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Hot topic: Early postpartum treatment of commercial dairy cows with nonsteroidal antiinflammatory drugs increases whole-lactation milk yield

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ABSTRACT

Previous research has shown that postpartum administration of the nonsteroidal antiinflammatory drug (NSAID) sodium salicylate can increase 305-d milk yield in older dairy cattle (parity 3 and greater). However, in this prior work, sodium salicylate was delivered to cows via the drinking water, a method that does not align well with current grouping strategies on commercial dairy farms. The objective of the current study was to replicate these results on a commercial dairy farm with a simplified treatment protocol and to compare sodium salicylate with another NSAID, meloxicam. Dairy cattle in their second lactation and greater (n = 51/treatment) were alternately assigned to 1 of 3 treatments at parturition, with treatments lasting for 3 d. Experimental treatments began 12 to 36 h after parturition and were (1) 1 placebo bolus on the first day and 3 consecutive daily drenches of sodium salicylate (125 g/cow per day; SAL); (2) 1 bolus of meloxicam (675 mg/cow) and 3 drenches of an equal volume of water (MEL); or (3) 1 placebo bolus and 3 drenches of water (CON). Blood samples were collected on the first day of treatment, immediately following the last day of treatment, and 7 d after the last day of treatment; plasma was analyzed for glucose, β-hydroxybutyrate (BHB), free fatty acids, haptoglobin, and paraoxonase. Milk production, body condition score, reproductive status, and retention in the herd were monitored for 365 d posttreatment, and effects of treatment, parity, days in milk, and interactions were evaluated in mixed effects models. Significance was declared at $P < 0.05$. Whole-lactation milk and protein yields were greater in NSAID-treated cows, although 305-d fat production was not affected. There was a significant interaction of treatment and parity for plasma glucose concentration; MEL increased plasma glucose concentrations compared with CON and SAL in older cows. Sodium salicylate decreased plasma BHB concentration compared with MEL at 7 d posttreatment, although no difference was detected immediately following treatment. Haptoglobin concentrations were elevated in SAL cows compared with CON. There was a tendency for CON cows to be removed from the herd more quickly than MEL cows (42 vs. 26% at 365 d posttreatment). Body condition score, concentrations of plasma free fatty acids and paraoxonase, and time to pregnancy were not affected by treatment. These results indicate that NSAID administration in postpartum cows has the potential to be a viable way to improve productivity and potentially longevity in commercial dairies, although further research is necessary to optimize recommendations for producers.
Key words: sodium salicylate, meloxicam, nonsteroidal antiinflammatory drug (NSAID), transition cow

Hot Topic

Despite ongoing research, the transition period remains a high-risk period for dairy cattle. A growing body of research indicates that systemic metabolic inflammation occurs in dairy cows following parturition and that this inflammation may be linked to negative production outcomes. Bionaz et al. (2007) demonstrated that reduced levels of the liver hydrolase paraoxonase are associated with increased markers of inflammation such as haptoglobin and globulin in early-lactation dairy cattle. Those authors reported that animals in the experiment with the greatest plasma paraoxonase activity during the first 30 d of lactation produced 10,090 ± 1,504 kg of milk in a 305-d lactation, whereas those with the least activity produced 8,119 ± 2,042 kg, a 1,971-kg difference. Bertoni et al. (2008) reported that cows in the highest quartile of an inflammatory index had decreased milk production in the first month of lactation compared with their counterparts with the low-

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est inflammatory markers (24.4 vs. 30.9 ± 2.11 kg/d). Farney et al. (2013b) administered dairy cattle with the nonsteroidal antiinflammatory drug (**NSAID**) sodium salicylate via drinking water in the week following calving in an attempt to suppress inflammation. Cows in their third lactation and greater that received sodium salicylate produced 21% more milk over a 305-d lactation than did parity-matched controls. Interestingly, although the initial hypothesis was that inflammation was linked to suboptimal metabolism, this productivity response occurred even though both the control and treatment groups had low incidence of clinical metabolic disorders.

Meloxicam is another drug in the NSAID class that has high oral bioavailability and a long plasma elimination half-life in cattle compared with sodium salicylate (Coetzee et al., 2009; Malreddy et al., 2013). Although no published studies have demonstrated that meloxicam affects milk production, research in lactating cattle has focused on its use during clinical mastitis (McDougall et al., 2009) and following assisted parturition (Newby et al., 2013). Considering the effect of sodium salicylate on production, it is likely that meloxicam, with a longer elimination half-life, may also have beneficial effects in lactation after a single dose. Therefore, the objective of this study was to determine if NSAID treatment in the first days following parturition would positively affect milk production and health of cows on a commercial dairy farm.

Multiparous cows from a commercial dairy (n = 51/treatment) were enrolled in the study 12 to 36 h after calving. Animals were managed similarly throughout the dry period and early lactation. Cows assigned to sodium salicylate treatment (**SAL**) received a placebo bolus on d 1 of treatment and an oral drench containing 125 g/d of sodium salicylate (estimated to be approximately 185 mg/kg of BW; Wintersun Chemical, Ontario, CA) in 375 mL of water for 3 consecutive days beginning on d 1 of treatment. Cows assigned to meloxicam treatment (**MEL**) received 675 mg of meloxicam (estimated to be approximately 1 mg/kg of BW; Unichem Pharmaceuticals, Rochelle Park, NJ) as a bolus on d 1 of treatment as well as 3 consecutive daily drenches of 375 mL of water. Control cows (**CON**) received a placebo bolus on d 1 and water drenches (375 mL) for 3 d. The placebo and meloxicam boluses both contained casein as a filler. Only cows entering their second lactation and greater were enrolled in the study (CON = 18 cows in parity 2 and 33 cows in parity ≥3; MEL = 27 cows in parity 2 and 24 cows in parity ≥3; SAL = 20 cows in parity 2 and 31 cows in parity ≥3). Cows were blocked by mastitis at parturition (CON = 1, MEL = 2, SAL = 2), breed (CON = 6, MEL = 6, SAL = 4 crossbred; all others were Holstein), dystocia (calving difficulty score ≥3; CON = 5, MEL = 5, SAL = 6), and twin births (CON = 4, MEL = 4, SAL = 3) and were sequentially assigned to treatment within block between July 15 and September 2, 2013. Mastitis was determined by farm staff for blocking purposes, and was defined as clinical mastitis with abnormal appearance of milk, such as clots. Milk from treated cows was discarded for 10 d after the start of treatment to ensure that no drug residue entered the saleable milk stream, particularly for meloxicam (Malreddy et al., 2013).

Blood samples were collected via the coccygeal vein on the first and last day of treatment and 7 d after the completion of treatment. Plasma was collected and stored at −20°C until analyzed for glucose by a colorimetric kit (kit #439-90901; Wako Chemicals USA Inc.), free fatty acids using an enzymatic colorimetric procedure (NEFA-HR; Wako Chemicals USA Inc., Richmond, VA), and BHB using a commercial kit (kit #H7587-58; Pointe Scientific Inc., Canton, MI). Haptoglobin was measured by the method of Cooke and Arthington (2013), a colorimetric technique that uses differences in peroxidase activity to measure haptoglobin-hemoglobin complexing. Absorbance was measured with a spectrophotometer (PowerWave XS; BioTek Instruments Inc., Winooski, VT) and calculations were performed using Gen5 software (BioTek Instruments Inc.). Paraoxonase was measured by the method of Ferré et al. (2002).

Reproduction and culling data were recorded in PC-Dart (Dairy Records Management Services, Raleigh, NC) by the farm staff, who were blinded to treatments. Reasons for culling were grouped into the following 7 categories: injury, lameness, low milk, mastitis, SCC, unknown, and other disease. Milk weights were collected electronically at each milking and stored in PC-Dart. Milk composition (including SCC) and yield were tested for individual cows at approximately 6-wk intervals by DHIA technicians, and 305-d mature-equivalent lactation yields were calculated by DHIA for animals that remained in the herd for at least 90 d. Body condition score was recorded as the average of responses from at least 3 independent observers on the last day of treatment (3 d after enrollment) and approximately 2, 5, and 8 mo following enrollment.

Statistical analyses were carried out using SAS (version 9.3; SAS Institute Inc., Cary, NC) and JMP (version 10; SAS Institute Inc.). Plasma variables were analyzed using d-0 values as a covariate along with fixed effects of block, parity (2 or 3+), treatment, sample day, and treatment by day interaction, and the random effect of cow. Milk data were analyzed with fixed effects