Journal of Animal and Feed Sciences, 13, Suppl. 1, 2004, 597–600

Reduction of lactational performance following bovine TNF-α administration to dairy cows

S. Kushibiki[1,5], K. Hodate[2], H. Shingu[3], Y. Obara[4], F. Itoh[1], and T. Komatsu[1]

[1]Department of Animal Physiology and Nutrition, National Institute of Livestock and Grassland Science, Tsukuba, Ibaraki, 305-0901, Japan
[2] School of Veterinary Medicine and Animal Sciences, Kitasato University Towada, Aomori, 034-8628, Japan
[3]Department of Animal Production and Grasslands Farming, National Agricultural Research Center for Tohoku Region, Morioka, Iwate, 020-0198, Japan
[4]Graduate School of Agricultural Science, Factory of Agriculture, Tohoku University Sendai, Miyagi, 981-8555, Japan

ABSTRACT

Twelve lactating Holstein cows were injected subcutaneously with recombinant bovine Tumor Necrosis Factor-α (rbTNF, 2.5 μg/kg/day) or saline (3 ml/head/day) at 12.00 h daily for 7 d (d 0 - 6). Milk yield was reduced by rbTNF injection from d 1 to 8. The milk fat content was increased on d 1 - 7 by rbTNF treatment, but milk protein content in the rbTNF group was decreased on d 5 and 7 as compared with that of the control group. The somatotropin (ST) response to ST-releasing hormone (0.25 μg/kg) was smaller in the rbTNF group than in the control. These results support the possibility that TNF is responsible for the changes in hormone secretion, milk production and composition observed during coliform mastitis.

KEY WORDS: TNF-α, milk yield, acute phase response, hormone, mastitis

INTRODUCTION

Coliform mastitis has adverse effects on the economics of milk production by reducing the quantity and quality of milk (Shuster et al., 1991). A recent study suggested that Tumor Necrosis Factor-α (TNF) plays a vital role in the pathophysiology associated with coliform mastitis and/or acute phase response (Hoeben et al., 2000). Bovine mammary macrophages secrete TNF in response

[5] Corresponding author: e-mail: mendoza@affrc.go.jp

to endotoxin (Pighetti and Sordillo, 1994), and the serum TNF level increases in coliform mastitis (Hoeben et al., 2000). Studies using endotoxin in lactating cows have been reported (Shuster et al., 1991), but the effects of exogenous TNF treatment on hormonal response, lactational performance and mastitic parameters have not yet been studied. Moreover, little information has been reported on somatotropin (ST), insulin-like growth factor-1 (IGF-1), cortisol, and thyroid hormones that are important regulators of mammary gland function.

The objective of the present study was to investigate some metabolic and hormonal changes and lactational performance during recombinant bovine TNF (rbTNF)-induced acute phase response in lactating cows in order to provide evidence that TNF is an in vivo mediator of mastitis-stimulated systemic changes.

MATERIAL AND METHODS

Twelve non-pregnant, lactating Holstein cows of 1st to 3rd parity between 10 and 14 wk after parturition were used in a crossover design in this study. They were milked twice daily at 06.00 and 16.00 h with a quarter milking machine. The diet consisted of, % dry matter basis: mixed concentrate 41.4, maize silage 22.0, lucerne hay cube 12.6, and orchardgrass hay 24.0. The cows were randomly divided into a rbTNF treatment group (n=6) and a saline treatment group (n=6) as control. The rbTNF (2.5 μg/kg/d) or saline (3 ml/head/d) was injected subcutaneously at 12.00 h daily for 7 consecutive days (d 0-6). On d 6 in the experiment period, we determined the effect of daily administration of rbTNF on ST-releasing hormone (STRH, 0.25 μg/kg) stimulated ST release. Milk fat and protein were measured with an infrared milk analyzer. The concentrations of plasma ST, cortisol, triiodothyronine (T_3), IGF-1, haptoglobin, and NEFA were measured.

RESULTS

Treatment with rbTNF decreased the milk yield ($P<0.05$) during the period between d 1 and 8 (Table 1). The milk fat percentage was elevated ($P<0.05$) at d 1 following rbTNF treatment and remained higher until d 7 in comparison with that in the control cows (Table 2). The protein content in milk was lower ($P<0.05$) in the rbTNF-treated cows than in the control cows on d 5 and 7 (Table 2). The plasma concentrations of cortisol, haptoglobin, and NEFA were increased ($P < 0.05$) by daily administration of rbTNF. The plasma T_3 and IGF-1 concentrations in the rbTNF-injected cows were lower ($P<0.05$) than those in the controls. The plasma ST concentration was lower ($P<0.05$) in the rbTNF group than in the control group from 15 to 120 min after STRH injection.

Table 1. Milk yield of cows treated with saline (control, 3 ml/head) or rbTNF (2.5 μg/kg) during the pre-treatment (d -1), treatment (d 0 - 6), and post-treatment (d 7 - 10) periods[1]

Period[1]	Milk yield[2]	
	control	RbTNF
Day -1	28.0 ± 1.0	28.4 ± 1.0
0	28.6 ± 1.0	28.3 ± 1.0
1	28.4 ± 1.2	23.8 ± 0.8*
2	28.4 ± 1.3	24.2 ± 0.9*
3	28.5 ± 1.3	24.3 ± 0.9*
4	28.1 ± 1.4	23.9 ± 0.8*
5	28.0 ± 1.3	23.8 ± 1.0*
6	28.6 ± 1.4	23.7 ± 0.7*
7	28.3 ± 1.3	23.6 ± 1.0*
8	28.2 ± 1.1	24.3 ± 0.9*
9	27.9 ± 1.4	24.6 ± 1.1
10	28.3 ± 1.4	25.1 ± 1.2

values are mean ± SE for 12 cows

[2] milk yield, kg/d

Asterisks indicate significant differences from control cows: *P<0.05

Table 2. Percentages of fat and protein in milk of cows treated with saline (control, 3 ml/head) or rbTNF (2.5 μg/kg) for 7 days (d 0 - 6)

Day	Fat		Protein	
	control	RbTNF	control	RbTNF
0	3.3 ± 0.2	3.2 ± 0.3	3.1 ± 0.1	3.0 ± 0.1
1	3.1 ± 0.1	3.8 ± 0.3*	3.2 ± 0.1	2.9 ± 0.1
3	3.2 ± 0.3	3.8 ± 0.2*	3.2 ± 0.1	2.8 ± 0.1
5	3.3 ± 0.3	4.2 ± 0.2*	3.3 ± 0.1	2.7 ± 0.1*
7	3.2 ± 0.2	4.3 ± 0.2*	3.2 ± 0.1	2.7 ± 0.1*

values are mean ± SE for 12 cows

Asterisks indicate significant differences from control cows: *P<0.05

DISCUSSION

Daily treatment with rbTNF influenced lactational performance, and altered metabolites and hormone concentrations in lactating cows. In studies using the mastitis model to investigate the pathophysiological causes of reduced lactational performance during mastitis, milk yields in the stage of early lactation were depressed in quarters not receiving *E. coli* despite the absence of inflammation in these quarters (Hoeben et al., 2000). The suppression of milk production was apparently mediated in part by systemic effects of intramammary *E. coli* infusion,

and may be caused by changes in the concentrations of stimulatory or inhibitory hormones (e.g., ST, IGF-1, T_3, and cortisol) (Hoeben et al., 2000). Data from the present study indicated that rbTNF induced systemic responses (e.g., acute phase response) associated with coliform mastitis in peak lactation, including a decrease in milk production, an increase of fat content and a decrease of protein content in milk. These changes in milk composition were similar to those observed following i.v. endotoxin treatment (Shuster et al., 1991). The reduction of plasma ST response to STRH in the rbTNF-treated cows is in agreement with the result obtained in our previous study (Kushibiki et al., 2000). It has been reported that TNF receptors are found in the bovine pituitary gland, and TNF inhibits STRH-stimulated ST release in cultured bovine pituitary cells (Elsasser et al., 1991).

CONCLUSIONS

This study showed that exogenous rbTNF injection induced many of the systemic responses associated with coliform mastitis in the plasma and milk of lactating cows. These findings support and confirm the hypothesis that TNF, rather than endotoxin, is absorbed from the mammary gland and released into the circulation, and that TNF is responsible for the systemic changes observed during coliform mastitis.

REFERENCES

Elsasser T.H., Caperna T.J., Fayer R., 1991. TNF-alpha affects GH secretion by a direct pituitary interaction. Proc. Soc. Exp. Biol. Med. 198, 547-554

Hoeben D., Burvenich C., Trevisi E., Bertoni G., Hamann J., Bruckmaier R. M., Blum, J.W., 2000. Role of endotoxin and TNF in the pathogenesis of experimentally induced coliform mastitis in periparturient cows. J. Dairy Res. 67, 503-514

Kushibiki S., Hodate K., Ueda Y., Sgingu H., Mori Y., Itoh T., Yokomizo Y., 2000. Administration of rbTNF affects intermediary metabolism and insulin and growth hormone secretion in dairy heifers. J. Anim. Sci. 78, 2164-2171

Pighetti G.M., Sordillo L.M., 1994. Regulation of mammary gland macrophage TNF production with IFN-ganma. Res. Vet. Sci. 56, 252-255

Shuster D.E., Harmon R.J., Jackson J.A., Hemken R.W., 1991. Reduced lactational performance following intravenous endotoxin administration to dairy cows. J. Dairy Sci. 74, 3407-3411