Effects of Recombinant Bovine Tumor Necrosis Factor-alpha Administration on Plasma Glucose, Triglyceride and Insulin Concentrations, and on Growth Hormone Secretion in Dairy Heifers.

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The cytokine tumor necrosis factor-alpha (TNFα) has been shown to act systemically as an endogenous pyrogen, and to affect glucose homeostasis, lipid metabolism and hormone secretion in humans and rats (Grunfeld et al., 1991). Data indicating that TNF is produced by fat cells and interferes with insulin action, have emerged over the last few years (Hotamisligil and Spiegelman, 1996). In ruminants, we have demonstrated that recombinant bovine TNF (rbTNF) injection induces marked changes in plasma glucose, triglyceride (TG), insulin and growth hormone (GH) concentrations in Holstein calves (Kushibiki et al., 2000). However, a previous report indicated that the concentration of plasma TG was not affected by rb TNF administration to calves (Kenison et al., 1991). In addition, it has been reported that TNF can directly inhibit GH secretion from bovine pituitary cells in culture (Sartin et al., 1991). There was also a report that TNF did not influence basal release of GH from cultured sheep pituitary cells (Sartin et al., 1998).

The objectives of this study were to clarify the effects of intravenous (iv) administration of rbTNF on plasma glucose, TG and insulin concentrations and on growth hormone-releasing hormone (GHRH)-stimulated GH release in Holstein heifers.

In experiment 1, six Holstein heifers with average body weight (BW) of 347kg, were used to clarify the effects of iv administration of rbTNF on selected plasma metabolites and insulin responses. Highly purified rbTNF was provided by HIGETA SHOYU CO., LTD., Choshi, Japan. Heifers were randomly assigned to treatment protocols arranged factorially in a 3 × 3 Latin square design. Treatments were iv injections of rbTNF at dosages of 0 (CONT), 2.5 (TNF2.5), or 5.0 (TNF5) μg/kg BW.

In Exp. 2, after the end of Exp. 1, the heifers were used to investigate the effects of iv administration of rbTNF (5.0 μg/kg BW) on GHRH-stimulated GH release. Heifers were assigned randomly to one of two iv treatment protocols: GHRH (0.25 μg/kg BW) + rbTNF or GHRH + saline. The treatment was conducted using a 2 × 2 Latin square design.

In Exp. 1, plasma glucose and TG concentrations were at first elevated by rbTNF treatment in both the TNF2.5 and TNF5 groups, and then decreased. Thereafter, in both groups there were gradual increases in glucose and TG concentration, which returned to the pretreatment levels at 12 h after rbTNF injection. The injection of rbTNF resulted in an increase in plasma insulin concentration during the period from 2 to 24 h, except for from 6 to 8 h, after the treatment.

In Exp. 2, rbTNF inhibited the GHRH-stimulated GH secretion during the initial phase as shown in the Figure 1. These results suggest that TNF directly and/or indirectly affects the intermediary metabolism and GH secretion in Holstein heifers.

**Figure 1.** Change of plasma GH concentration (means ± SEM) in Exp. 2. Time 0 represents the time of injection. *P < 0.05.

This study was supported by a Grant-in-Aid of Recombinant Cytokine’s Project provided by the Ministry of Agriculture, Forestry and Fisheries, Japan (RCP 1998-4330).


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