J. Dairy Sci. 98:4392–4400
http://dx.doi.org/10.3168/jds.2014-8235

Effect of administration of recombinant bovine somatotropin on health and performance of lactating dairy cows diagnosed with hyperketonemia

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ABSTRACT

The effect of administering recombinant bovine somatotropin (rbST) to cows with hyperketonemia during the early postpartum period on health, metabolic parameters, milk production, and early reproductive performance was evaluated in a double-blinded clinical trial. Cows from 8 dairy herds in New York State were tested weekly between 3 and 16 d in milk for elevated serum β-hydroxybutyrate. Cows were enrolled in the study when blood β-hydroxybutyrate was ≥1.3 mmol/L for the first time. Enrolled cows were randomly assigned to a treatment (n = 273) or placebo control (n = 270) group. Treated cows were given 325 mg of rbST subcutaneously on the day of enrollment and again 14 d later. Control cows received the same regimen except the syringe contained only the carrier without somatotropin. After enrollment, blood samples were collected weekly for 4 wk and submitted to the laboratory to be analyzed for selected metabolites. Risk ratios for clinical diseases subsequent to treatment were calculated using Poisson regression. Continuous data were analyzed using linear mixed models. Time to first insemination was assessed with survival analysis. In the 42 d following the first administration of rbST, incidence risks of displaced abomasum, clinical ketosis, metritis, clinical mastitis, and lameness were not different between treatment groups. Cows treated with rbST had a slightly lower body condition score 28 d after enrollment compared with control cows. In the 4 wk following enrollment, serum nonesterified fatty acids and aspartate amino-transferase were slightly higher for treated than control cows, respectively. Serum glucose, calcium, haptoglobin, and β-hydroxybutyrate were similar between groups. Treatment had no effect on resolution of hyperketonemia in any of the 4 wk after enrollment. Milk production in either of the 2-wk periods after each treatment was not different between treated and control cows. Furthermore, milk production was not different between groups from enrollment to 98 d in milk (42.6 ± 0.6 and 42.1 ± 0.7 kg/d for treatment and control groups, respectively). Treatment had no effect on time to first insemination (83 and 74 d in milk for treatment and control groups, respectively; hazard ratio = 0.72) or first insemination pregnancy risk (27 and 29% for treatment and control groups, respectively; risk ratio = 0.92). Based on the current results, it is not recommended to use a low dose of rbST as therapy for cows with hyperketonemia.
Key words: dairy cow, hyperketonemia, ketosis treatment, recombinant bovine somatotropin

INTRODUCTION

Essentially all dairy cows go through a period of negative energy balance, decreased DMI, insulin resistance, and immune suppression around the time of calving. The ability to adapt to these changes is part of what separates cows that remain healthy from those that develop metabolic or infectious diseases associated with early lactation (LeBlanc, 2010). One of the important metabolic problems in early-lactation dairy cows is hyperketonemia. Hyperketonemia in lactating dairy cows is defined as an elevated concentration of ketone bodies in the blood, which may or may not be accompanied by clinical signs (Andersson, 1988; Kelton et al., 1998), but is associated with decreased production and impaired reproduction and health measures (Duffield et al., 2009; Ospina et al., 2010; McArt et al., 2011), resulting in significant economic effects. A lack of gluconeogenic substrates is thought to contribute to hyperketonemia; therefore, many therapies for hyperketonemia target the provision of glucogenic substrates. The plethora of physiological, environmental, and genetic factors that interact to cause a cow to become hyperketonemic can make it difficult to determine the best method of treatment because this may vary depending on herd and cow-level factors. However, a considerable amount of work has been done to try to identify effective treatments as well as preventative measures to mitigate

Received April 14, 2014.
Accepted March 25, 2015.
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the negative effects of hyperketonemia (Duffield et al., 1998; McArt et al., 2011; Gordon et al., 2013).

Some studies have shown that administration of recombinant bST (**rbST**) during the late dry period may have beneficial effects on metabolic diseases. Prepartum rbST treatment decreased prepartum plasma concentrations of NEFA and BHBA (Putnam et al., 1999). Similarly, rbST administered during the transition period (both before and following calving) resulted in some positive effects such as increased BW and BCS (Gulay et al., 2000, 2003). Increased DMI by cows treated with rbST in the transition period has also been documented in a few studies (Gulay et al., 2000, 2004a), and this is likely the mechanism through which increased BW and BCS would occur. These authors hypothesized that the increased body condition and BW may help cows to cope better with negative energy balance during the transition period.

Bovine somatotropin can positively influence glucose metabolism by increasing hepatic gluconeogenesis, reducing glucose oxidation, and increasing glycogen mobilization; all actions combined result in an increase of blood glucose concentrations (Peel and Bauman, 1987; Bauman et al., 1989). When cows diagnosed with left displacement of the abomasum were treated with 500 mg of rbST immediately after surgical correction, blood glucose increased and urine ketones were reduced (Fetrow et al., 1999). Therefore, administration of rbST to cows with hyperketonemia may increase blood glucose and reduce fat mobilization and so might be useful as a treatment for hyperketonemia.

The objective of this study was to evaluate the effect of administration of 2 doses of 325 mg of sometribove zinc to lactating dairy cows diagnosed with hyperketonemia on milk production in early lactation, early reproductive performance, and health and metabolic parameters.

MATERIALS AND METHODS

Study Population

The study population was a convenience sample (herds with good record-keeping practices, proximity to the investigators, and willingness to participate in the study) of Holstein cows of all parities from 8 herds in New York State. Farms ranged in size from 624 to 1,600 milking cows, with an average herd size of approximately 1,000 milking animals. Facilities were freestall design, and animals were fed a TMR representative of commercial rations formulated to meet NRC requirements. All farms used the farm management program DairyComp 305 (Valley Agricultural Software, Tulare, CA). Animals were excluded if they were not clinically healthy at the time of enrollment or if they had a displaced abomasum, metritis, or severe clinical mastitis in the current lactation before being enrolled. Data were collected from April 14, 2010, until September 27, 2011. The Animal Care Committee at the University of Guelph approved the Animal Utilization Protocol (AUP number: 10R008) before the trial was started.

Data Collection and Study Design

Lactating cows of all parities between 3 and 16 DIM, inclusive, were screened once a week for blood BHBA concentration $\geq$1.3 mmol/L using a validated point-of-care meter (Precision Xtra; Abbott Diabetes Care Canada Inc., Mississauga, ON, Canada). Cows were enrolled in the study when blood BHBA concentration was $\geq$1.3 mmol/L for the first time. Cows enrolled in the study were blocked by herd and parity group and were sequentially randomized to the treatment group to receive 325 mg of sometribove zinc suspension (Posilac; Elanco Animal Health, A Division of Eli Lilly and Co., Greenfield, IN) or the control group to receive placebo injections with carrier (no sometribove) based on predetermined random number tables. The dose of rbST used in this trial was an average of doses used in studies done previously that provided evidence of positive outcomes when rbST was administered at a dose between 143 to 500 mg (Putnam et al., 1999; Gulay et al., 2007). Cows were injected twice, 14 d apart, at the depression on either side of the tail head. All trial staff were blinded to the identity of the treatments until statistical analysis was completed.

In addition to the blood sample obtained at the time of enrollment, 4 blood samples were obtained from the coccygeal vessels on d 7, 14, 21, and 28 after enrollment with a 10-mL vacuum tube containing no anticoagulant. Blood samples were allowed to clot at room temperature for approximately 1 h, then were stored in a cooler and transported to a local veterinary clinic for processing within 6 h. Blood was centrifuged at 1,200 $\times$ g at 20°C for 10 min, and serum was separated and frozen at −20°C before submission to the Animal Health Laboratory at the University of Guelph for analysis of BHBA, glucose, NEFA, total calcium, aspartate amino-transferase (**AST**), and haptoglobin using a Roche Cobas 6000 c501 automated chemistry analyzer (Roche Canada, Laval, Quebec). Test reagents for glucose, calcium, and AST were supplied by Roche diagnostics (Indianapolis, IN) and for BHBA and NEFA, Randox Laboratories (UK). They were prepared by the Animal Health Laboratory staff to measure haptoglobin.