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Synergism between a human growth hormone-releasing factor and thyrotropin-releasing factor on growth hormone release in relation with the stage of lactation of Holstein dairy cows (1)

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Résumé. Trois groupes de 6 vaches Holstein en début, au pic et en fin de lactation (18, 72 et 210 jours, respectivement) ont reçu par voie sous-cutanée à 10,00 h les traitements suivants : hGRF(1-29)NH_2 (3,3 $\mu g.kg^{-1}$), TRF (1,1 $\mu g.kg^{-1}$) ou la combinaison des deux facteurs hypothalamiques aux mêmes doses. Le pic atteint et la surface sous la courbe de la GH (SSC) ont été respectivement 2,5 et 3,4 fois plus grands après l'injection combinée du hGRF(1-29)NH_2 et du TRF que la somme des réponses après leurs injections séparées. La sécrétion de la GH mesurée par la SSC a diminué de façon linéaire ($P < 0,05$) en fonction des jours de lactation.

Human growth hormone-releasing factor (hGRF) and its fragment, (1-29)NH_2, stimulate GH release in cattle (Moseley *et al.*, 1984 ; Petitclerc *et al.*, 1987). In addition, thyrotropin-releasing factor (TRF) induces GH release in cattle (Convey *et al.*, 1973). Used together, these two hypothalamic factors act in synergy to increase GH secretion in dairy cattle (Hodate *et al.*, 1985). In this experiment, our objectives were to determine if GH responses to hGRF and TRF were synergistic and related to the stages of lactation of Holstein cows.

Three groups of six cows at the beginning (18 $\pm$ 6 days), at the peak (72 $\pm$ 8 days) or in mid to late lactation (210 $\pm$ 14 days) were used. Each group was divided in two replicates and each cow within each replicate received the three following treatments over three consecutive days according to a 3 $\times$ 3 latin square design : 1) hGRF(1-29)NH_2 (3.3 $\mu g.kg^{-1}$), 2) TRF (1.1 $\mu g.kg^{-1}$) and 3) hGRF(1-29)NH_2 plus TRF (same doses). All the injections were done sc at 10.00 h. Bovine GH was analysed by a double antibody RIA (Petitclerc *et al.*, 1987). The basal level was the mean of samples taken prior to the injection. The peak was the highest level reached after the injection. The area under the curve (AUC) was calculated using the trapezoidal method, excluding the area under the basal level.

The GH response following sc injections of hypothalamic peptides is depicted in figure 1. There were significant effects ($P < 0.01$) of treatments and stages of lactation but no significant interaction ($P > 0.05$) between both factors. After hGRF(1-29)NH_2, TRF, or both peptide injections, GH peaks ($ng.ml^{-1}$) were 36.2,

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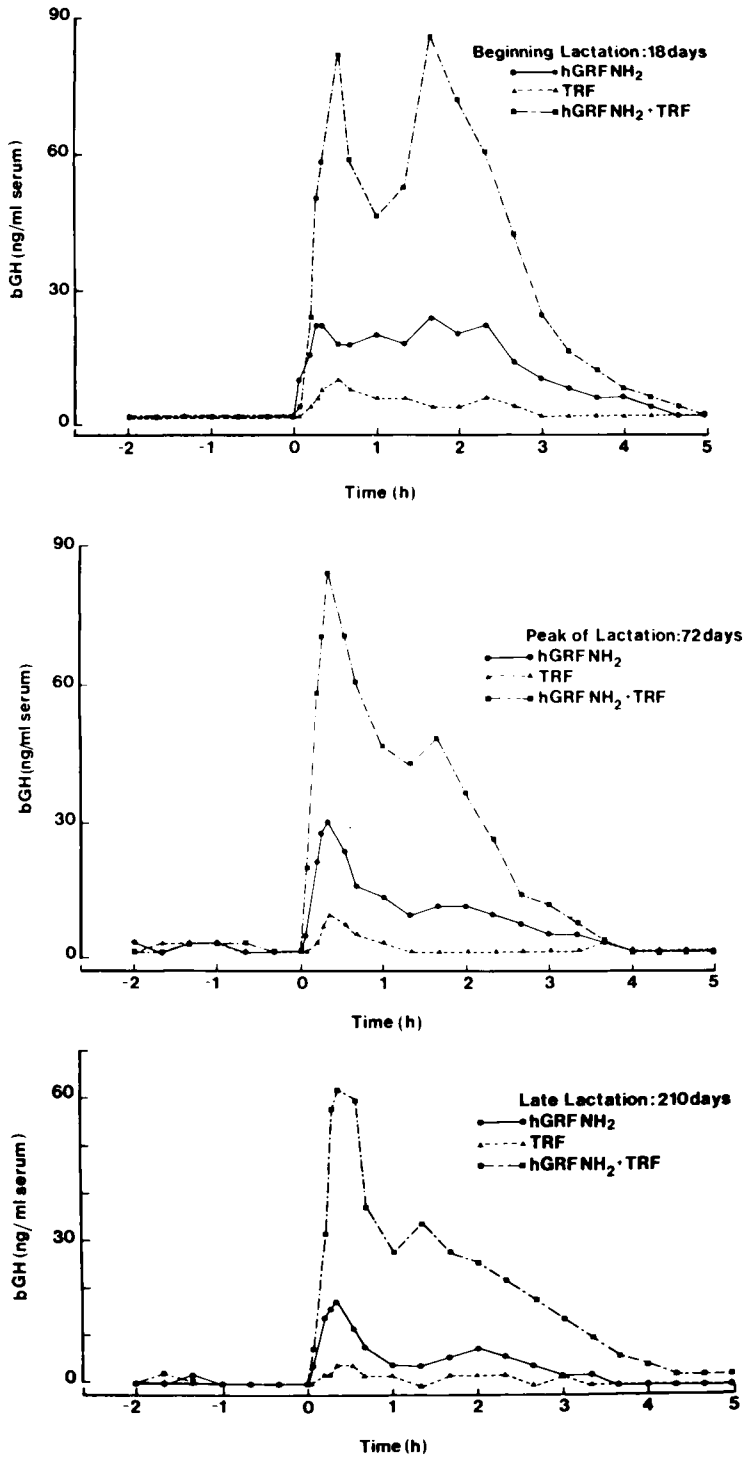

FIG. 1. — *Profile of serum bovine growth hormone* (bGH) *after subcutaneous injection of hGRF(1-29) NH_2* (3.3 $\mu g.kg^{-1}$), *TRF* (1.1 $\mu g.kg^{-1}$) *or both peptides* (same doses) *in Holstein cows at three different stages of lactation* (18, 72 and 210 days, respectively).

10.7 and 127.1 on day 18 ; 33.5, 11.0 and 89.1 on day 72 ; and 20.5, 4.0 and 71.6 on day 210, respectively (pooled SE = 14.2). AUC ($ng.ml^{-1}.min$) were 3 343, 699 and 10 574 on day 18 ; 1 958, 291 and 6 945 on day 72 ; and 1 122, 203 and 5 707 on day 210 of lactation (pooled SE = 982). The AUC following hGRF(1-29)NH_2 injection was higher ($P < 0.05$) than following TRF injection, but smaller ($P < 0.001$) than following GRF + TRF injection. Our results clearly show an important synergism between hGRF(1-29)NH_2 and TRF on GH release at all three stages of lactation. In addition, a biphasic pattern of GH release after GRF + TRF injection was observed in the beginning lactation cows. GH peaks and AUC following the combined injection were respectively 2.5 and 3.4 times higher than the sum of the responses following their separate injections. These results confirm the observation of Hodate *et al.* (1985) in dairy calves. GH basal levels at the beginning and peak of lactation were not different, but were higher ($P = 0.02$) than basal level at the end of lactation. They were respectively 1.9, 3.0 and 0.7 $ng.ml^{-1}$ (pooled SE = 0.1). This phenomenon has also been reported by Koprowski and Tucker (1975). GH response as measured by AUC declined linearly ($P < 0.05$) with stages of lactation, but GH peaks were not different ($P = 0.12$). Following TRF injections, Vines *et al.* (1977) reported that GH secretion was higher at two months of lactation compared with 4, 6, 8 and 10 months. They proposed that the higher response at the beginning of lactation could be due to a higher ability of the pituitary to secrete GH at a time when milk production is higher and GH probably more needed. Overall, these two hypothalamic factors could be useful to manipulate GH secretion in order to stimulate growth and lactation of dairy cattle.

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