (SCFP) from d 63 ± 5 before expected parturition date to 42 DIM

Item	CTR n = 17	SCFP n = 15
LFI, mean (SD)	−0.30 (2.43)	−0.08 (2.31)
Cows with negative LFI, no.	8	7
Disease incidence, number of cows		
Clinical diseases ¹	7	3
Fever	1	0
Retained placenta	3	1
Mastitis	3	1
Abomasal displacement	0	1

¹Clinical diseases is the sum of fever, retained placenta, mastitis, and abomasal displacement.

al. (1998). The statistical model included the fixed effect of the diet (CTR and SCFP), LFI group (LLFI and HLFI), time (d −60, −7, 7, and 28 relative to parturition for blood parameters and d 7, 14, 21, 28, 35, and 42 DIM for milk parameters), and their interaction. The time (day) was considered as a repeated measure for each cow. The analysis was conducted using the following 3 covariance structures: autoregressive order,

compound symmetry, and spatial power. These were ranked according to their Akaike information criterion, with the one having the lowest criterion being chosen for the eventual analysis (Littell et al., 1998). Incidence of diseases was analyzed with χ^2 test (FREQ procedure of SAS). The post hoc comparisons were determined when the *P*-value for the main effect was ≤0.05. Main effects at 0.05 < *P* ≤ 0.10 are discussed in the context of tendencies. Data are presented as the mean ± standard error.

RESULTS

Health Parameters, Blood Parameters, BCS Change, SCC, and Rumination

Two cows from SCFP group were removed from the study due to severe parturition difficulties with large bull calves. The LFI values averaged −0.30 and −0.08 with standard deviations of 2.43 and 2.24, respectively, for the CTR and SCFP groups. Clinical diseases observed in the study are reported in Table 3, and no differences due to treatment were observed. Overall, 47.1% of the cows in the CTR group reported values

Table 4. Least squares means of plasma biomarkers from dry-off to 28 d of lactation in dairy cows grouped by liver functionality index (LFI) and dietary treatment as follows: cows with high LFI fed with control diet (HLFI-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFI-SCFP), cows with low LFI fed with a control diet (LLFI-CTR), and cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFI-SCFP)

Biomarker ¹	HLFI-CTR	HLFI-SCFP	LLFI-CTR	LLFI-SCFP	SEM ²	LFI ³	Diet ⁴	LFI × diet ⁵
Hematocrit, L/L	0.30	0.30	0.31	0.31	0.01	0.05	0.83	0.83
Glucose, mmol/L	4.15	4.17	4.20	4.01	0.12	0.51	0.27	0.12
NEFA, mmol/L	0.32	0.33	0.55	0.32	0.09	0.06	0.03	0.02
BHB, mmol/L	0.49	0.62	0.64	0.65	0.10	0.11	0.21	0.24
Urea, mmol/L	5.38	5.57	4.89	4.50	0.32	<0.01	0.54	0.07
Creatinine, μmol/L	86.6	83.2	87.9	78.9	2.57	0.50	<0.01	0.13
Calcium, mmol/L	2.50	2.55	2.46	2.47	0.05	0.05	0.30	0.52
Phosphorus, mmol/L	1.75	1.57	1.69	1.65	0.11	0.80	0.11	0.25
Magnesium, mmol/L	1.00	1.00	0.98	0.95	0.03	0.07	0.43	0.41
Zinc, μmol/L	12.0	11.6	10.9	12.3	0.81	0.72	0.38	0.13
Cholesterol, mmol/L	3.81	3.84	3.32	3.50	0.23	<0.01	0.57	0.51
Ceruloplasmin, μmol/L	2.52	2.49	2.68	2.49	0.16	0.53	0.20	0.41
Total protein, g/L	78.5	77.8	76.7	76.2	1.42	0.11	0.53	0.92
Albumin, g/L	36.7	37.1	36.7	35.6	0.70	0.08	0.35	0.07
Globulin, g/L	41.7	40.8	40.1	40.7	1.65	0.52	0.88	0.43
AST-GOT, U/L	118.6	111.4	111.8	113.6	9.83	0.69	0.63	0.45
GGT, U/L	26.7	26.1	22.1	23.2	2.50	0.09	0.94	0.60
Bilirubin, μmol/L	3.68	3.61	5.63	4.86	0.78	<0.01	0.20	0.29
Haptoglobin, g/L	0.34	0.19	0.33	0.42	0.11	0.03	0.52	0.01
Paraoxonase, U/mL	89.3	95.0	77.7	79.3	6.07	<0.01	0.27	0.48
ROM, mg of H ₂ O ₂ /100 mL	15.6	15.3	16.2	15.6	0.85	0.42	0.34	0.70
Myeloperoxidase, U/L	476	471	466	476	20.0	0.77	0.89	0.59
FRAP, μmol/L of TE	132.1	130.3	132.0	135.2	6.35	0.58	0.88	0.48

¹NEFA = nonesterified fatty acids; AST-GOT = aspartate aminotransferase–glutamate oxaloacetate transaminase; GGT = γ -glutamyltransferase; ROM = reactive oxygen metabolites; FRAP = ferric-reducing ability of plasma.

²Greatest SEM.

³Overall effect of the LFI.

⁴Overall effect of the diet.

⁵Interaction of LFI × diet.

of LFI less than 0, and 41.2% manifested clinical signs of disease as follows: 1 case of fever, 3 cases of retained placenta, and 3 cases of mastitis. In the SCFP group, 46.7% of the cows had values of LFI less than 0, and 20% manifested clinical signs of disease as follows: 1 case of metritis, 1 case of mastitis, and 1 case of displaced abomasum.

In this study, plasma samples were analyzed for metabolic markers, inflammatory markers, minerals, and markers of the oxidative status (Table 4). The cows with greater LFI showed increased concentrations of urea ($P < 0.01$), calcium ($P < 0.05$), magnesium ($P < 0.07$), cholesterol ($P < 0.01$), and albumin ($P < 0.08$), as well as reduced concentrations of haptoglobin ($P < 0.05$) and bilirubin ($P < 0.01$). Concentrations of haptoglobin were significantly affected by the interaction LFI $\times$ diet ($P < 0.01$). The haptoglobin of cows fed SCFP was reduced if they were HLF, but increased for LLFI. Taking into consideration the inflammatory condition of the cows, the SCFP supplementation affected the plasmatic concentration of NEFA (LFI $\times$ diet, $P < 0.02$). In both high LFI groups, there was no effect of SCFP supplementation. Whereas, in the low LFI groups, the LLFI-CTR reported higher concentration of NEFA during lactation on d 7, compared with the other groups (1.03 vs. 0.59 mmol/L, $P < 0.05$; Figure 1A). The diet supplementation also affected the concentrations of creatinine (effect of diet, $P < 0.01$) in that creatinine was reduced for cows of SCFP (81.5 $\mu\text{mol/L}$) versus CTR (87.4 $\mu\text{mol/L}$). No other relevant differences were observed in the other plasma parameters related to the diet, LFI, and LFI $\times$ diet interaction effects.

During the period from d -7 until 28 relative to parturition, BCS changed as follows: -0.3 , -0.2 , -0.6 , and -0.4 for HLF-CTR, HLF-SCFP, LLFI-CTR, and LLFI-SCFP groups respectively. The only significant difference of BCS change was for cows of LLFI-CTR compared with the other groups ($P < 0.05$; Figure 1B). Somatic cell counts were not different among the groups with averages of 175, 169, 384, and $126 \times 1,000$ cells/mL for the HLF-CTR, HLF-SCFP, LLFI-CTR, and LLFI-SCFP groups, respectively. However, the LLFI-CTR had the greatest SCC during the study period when compared with other groups on 42 DIM ($P < 0.05$; Figure 2).

Rumination time (Figure 3) was similar at -60 DIM (baseline number) for the 4 groups (averaged 429 min/d). On the week before parturition, the LLFI-CTR group had reduced rumination time compared with the other 3 groups ($P < 0.05$), but was only statistically different between LLFI-CTR and LLFI-SCFP, with 469 and 516 min/d, respectively. Rumination time was 359 min for LLFI groups and 440 min for HLF groups dur-

ing the first week of lactation ($P < 0.01$). In the second and third weeks of lactation, rumination times were similar between groups; however, the minutes of daily rumination of the LLFI-CTR cows were 40 less minutes compared ($P > 0.05$) to the other 3 groups (Figure 3).

Milk Production and Milk Composition

Milk production (Figure 4) of cows was different between LFI groups (50.2 vs. 46.7 kg/d for HLF and LLFI, respectively; $P < 0.05$). Interestingly, there were no differences due to diet treatment for the HLF cows. Although the LFI $\times$ diet interaction was not significant

Figure 1. Least squares means ($\pm$ SE) of plasma nonesterified fatty acid (NEFA; A) from -60 to 42 d relative to parturition and difference in body condition score (dBCS; B) between values measured at -7 d relative to parturition and values measured at $+28$ DIM in dairy cows grouped by liver functionality index (LFI) and diet as follows: cows with high LFI fed with control diet (HLFI-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFI-SCFP), cows with low LFI fed with a control diet (LLFI-CTR), and cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFI-SCFP). Different letters (a, b) at the same time point indicate a significant difference ($P < 0.05$).

($P < 0.13$), in LLFI groups, cows that were supplemented with SCFP produced 49.1 kg/d compared with 44.3 kg/d of the LLFI-CTR group. The main differences occurred in the first month of lactation ($P < 0.05$ at 21 and 28 DIM).

During the first week after parturition, milk fat compositions were 4.18, 4.29, 4.88, and 4.65% for the HLF-CTR, HLF-SCFP, LLFI-CTR, and LLFI-SCFP groups, respectively (Figure 5A). Milk fat percent was greatest for the LLFI-CTR group in the first week after parturition compared with the other 2 HLF groups ($P < 0.01$). In the later weeks, milk fat percent was similar between groups. Milk fat yield (Figure 5B) was greater ($P < 0.09$) for cows with HLF compared with cows of LLFI (1.99 and 1.88 kg/d, respectively). Milk fat yield of LLFI-CTR cows were lower (1.76 kg/d) compared with HLF-CTR, HLF-SCFP, and LLFI-SCFP groups (2.01, 1.96, and 2.02 kg/d, respectively, LFI $\times$ diet interaction; $P < 0.08$). From 14 to 35 DIM, the milk fat yield was significantly lower ($P < 0.05$) in LLFI-CTR cows compared with HLF-CTR and LLFI-SCFP cows, and also compared with HLF-SCFP on 14 DIM.

Milk protein percent was similar throughout the experimental period (Figure 6A). The milk protein yield did not show any differences that could be attributed to the effect of diet or LFI. However, during first and second week after parturition, the LLFI-CTR group had the reduced milk protein output compared with the HLF groups ($P < 0.05$; Figure 6B).

DISCUSSION

The temporal patterns of blood metabolic parameters of this study reflected the typical changes that occur during the transition period of dairy cows (Bionaz et al., 2007; Trevisi et al., 2012). Other studies investigating SCFP supplementation of transition cows also reported minimal alterations to metabolic markers, inflammatory proteins, and minerals (Ramsing et al., 2009; Zaworski et al., 2014). Recently, Knoblock et al. (2019) found that serum haptoglobin concentrations were decreased in SCFP cows on d 7 after parturition compared with control cows, which suggests reduced inflammation of cows fed SCFP in very early lactation.

Figure 2. Least squares means ($\pm$ SE) of milk SCC from 7 to 42 d from parturition in dairy cows grouped by liver functionality index (LFI) and diet as follows: cows with high LFI fed with control diet (HLFI-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFI-SCFP), cows with low LFI fed with a control diet (LLFI-CTR), and cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFI-SCFP). Different letters (a,b) at the same time point indicate a significant difference ($P < 0.05$).

In our study, these results were consistent for animals with HLF. Olagaray et al. (2019) reported an increase in plasma cholesterol for the treatment cows at the second and fifth week after parturition, also suggesting a reduced inflammation of SCFP cows. Cholesterol is one of the parameters included in the LFI, as it is an indirect marker of $-APP$. Greater concentrations of cholesterol involve greater apo-lipoprotein synthesis (Bertoni and Trevisi, 2013) and thus better liver functionality (i.e., not being impaired by severe inflammation). In the present experiment, the overall concentrations of haaptoglobin (the main positive APP) and cholesterol were unaffected by SCFP supplementation; nevertheless, the great variability of their concentrations suggests a presence of severe challenges to the immune system in both groups (CTR and SCFP). The determination of the LFI (Bertoni and Trevisi, 2013) that measures the ability of cows to respond to inflammatory challenges during the transition period may identify cows that are less resilient to inflammation in early lactation. In particular, the values of LFI less than 0 are representative of cows that encountered health problems around parturition (clinical and subclinical) and recovered slowly. In our

study, the large standard deviations of LFI within groups of diet treatments confirmed that some animals faced a severe inflammation event around parturition, which was not always clinically manifested. However, other animals had a smooth transition into lactation. This information led to the investigation of the effects of SCFP on cow performance controlling for LFI (i.e., the severity of the inflammatory condition). When grouping cows based on their LFI value, we discovered that about 50% of the experimental cows had negative LFI values, regardless of dietary treatment assignment. These cows experienced severe inflammation during the very early days of their lactation (low LFI, negative values) and had significant reduction of milk production. Low LFI cows reached similar milk production compared with high LFI cows by 42 DIM. However, milk production of LLFI-SCFP recovered faster compared with LLFI-CTR cows. Our understanding from the results of this experiment is that cows under inflammatory conditions synthesized $+APP$, and diet supplementation did not influence it. For example, cows facing inflammatory insults such as a difficult parturition, heat stress, overcrowding, and mastitis will have a low

Figure 3. Least squares means ($\pm$ SE) of rumination time from -60 to 42 d from parturition in dairy cows grouped by liver functionality index (LFI) and diet as follows: cows with high LFI fed with control diet (HLFI-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFI-SCFP), cows with low LFI fed with a control diet (LLFI-CTR), and cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFI-SCFP). Different letters (a, b) at the same time point indicate a significant difference ($P < 0.05$).

LFI. The SCFP inclusion in the diet may not influence the overall inflammatory challenge because it may only have an effect in the gastrointestinal tract to maintain its stability (Tun et al., 2020). The better stability of the forestomachs immediately after parturition may allow a cow's rumination time and milk production to be more resilient. For instance, in the week before parturition, cows in the LLFI-SCFP group ruminated for more minutes compared with the LLFI-CTR group. This suggests that feeding SCFP during the entire dry period may have contributed positively to the rumen environment. Thus, allowing cows in LLFI-SCFP to recover rumination time and production faster postpartum compared with CTR-LLFI cows. Other authors have reported that SCFP positively affected rumen pH (Li et al., 2016; Shi et al., 2019a) or improved energy availability by promoting cellulolytic, proteolytic, and lactate-utilizing bacteria in the rumen (Harrison et al., 1988; Callaway and Martin, 1997; Poppy et al., 2012; Mullins et al., 2013). The greater stability of the rumen environment in the SCFP-LLFI cows could result in lower energy demand by the immune system (Trevisi et al., 2010) and would allow more energy to be directed

to milk production, as observed for the LLFI-SCFP group of cows. We can speculate that, as suggested by Minuti et al. (2015), the improved rumen functionality of the LLFI-SCFP could have improved the functionality of the liver epithelium, resulting in better utilization of nutrients for milk production.

In previous studies, Soriani et al. (2012) and Calamari et al. (2014) observed that cows affected by more serious inflammatory events around parturition showed a modified daily pattern of feed intake and reduced rumination activity. The meta-analysis by Poppy et al. (2012) revealed that SCFP allowed for greater DMI in early lactation. Olagaray et al. (2019) reported that supplementation with SCFP during the transition period altered prepartum and postpartum feeding behavior, with increased meals per day and decreased time between those meals. In our research, we speculated that SCFP reduced the stress in the forestomach and contributed to greater rumen activity due to stability of rumen fermentation and pH. Additionally, SCFP supplementation supports better intake around parturition, as indicated by behaviors of rumination activity and the lower mobilization of adipose tissue. Further

Figure 4. Least squares means ($\pm$ SE) of milk yield from 7 to 42 d from parturition in dairy cows grouped by liver functionality index (LFI) and diet as follows: cows with high LFI fed with control diet (HLFi-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFi-SCFP), cows with low LFI fed with a control diet (LLFi-CTR), cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFi-SCFP). Different letters (a, b) at the same time point indicate a significant difference ($P < 0.05$).

Figure 5. Least squares means ($\pm$ SE) of milk fat concentration (A) and milk fat yield (B) from 7 to 42 d from parturition in dairy cows grouped by liver functionality index (LFI) and diet as follows: cows with high LFI fed with control diet (HLFI-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFI-SCFP), cows with low LFI fed with a control diet (LLFI-CTR), and cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFI-SCFP). Different letters (a, b) at the same time point indicate a significant difference ($P < 0.05$).

Figure 6. Least squares means ($\pm$ SE) of milk protein concentration (A) and milk protein yield (B) from 7 to 42 d from parturition in dairy cows grouped by liver functionality index (LFI) and diet as follows: cows with high LFI fed with control diet (HLFI-CTR), cows with high LFI fed with *Saccharomyces cerevisiae* fermentation product (HLFI-SCFP), cows with low LFI fed with a control diet (LLFI-CTR), and cows with low LFI fed with diet supplemented with *Saccharomyces cerevisiae* fermentation product (LLFI-SCFP). Different letters (a, b) at the same time point indicate a significant difference ($P < 0.05$).

research should examine the circadian patterns instead of weekly patterns of rumen activity and functions as well as metabolic markers.

The inclusion of the LFI factor in the analysis of SCFP effects on cow performance has never been considered before. Differentiating low LFI cows from high LFI cows revealed that low LFI cows benefited from SCFP supplementation with improved performance. These results make sense in that animals that are suffering from an inflammatory event would be expected to have reduced feed intake and performance, and thus be more likely to show the benefits of supplementation of SCFP. Further study is warranted to describe the SCFP effect on cows with high LFI using a greater number of cows. This information complements the conclusions from the meta-analysis by Poppy et al. (2012) where they reported 1.43 extra kilograms of milk for SCFP-fed cows during early lactation.

CONCLUSIONS

Supplementation with SCFP during the dry period until 42 DIM affected performance of cows facing severe inflammation as indicated by LFI during the transition period. In cows of the LLFI groups, the supplementation with SCFP contributed to a faster recovery of milk production, lower SCC, and lower plasma NEFA concentration compared with cows in the LLFI-CTR group. Future research on SCFP should include LFI analysis along with the evaluation of diurnal patterns of rumen and metabolic markers.

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