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Sodium salicylate treatment in early lactation increases whole-lactation milk and milk fat yield in mature dairy cows

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ABSTRACT

Multiple lines of inquiry have suggested that a high degree of inflammation in early lactation cows is associated with low productivity and increased disease incidence. In addition, some small studies have suggested that milk production increases in response to antiinflammatory treatment in the first week of lactation. Our objective was to determine if administration of sodium salicylate (SS), a nonsteroidal antiinflammatory drug (NSAID), in the first week of lactation changes whole-lactation productivity and retention in the herd. At calving, 78 cows [n = 39 primiparous (1P); n = 24 second parity (2P); n = 15 third parity or greater (3P)] were alternately assigned to either control (CON) or SS treatments for 7 d postpartum. Sodium salicylate treatment was administered via individual water bowls at a concentration of 1.95 g/L, delivering a mean of 123.3 ± 5.5 g of salicylate/d during the 7-d treatment. For the first 21 d of lactation, dry matter intake, water intake, milk yield, and health were monitored daily, and milk samples were collected twice weekly for milk component analysis. Monthly milk yield and component testing through the rest of the lactation provided data to assess long-term responses, and the effects of treatment on the risk of leaving the herd and on 305-d milk, fat, and protein yields were assessed. During the first 21 d of lactation, we observed no differences in morbidity, except for increased risk of metritis in 3P SS cows. Treatment interacted with parity to influence both 305-d milk and milk fat yields, and a tendency for an interaction was detected for 305-d milk protein yield. Milk yield was 2,469 ± 646 kg greater over the lactation in 3P SS cows compared with 3P CON cows (21% increase) and tended to decrease by 8% in 1P cows treated with SS; no effects were detected in 2P cows. Furthermore, 3P SS cows produced 130 ± 23 kg more milk fat over the lactation (30% increase), with no effects detected for 1P or 2P. Treatment with SS tended to increase 305-d milk protein yield in 3P cows by 14%, with no effects in 1P or 2P cows. A tendency for a treatment × parity interaction was also observed for the risk of leaving the herd. First-parity cows treated with SS tended to have greater risk of leaving the herd than controls (30 vs. 6% risk); however, 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 of mature dairy cows, particularly on fat yield, but may have negative effects for primiparous cows.

Key words: nonsteroidal antiinflammatory drug, inflammation, programming

INTRODUCTION

The presence of an inflammatory state in postpartum dairy cows is well established. Although early studies focused on associations between inflammatory markers and diseases such as mastitis and metritis, numerous studies in the past decade have demonstrated that inflammatory and acute-phase mediators are elevated in the days after parturition, even in cows that are apparently healthy (Humblet et al., 2006; Bionaz et al., 2007; Huzzey et al., 2009; Graugnard et al., 2012; Mullins et al., 2012). This growing body of evidence suggests that either the processes of parturition and galactopoiesis induce inflammation directly or that infections or endotoxin affect far more postpartum cows than is currently recognized. Whatever the explanation, the prevalence of postpartum inflammation raises important questions about the implications of this inflammation across numerous organs.

Although most transition dairy cows apparently experience a period of inflammation, the magnitude of this inflammatory condition varies greatly between cows. Bertoni et al. (2008) assessed the importance of this variation by measuring a panel of inflammatory markers and separating transition cows into quartiles for degree of inflammation. Cows in the highest quartile had significantly lower milk yields than those in the lowest quartile throughout the first month of lactation, differing by 20% on d 28 of lactation (Bertoni et al.,

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2008). One metric that has been used in this respect is paraoxanase, a plasma biomarker that is potently suppressed by a variety of inflammatory stimuli. Transition cows with high paraoxanase concentrations, in addition to having lower concentrations of acute phase proteins and reactive oxygen metabolites, produced 1,971 kg more milk (24%) over 305 d than did those in the lowest quartile for paraoxanase (Bionaz et al., 2007).

It is possible that these studies identified cows with primary inflammatory conditions that impaired milk production capacity, but it is also possible that the primary issue in these cows was a health disorder (e.g., metritis, displaced abomasum) that was the causative factor underlying both inflammation and the decrease in milk production (Ingvartsen, 2006). Experimental strategies to alter endogenous inflammation in apparently healthy cows must be employed to accurately assess the effects of periparturient inflammation on milk production.

One approach to assessing the effects of inflammation during the transition period is to block endogenous inflammation through the use of nonsteroidal antiinflammatory drugs (**NSAID**). Nonsteroidal antiinflammatory drugs are classified into 5 broad categories with slightly different modes of action (Gallo et al., 2008). Salicylate, a long-studied compound found in willow bark, is a weak inhibitor of cyclo-oxygenase (**COX**)-1 and COX-2 (Mitchell et al., 1993), and its probable mode of action is impairing the activation of nuclear factor κB, a common mediator of inflammation (Kopp and Ghosh, 1994; Pierce et al., 1996). This mode of action is not shared by all NSAID. Most NSAID are COX inhibitors, and neither genetic ablation nor pharmacological inhibition of COX enzymes replicated the beneficial metabolic responses induced by salicylates in mice (Yuan et al., 2001). If metabolic inflammation in transition dairy cows has a similar molecular architecture to the inflammation that occurs in rodent models of obesity, then COX inhibitors may have less potential to alter transition cow physiology than salicylate-class compounds.

Based partly on responses to exogenous cytokine administration (Bradford et al., 2009), we hypothesized that elevated plasma concentrations of NEFA and cytokines in early lactation cause an inflammatory response in the liver of transition dairy cows, resulting in partitioning of fatty acids toward triglyceride synthesis, depressed gluconeogenesis, and continued adipose tissue mobilization. This metabolic scenario could limit nutrient supply to the mammary gland, decreasing milk yield during peak lactation and affecting whole-lactation productivity. Therefore, we further hypothesized that the antiinflammatory effects of salicylate could improve metabolic function and enhance productivity. The specific objective of this study was to determine the effects of sodium salicylate (**SS**) treatment in the first week of lactation on production and health through the entire lactation.

MATERIALS AND METHODS

All experimental procedures were approved by the Kansas State University Institutional Animal Care and Use Committee. The experimental design, treatments, and sampling protocols have been previously described in a companion paper (Farney et al., 2013).

Design and Treatments

A total of 78 cows [n = 39 primiparous (**1P**), n = 24 second parity (**2P**), and n = 15 third and greater parity (**3P**)] from the Kansas State University Dairy Teaching and Research Facility (Manhattan) were blocked by parity and alternately assigned to treatment at parturition. Cows that were enrolled were apparently healthy, had a dystocia score <2 (1 to 5 scale), and were not visibly lame. Treatments consisted of administration of sodium salicylate (1.95 g/L) in a molasses carrier (0.14 g/L) via individual water bowls for 7 d postpartum. Control cows received water with the same molasses concentration for 7 d (**CON**). Neither water nor DM intake was affected by treatment during the 7-d treatment period (Farney et al., 2013). On d 8 postpartum, all cows were given untreated water for the remainder of the experiment. Cows were housed in a tiestall facility in randomly assigned stalls through d 21 postpartum. Cattle were milked 3 times daily (0200, 1000, and 1800 h) and fed ad libitum twice daily (0630 and 1800 h) with a diet formulated to meet all nutrient requirements (Table 1). Feed and water intakes and milk yield were recorded daily during the first 21 d of lactation. After cows were removed from the tiestall facility (d 22 postpartum), they were returned to the general herd freestall facility, managed similarly, and received the same diet that they consumed while in the tiestall facility.

Disease Incidence

Cows were assessed daily for health status by trained personnel, including daily recording of rectal temperature and urine ketones (ReliOn ketone test strips, Bayer Healthcare LLC, Mishawaka, IN). Ketosis was defined as the detection of urine acetoacetate concentrations exceeding 80 mg/dL on any one day, or exceeding 40 mg/dL for 2 consecutive days to reduce the risk of false-positive responses at the lower threshold

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