Kansas Agricultural Experiment Station Research Reports

Volume 0
Issue 2 *Dairy Research (1984-2014)*

Article 175

2012

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Recommended Citation

Farney, Jaymelynn K.; Mamedova, Laman; Minton, J. Ernest; and Coetzee, J. F. (2012) "Sodium salicylate during the first 7 days of lactation affects the entire lactation," *Kansas Agricultural Experiment Station Research Reports*: Vol. 0: Iss. 2. https://doi.org/10.4148/2378-5977.3100

Sodium salicylate during the first 7 days of lactation affects the entire lactation

Abstract

Inflammation has been proposed as a contributor to metabolic disorders in transition dairy cows. The purpose of this experiment was to determine if a non-steroidal anti-inflammatory drug, sodium salicylate (SS), benefits transition cows. At calving, 78 cows [primiparous (1P) n = 39; 2nd lactation (2P) n = 24; ≥3 lactations (3P) n = 15] were assigned alternately to either a control or SS treatment for 7 days and production responses were evaluated through the entire lactation. Treatment was administered via individual water bowls, delivering a mean of 123 ± 5.5 (mean ± standard deviation) grams salicylate per day during the 7 days of treatment. Cows were followed throughout the lactation by monthly milk yield and component testing, and the effects of treatment on the risk of leaving the herd and on normalized 305-day milk, fat, and protein yields were determined by Fisher's exact test and mixed model analysis, respectively. Treatment influenced both 305-day milk and fat yields differently across parities. Milk yield was increased by 17% in 3P SS cows (4,374 ± 1,549 lb greater for 3P SS cows). Primiparous SS cows tended to produce 2,155 ± 824 lb less 305-day milk than control cows; no differences were detected for 2P cows. Furthermore, 3P SS cows produced 285 ± 50 lb more 305-day milk fat and tended to produce 108 ± 40 lb more 305-day milk protein. No effects were detected in 1P or 2P cows. A treatment by parity interaction was observed for the risk of leaving the herd where 1P cows treated with SS tended to have a greater risk of leaving the herd than controls (30% vs. 6% risk). Treatment did not alter herd retention in 2P or 3P groups, and SS had no effect on the risk of leaving the herd overall. Results indicate that SS has long-term effects on lactation characteristics of aged cows, particularly on fat metabolism, but has potential negative effects for primiparous cows.; Dairy Day, 2012, Kansas State University, Manhattan, KS, 2012; Dairy Research, 2012 is known as Dairy Day, 2012

Keywords

Dairy Day, 2012; Kansas Agricultural Experiment Station contribution; no. 13-030-S; Report of progress (Kansas Agricultural Experiment Station and Cooperative Extension Service); 1075; Dairy cows; Lactation; Postpartum health; Sodium salicylate

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Sodium Salicylate during the First 7 Days of Lactation Affects the Entire Lactation

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Summary

Inflammation has been proposed as a contributor to metabolic disorders in transition dairy cows. The purpose of this experiment was to determine if a non-steroidal anti-inflammatory drug, sodium salicylate (**SS**), benefits transition cows. At calving, 78 cows [primiparous (**1P**) n = 39; 2nd lactation (**2P**) n = 24; ≥3 lactations (**3P**) n = 15] were assigned alternately to either a control or SS treatment for 7 days and production responses were evaluated through the entire lactation. Treatment was administered via individual water bowls, delivering a mean of 123 ± 5.5 (mean ± standard deviation) grams salicylate per day during the 7 days of treatment. Cows were followed throughout the lactation by monthly milk yield and component testing, and the effects of treatment on the risk of leaving the herd and on normalized 305-day milk, fat, and protein yields were determined by Fisher's exact test and mixed model analysis, respectively. Treatment influenced both 305-day milk and fat yields differently across parities. Milk yield was increased by 17% in 3P SS cows (4,374 ± 1,549 lb greater for 3P SS cows). Primiparous SS cows tended to produce 2,155 ± 824 lb less 305-day milk than control cows; no differences were detected for 2P cows. Furthermore, 3P SS cows produced 285 ± 50 lb more 305-day milk fat and tended to produce 108 ± 40 lb more 305-day milk protein. No effects were detected in 1P or 2P cows. A treatment by parity interaction was observed for the risk of leaving the herd where 1P cows treated with SS tended to have a greater risk of leaving the herd than controls (30% vs. 6% risk). Treatment did not alter herd retention in 2P or 3P groups, and SS had no effect on the risk of leaving the herd overall. Results indicate that SS has long-term effects on lactation characteristics of aged cows, particularly on fat metabolism, but has potential negative effects for primiparous cows.

Key words: lactation, postpartum health, sodium salicylate

Introduction

The transition period is a time of metabolic problems for dairy cattle, which causes substantial costs for producers. A majority of the metabolic issues stem from the negative energy balance associated with the increase in nutrients needed for the mammary gland. It has been hypothesized that inflammation also plays a role in the development of metabolic disorders such as fatty liver and ketosis. Non-steroidal anti-inflammatory drugs (**NSAID**) are used to combat the effects of inflammation (i.e., pain, redness, and swelling). These types of drugs have been used in dairy research as a component of treatment protocols for bacterial infections (primarily mastitis); however, a few NSAIDs have been used in metabolic disorders.

We recently conducted a study to evaluate responses to oral delivery of the NSAID sodium salicylate (**SS**; the parent compound for aspirin) during the first week of lactation. Intensive measurements were conducted during the first 21 days of lactation for this trial, during which we observed an increase in milk yield and incidence of metritis in older cows as well as an increase in energy-corrected milk and milk fat yield by week 3 across all cows treated with SS.

The purpose of this investigation was to determine if oral SS treatment during the first 7 days in milk (**DIM**) has sustained impacts through the entire lactation.

Experimental Procedures

Seventy-eight Holstein cows [primiparous (**1P**), n=39; 2nd lactation (**2P**), n=24; ≥3rd lactation cows (**3P**,) n=15] from the Kansas State University Dairy Teaching and Research Center were used in the trial. Cows were assigned to two treatments on the day of parturition. Cows that had lameness issues or milk fever before the initiation of treatment were excluded. Treatments were balanced for parity and consisted of 7-day control or SS treatments administered through individual water bowls. Cows were housed in tie-stall facilities, fed ad-libitum at 6:00 a.m. and 6:00 p.m., and milked thrice daily (2:00 a.m., 10:00 a.m., and 6:00 p.m.). On the eighth day after calving, all cows were provided regular water for the remainder of lactation. Herd management data and DHIA production records were used for a retrospective analysis of whole-lactation production and risk of leaving the herd. Cows that did not remain in the herd for a subsequent calving were considered to have left the herd, and the reason entered was recorded. Predicted 305-day yields of milk, fat, and protein generated by DHIA were used for all cows for which a value was generated. Predictions were not available for 3 cows that left the herd prior to 95 DIM. To test for randomization bias in milk production, treatment effects on predicted transmitting ability (**PTA**) for milk, fat, and protein yield were tested, and no significant differences between treatments were observed (all $P < 0.50$). An additional potential confounding factor was the enrollment of 27 of the cows (14 control and 13 SS cows) in a nutrition study following the completion of the salicylate study. The study was a Latin square design with treatments that failed to influence any measured outcome. Therefore, the simple effect of enrollment in the study was included in the model. Statistical analysis of 305-day milk, fat, and protein yields were carried out using JMP (version 8.0) to estimate the fixed effects of treatment, parity, treatment by parity interaction, and subsequent study enrollment. The PTA for the variable of interest was included as a covariate to account for genetic contributions to variance.

Results and Discussion

No overall treatment effect ($P = 0.16$) was observed for the 305-day milk yield, but an interaction of treatment and parity ($P < 0.01$, Table 1) was detected. Salicylate administration increased ($P = 0.05$) 305-day milk yield in 3P cows by 4,384 ± 1,552 lb but decreased it in 1P cows by 2,155 ± 824 lb (Figure 1). Estimated 305-day milk fat yield was increased by 13% in SS cows ($P < 0.001$; Table 1). A treatment by parity interaction was observed, where 3P SS cows produced 318 ± 55 lb more fat during the entire lactation than 3P controls (34% increase, $P < 0.001$; Figure 2). The 305-day protein yield was not affected by treatment ($P > 0.50$), but a treatment by parity interaction was detected in which 3P SS cows tended ($P = 0.06$) to have greater protein yield than 3P CON (14% increase; Figure 3).

A treatment by parity interaction was observed ($P < 0.05$) for risk of leaving the herd; 1P SS cows tended ($P < 0.10$) to have a greater risk of leaving the herd than 1P controls (6% risk vs. 30% risk, Table 2). No differences were observed between treatments in 2P and 3P groups. The specific causes of removal from the herd also were statistically evaluated, but treatment did not impact any of these conditions. The most common reasons that cows left the herd were reproductive issues and chronic mastitis (Table 2).

Milk and fat yields were increased in cows treated with sodium salicylate, with the greatest differences observed in third or greater lactation cows. The divergence in milk yield observed in

3P cows at the end of the third week of lactation was confirmed to affect the entire lactation. Others who have administered aspirin to transition dairy cows reported increases in milk yield around peak lactation compared with controls. Conversely, flunixin meglumine administered for 3 days postpartum did not affect milk yield, suggesting that the type of NSAID administered is critical in determining milk production responses. Overall, SS administration during the first week of lactation seems to increase production and potentially profit in ≥3rd lactation cows, but it is not a beneficial management practice for primiparous cows, in which SS tended to decrease milk production and increase cows' risk of being removed from the herd.

It is important to note that SS is not approved for commercial use for the purposes as described in this paper. In addition, although veterinary forms of aspirin are marketed with label indications for pain, fever, and inflammation in the U.S., the FDA has not formally approved this drug; consequently, withdrawal times have not been established for food-producing animals. These results should be viewed as establishing a critical role of inflammatory pathways during early lactation, with effects that endure throughout the lactation. Future research may reveal broadly applicable techniques to put this new knowledge to work.

Table 1. Estimated 305-day yields of milk, fat, and protein

				P-value		
Variable	Control	Sodium salicylate	SEM	Treatment	Parity	Treatment × parity
Milk yield (× 1,000 lb)	26.0	27.3	6.6	0.16	<0.01	<0.01
Fat yield (lb)	901.8	1023.1	24.3	<0.01	<0.01	<0.01
Protein yield (lb)	774.0	807.0	19.9	0.23	<0.01	0.08

Table 2. Reasons cows left herd[1]

	Parity						
	First		Second		Third or greater		
Reason	Control	SS[2]	Control	SS	Control	SS	Total
Foot or leg	....	....	....	....	1	....	1
Low production	....	1	1	....	....	....	2
Reproduction	1	3	1	2	1	1	9
Injury	....	....	....	....	....	1	1
Death	....	....	1	1	1	....	3
Mastitis	....	2	2	2	1	....	7
Udder	....	....	1	....	....	....	1
Total	1	6	6	5	4	2	24

[1]All values are numerical counts based on parity and treatment for each specific reason cows were removed from the herd.
[2] SS: sodium salicylate treatment.

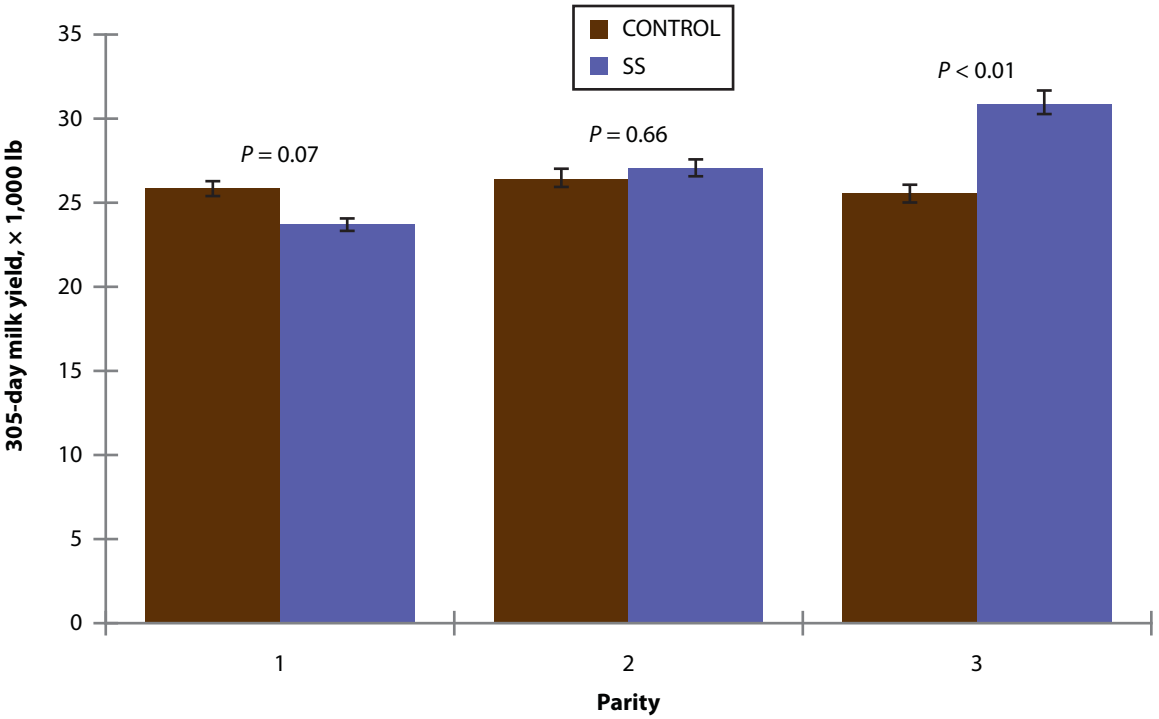

Figure 1. A treatment × parity interaction ($P < 0.01$) was detected for milk yield with third-parity sodium salicylate (SS) cows having greater milk yield and a tendency for first-parity SS cows to have a lesser milk yield. No difference was detected for second-parity cows.

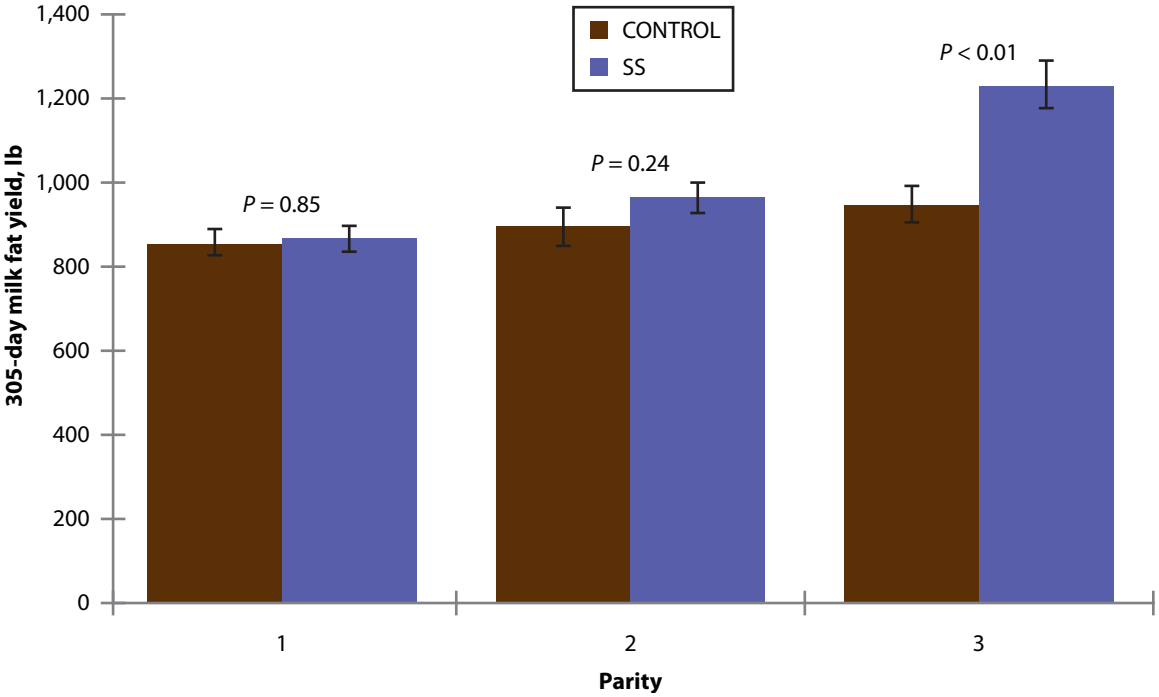

Figure 2. A treatment × parity interaction ($P < 0.01$) was observed for 305-day milk fat yield, reflecting greater milk fat yield in third-parity cows treated with sodium salicylate (SS).

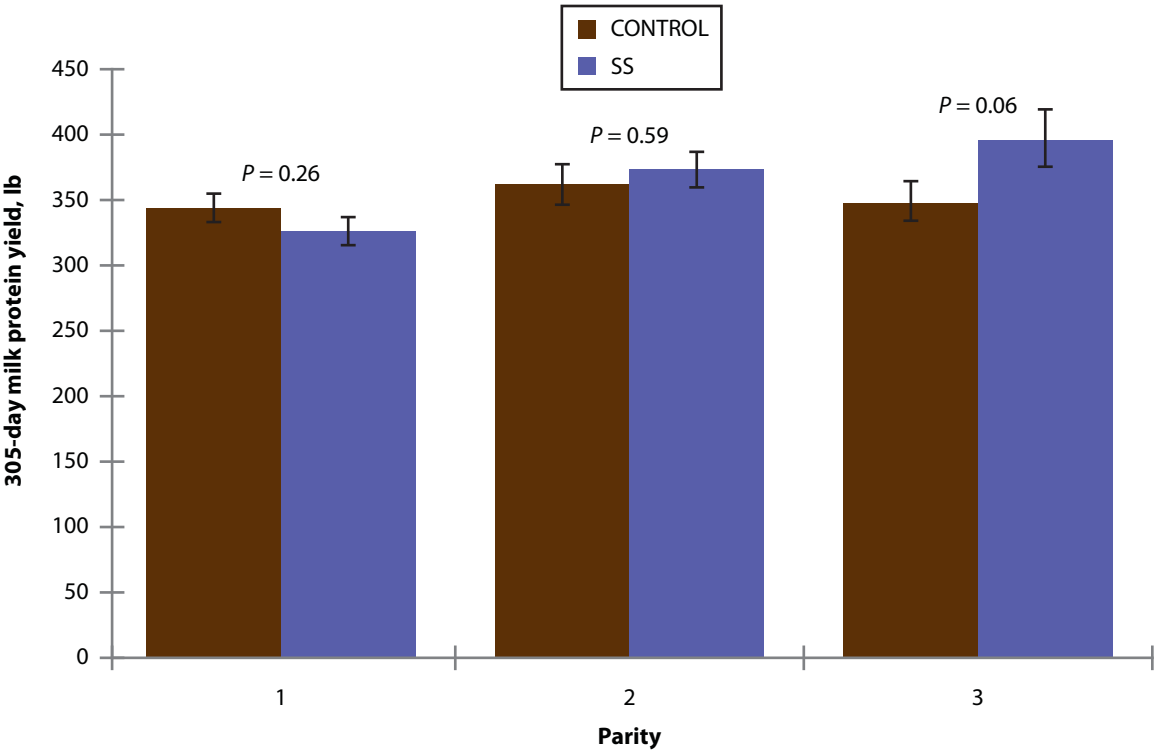

Figure 3. A tendency ($P = 0.08$) for a treatment × parity interaction was found for 305-day milk protein yield, with third-parity sodium salicylate (SS)-treated cows tending to have a greater milk protein yield through the lactation.