
THE PROCEEDINGS OF THE
NEW ZEALAND SOCIETY
OF
ANIMAL PRODUCTION
VOLUME 62 2002

Plasma hormone concentrations in pasture-fed Friesian cows treated with recombinantly-derived bovine somatotropin (bST)

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ABSTRACT

Friesian cows (25 per group) were treated with excipient or recombinantly-derived bovine somatotropin (bST,25 mg/day) by two-weekly injection of a controlled release formulation for 26 weeks commencing 7 to 11 weeks after calving. Responses in fat yield were significant during weeks 1 to 13 of treatment (spring/early summer) and weeks 21 to 25 (autumn) but not during the intervening dry summer period when pasture allowance was low. Ten randomly-selected cows per group were blood sampled (tail vein, 2 hours off pasture) in weeks 5,9,13,17,21 and 25 of treatment. Treatment of cows with bST significantly elevated plasma concentrations of immunoreactive bST (12.4 vs 18.5 ng/ml, Pooled se = 0.8 ng/ml, P<0.001) and insulin-like growth factor-1 (IGF-1) (178.5 vs 246.1 ng/ml, Pse = 7.5 ng/ml, P<0.001). Treatment x sampling date interactions were nonsignificant for plasma levels of both bST and IGF-1, reflecting parallel changes in the concentrations of these hormones across the treatment period. It is concluded that the inability of cows to respond to exogenous bST during periods of low pasture availability does not reflect a diminished IGF-1 response to bST at this time.

Keywords Bovine somatotropin, insulin-like growth factor-1, lactation.

INTRODUCTION

It is now well established that treatment of cows with pituitary- or recombinantly-derived bovine somatotropin (bST) substantially increases yield of milk and milk components. In studies where cows are offered *ad libitum* quantities of concentrate-based rations, responses to exogenous bST are relatively constant over long periods of treatment (Bauman *et al.*, 1985). However, we have recently shown that responses of pasture-fed cows treated with bST under commercial conditions are related to pasture allowance, being greatest in the spring and autumn but effectively zero in the intervening dry summer period (Hoogendoorn *et al.*, 1990). In that study, bST-treated cows exhibited only a small decline in condition score (0.2 condition score units) suggesting that the inability of cows to respond to bST during periods of low pasture availability may be related to factors other than nutrient supply *ad libitum*.

Nutritional effects on the response to exogenous bST in pasture-fed cows could potentially be related to changes in circulating concentrations of insulin-like growth factor-1 (IGF-1). Infusion of IGF-1 directly into the mammary gland via the pudic artery has been reported to stimulate milk yield in goats (Prosser *et al.*, 1989) and systemic treatment of cows with bST produces dose-dependent elevations in both milk yield and circulating IGF-1 concentrations (Breier *et al.*, 1991). Thus IGF-1 may mediate some of the galactopoietic effects of bST although Davis *et al.* (1989) observed no galactopoietic response to a jugular infusion of IGF-1 in goats. In steers, low levels of nutrition are associated with depressed circulating levels of IGF-1 and an inability of exogenous somatotropin to elevate circulating IGF-1 levels (Breier *et al.*, 1988a), apparently reflecting down-regulation of the high affinity hepatic somatotrophic receptor (Breier *et al.*, 1988b). The possibility thus exists that cows fail to respond to

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exogenous bST during periods of low pasture availability because they are unable to maintain elevated IGF-1 levels in response to bST stimulation. Accordingly we have, in this study, examined relationships between circulating bST and IGF-1 levels, and the galactopoietic response to bST, in cows at pasture.

MATERIALS AND METHODS

Details of the experimental animals and treatments have been published elsewhere (Hoogendoorn *et al.*, 1990). Briefly, 50 multiparous Friesian cows were allocated at random to two equal groups. One group was treated with recombinantly-derived bST at a dose equivalent to 25 mg/day for 26 weeks commencing 7 to 11 weeks after calving (late October). The bST was administered by two-weekly injection of a controlled release formulation (American Cyanamid Co., Princeton, N.J., U.S.A.). Control cows were injected with excipient, also at two-weekly intervals. Cows were grazed on mixed ryegrass/white clover pastures and were supplemented with greenfeed maize during weeks 16 to 23 of treatment (February/March). Cows were herd-tested every two weeks commencing one week after the first injection of bST or excipient.

For the purposes of this study, ten cows were selected at random from each of the control and bST-treated groups. These cows were blood sampled after the morning milking (i.e. two hours off pasture) in weeks 5,9,13,17,21 and 25 of treatment. In each case sampling occurred 7 days after the last injection of the two-weekly controlled release bST formulation. Blood samples (8 ml) were collected from the tail vein into EDTA-venoject tubes (Nipro Medical Industries Limited, Tokyo) and placed immediately on ice. Within 1h of collection they were centrifuged at 3000g and 4°C for 20 min. Plasma was harvested and stored in duplicate vials at -20°C until assay.

Plasma was analysed for concentrations of somatotropin and IGF-1. Somatotropin concentrations were determined by radioimmunoassay (Flux, *et al.*, 1984) using pituitary-derived bST for iodination (USDA-bGH-I1, 3.2 I.U./mg) and reference standards (USDA-bGH-B1, 1.9 I.U./mg). Plasma IGF-1 levels were determined by radioimmunoassay following acid-ethanol extraction (Gluckman *et al.*, 1983) and are expressed in terms of recombinant human Met-IGF-1 (batch no. 724-44, Dr B.D. Burleigh, International Minerals and Chemicals, Pitman-Moore, Northbrook, IL, USA).

Multivariate analysis of variance (MANOVA) was used to test the effects of treatment (bST vs control), sampling date (time) and the treatment x time interaction on plasma concentrations of each hormone and on milk fat yield.

RESULTS AND DISCUSSION

Patterns of milk fat yield in the control and bST-treated cows are shown in Figure 1. One week after the onset of bST injections, treated cows had exhibited an 18% response in fat yield ($P<0.05$). Thereafter the magnitude of the response to bST declined progressively, being non-significant during the dry summer period (weeks 13 to 19) when pasture covers were low. The onset of autumn rain, and accompanying increase in pasture cover, was associated with a divergence between the groups in fat yield and significant ($P<0.05$) treatment effects at weeks 21 and 25 of treatment. As a result both the bST treatment effect ($P<0.01$) and the treatment by time interaction ($P<0.01$) were significant with respect to fat yield. A similar changing pattern of response, which paralleled changes in pasture cover, was observed for milk and protein yields (Hoogendoorn *et al.*, 1990).

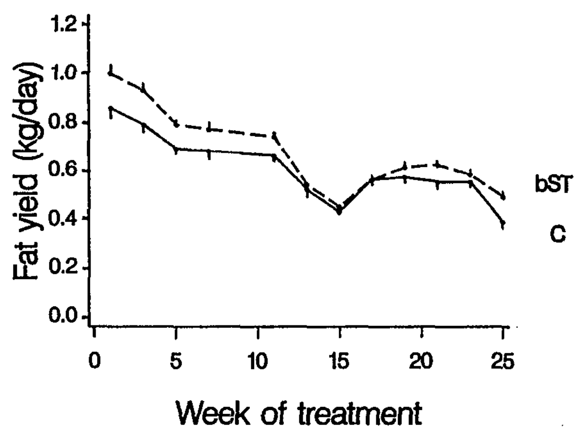

FIG 1 Milk fat yield in control (——) and bST-treated (– –) cows during 25 weeks of bST treatment (25 mg/day). Vertical bars represent standard errors about the mean. From Hoogendoorn *et al.* (1990).

Circulating concentrations of immunoreactive bST are in Fig. 2. Control cows maintained bST levels of 11 to 13 ng/ml throughout the study while levels in bST-treated cows were about 50% higher. Over the whole sampling period, mean circulating bST levels were 12.4 ng/ml in the control cows and 18.5 ng/ml in the treated group (Pooled s.e. = 0.8 ng/ml, P<0.001). Whereas the treatment effect was highly significant there was no treatment x time interaction (P>0.10), reflecting the parallel changes in plasma bST levels in the two groups.

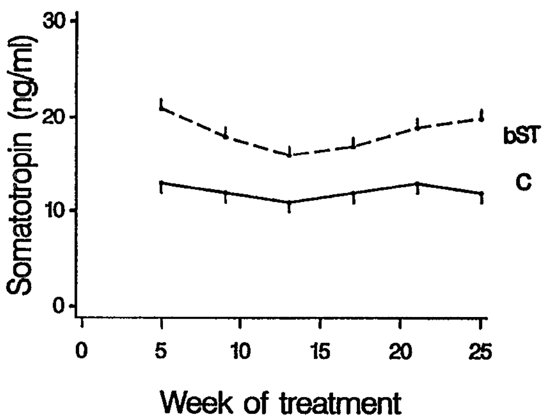

FIG 2 Plasma concentrations of bovine somatotropin in control (—) and bST-treated (– –) cows during 25 weeks of bST treatment (25 mg/day). Vertical bars represent standard errors about the mean.

Plasma IGF-1 levels are in Fig. 3. As expected, bST treatment was associated with a significant (P<0.001) elevation in circulating IGF-1, mean levels during the study being 178.5 ng/ml in control cows and 246.1 ng/ml in the treated group (Pooled s.e. = 7.5 ng/ml). There was no indication of a substantial decline in IGF-1 levels during the dry summer period. Moreover, temporal changes in IGF-1 levels in the control and bST-treated cows followed a similar pattern, as indicated by the non-significant (P>0.10) treatment x time interaction.

It is apparent from these results that, while there were marked changes through the season in the magnitude of the fat yield response to bST, apparently reflecting changes in the amount of pasture on offer to the cows (Hoogendoorn *et al.*, 1990), no similar pattern was evident with respect to circulating somatotropin and IGF-1 concentrations. Although treated cows maintained higher plasma levels of both bST and IGF-1, the magnitude of this difference was essentially constant throughout the treatment period (as indicated by the non-significant treatment x time interactions). While a constant difference in bST levels could be expected (unless the rate of release of bST from the controlled release formulation, or the clearance of bST, varied), it would have been reasonable to expect low IGF-1 levels (and a diminished difference between the groups) during the dry summer period when herbage yield was low (Breier *et al.*, 1988a). The difference between the groups in circulating IGF-1 levels was relatively small at week 17 (Fig.3) but this reflected the combined effects of decreased levels in the treated cows and elevated levels in the controls. Considering the whole treatment period, there was little association between the patterns of plasma IGF-1 levels and the galactopoietic response to bST. Thus the inability of cows to respond to bST during the dry summer period does not appear to reflect an inability to maintain elevated IGF-1 levels in response to exogenous bST stimulation.

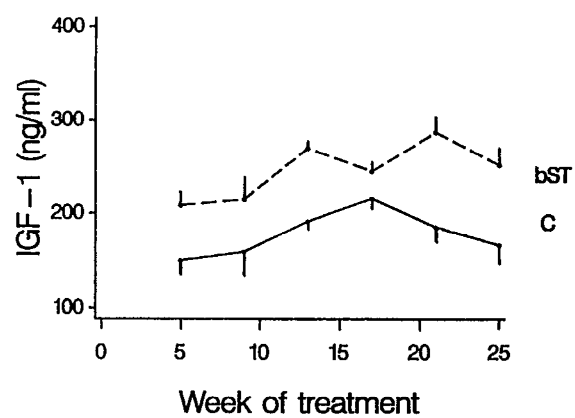

FIG 3 Plasma concentrations of insulin-like growth factor-1 (IGF-1) in control (—) and bST-treated (– –) cows during 25 weeks of bST treatment (25 mg/day). Vertical bars represent standard errors about the mean.

A number of possible reasons exist for the lack of association between temporal patterns in plasma IGF-1 concentrations and the galactopoietic response to bST. First, the degree of nutritional restriction experienced by cows during the dry summer period, while limiting the supply of nutrients for milk and milk fat synthesis, may have been insufficient to reduce circulating IGF-1 concentrations. Breier *et al.* (1986) found that, in steers, plasma IGF-1 levels were reduced only by marked nutritional restriction. Furthermore, chronic somatotropin therapy appears to upregulate the hepatic somatotropic receptor (see review by Breier *et al.*, 1991), an effect which would tend to overcome any nutritionally-induced decline in plasma IGF-1 levels. Second, changes in the distribution of IGF-1 between its two major binding proteins (Breier *et al.*, 1991) could have altered its delivery to target tissues in a manner not detected by the assay of circulating IGF-1 concentrations. Finally, and as suggested by the data of Davis *et al.* (1989), our results may indicate that circulating IGF-1 is not the principal mediator of the galactopoietic effects of bovine somatotropin.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge; Miss M.F. Scott and Miss Y.H. Cottam for technical assistance; American Cyanamid Co. for provision of the recombinant bovine somatotropin; and the financial support of the Livestock Improvement Corporation.

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