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Effects of treatment of preweaning dairy calves with recombinant bovine somatotropin on immune responses and somatotropic axis

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ABSTRACT

Weaning may be associated with negative energy balance and body weight loss when calves are still immunologically immature, predisposing them to infectious diseases. The aim of the present experiment was to investigate the effects of treatment of preweaning dairy calves with recombinant bovine somatotropin (rbST) on the somatotropic axis, selected immune parameters, and hematology of calves around weaning. Thirty-six Holstein female calves were randomly assigned to receive 1.5 to 1.8 mg of rbST (Posilac, Elanco Animal Health, Greenfield, IN) per kilogram of body weight or to receive injections of saline (saline solution 0.9%, Valley Vet Supply, Marysville, KS) every 7 d from 21 to 63 d of life. Calves were fed milk replacer ad libitum from birth to 38 d of age (d −11), when progressive weaning started, and calves were weaned at 49 d of age (d 0). Calves were weighed at birth and weekly from 21 to 63 d of age, when wither height also was measured. Calves were vaccinated with 0.5 mg of ovalbumin on study d −28 and −7. Blood samples were collected on d −28, −25, −21, −11, 0, 3, 7, and 14. Polymorphonuclear leukocytes were isolated and challenged ex vivo with *Escherichia coli* to determine phagocytosis and oxidative burst capacity. Additionally, expression of cluster of differentiation (CD)62L and CD18 by granulocyte, lymphocyte, and CD14+ monocyte were determined. Blood samples were also used to determine hematological parameters and concentrations of growth hormone, insulin-like growth factor-1, insulin, glucose, fatty acids, β-hydroxybutyrate, haptoglobin, and anti-ovalbumin IgG. Calves treated with rbST had greater concentrations of growth hormone and insulin-like growth factor-1 from d −25 to 14 than control calves, whereas insulin, fatty acid, and β-hydroxybutyrate concentrations did not differ. On d −11, glucose concentration was greater for rbST-treated calves. Treatment did not affect polymorphonuclear lymphocyte phagocytosis and oxidative burst, but intensity of expression of CD62L and CD18 by granulocytes tended to be increased by rbST treatment. Treatment did not affect the concentration of anti-ovalbumin IgG in serum. Haptoglobin concentration was reduced in rbST treated calves on d 3 and we noted a tendency for hematocrit to be lower in rbST-treated calves. Treatment did not affect body weight, wither height, and average daily gain, despite the fact that rbST-treated calves had lower daily milk replacer intake. The relatively minor improvements in immune responses resulting from rbST treatment of weaning calves may not be sufficient to reduce the incidence of infectious diseases.
Key words: dairy calves, somatotropin, immune parameters

INTRODUCTION

Neonatal calves are immunologically naive and rely heavily on passive transfer of immunoglobulins through colostrum and on innate immune mechanisms as their first line of defense against pathogens (Barrington and Parish, 2001). The development of the immune system to a mature state is a slow process and percentages of lymphocyte subpopulations [cluster of differentiation (**CD**)4+, CD8+, and γδ T cell receptor+] and PMN function (phagocytosis and respiratory burst) reach stable levels within the first 6 mo of life (Kampen et al., 2006). On the other hand, the immunoglobulins acquired from colostrum are practically extinguished from circulation by approximately 21 d of age (Chase et al., 2008; Hulbert and Moisá, 2016), creating a window of susceptibility.

Weaning, which in many herds is also associated with regrouping, is another challenging period for dairy

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calves. Common metabolic changes associated with weaning are decreased circulating concentrations of glucose, insulin, and IGF-1 and increased circulating concentrations of BHB and, in some instances, fatty acids (Omidi-Mirzaei et al., 2015; Schäff et al., 2016). Less is known about the associations between weaning and changes in immune parameters. Hulbert et al. (2011a) demonstrated that calves weaned at 47 d of age, after being fed 454 g/d of milk replacer (DM), had reduced percentage of PMN positive for phagocytosis and oxidative burst and reduced intensity of phagocytosis ex vivo from 45 to 66 d of age. Researchers have proposed that, to achieve proper weight gain, reproductive performance, and milk yield in the first lactation, calves should be fed 15 to 20% of their live BW of milk containing 20 to 25% fat and 28% protein (DM basis; Gelsinger et al., 2016; Soberon et al., 2012). A significant challenge for this strategy is the weaning period, because calves may not consume enough solid feed (starter and forage) to compensate for the nutritional needs in the absence of milk feeding (Miller-Cushon et al., 2013). Therefore, calves undergoing weaning may present negative energy balance and, consequently, alterations in metabolic profile that could impair immune function.

Insulin-like growth factor-1 is an important factor in proliferation, differentiation, and hypertrophy of various cell types, including immune cells (LeRoith and Roberts, 1991). Culture of human granulocytes in the presence of increasing concentrations of IGF-1 reduced the percentage of apoptotic granulocytes by 34 to 40% compared with culture of granulocytes in the absence of IGF-1 (Kooijman et al., 2002). Similarly, granulocyte cultured with 6.5 n*M* IGF-1 had a 45% decrease in DNA fragmentation compared with granulocytes cultured in the absence of IGF-1 (Kooijman et al., 2002). Culture of PMN with human growth hormone (**GH**; 100 to 1,000 ng/mL) or IGF-1 (100 to 1,000 ng/mL) increased the percentage of *Escherichia coli* killed and increased the expression of CD11 (Inoue et al., 1998). Treatment of humans and rats deficient in GH with somatotropin (**ST**) resulted in increased circulating concentrations of IGF-1, PMN, and total antibodies (Kimata and Yoshida, 1994; Ibañez et al., 2005; Sohmiya et al., 2005). Thus, the reduced concentration of IGF-1 observed during the weaning period could partly explain the immunosuppression observed during this phase of life. Piglets treated with porcine ST (0.5 mg/kg) for 5 d and subjected to weaning and transportation had increased circulating concentrations of IGF-1, neutrophils, and IgM in the first 24 h after weaning compared with piglets not treated with ST and subjected to weaning and transportation stress (Kojima et al., 2008). In recent experiments, our group demonstrated that cows treated with 125 mg of recombinant (**r**)bST from −21 to 28 d relative to calving, a period characterized by intense negative energy balance and immunosuppression, had greater intensity of phagocytosis and oxidative burst by PMN, greater circulating concentration of anti-ovalbumin IgG, and reduced incidence of retained fetal membranes and metritis (Silva et al., 2015, 2017a).

The hypotheses of the current experiment were that treatment of weaning calves with rbST would increase GH and IGF-1 concentrations and, consequently, improve selected innate and adaptive immune parameters. Additionally, we hypothesized that treatment of weaning calves with rbST would only minimally affect metabolic parameters. Therefore, the objectives of the current experiment were to evaluate the effects of treating weaning calves with rbST on GH and IGF-1 concentrations, on PMN phagocytosis and oxidative burst, on expression of adhesion molecules by granulocytes, lymphocytes, and CD14+ monocytes, on concentration of anti-ovalbumin IgG, and on hematological parameters. The secondary objectives of the current experiment were to evaluate the effects of treating weaning calves with rbST on metabolic parameters, growth, and intake of milk replacer.

MATERIALS AND METHODS

All procedures involving animals were approved by the animal care and use committee of the University of Florida (protocol #201609265).

Animals, Facilities, Nutrition, and Management

The experiment was conducted on a commercial dairy farm located in northern Florida. Calves were born in a loose housing sand-bedded pen. At birth, calves were individually weighed using an electronic scale and fed 2 L of colostrum within 30 min of birth and another 2 L of colostrum within 6 h of birth. At 48 h after birth, blood was sampled to determine serum total protein, a proxy for passive transfer of immunity. Only calves with total protein measured by refractometer between 5.5 and 8.5 g/dL were used in this experiment. Throughout the experiment, calves were group housed (8 calves/pen from 24 h after birth to 20 d of age, 20 to 30 calves/pen from 21 to 63 d of age) in sand-bedded pens.

From 24 h after birth to 36 d of age, calves were fed milk replacer ad libitum. Starting at 38 d of age, milk replacer allowance was progressively reduced until 49 d of age (d 0), when calves were completely weaned. From 21 to 49 d of age an automated milk replacer feeder recorded individual replacer intake. At 63 d of age, calves were moved to an open lot with capacity for approximately 60 calves. Calves had ad libitum access