

Involvement of endothelin B receptors in the increase of plasma glucose and NEFA with a GH-independent manner in cattle

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We have previously demonstrated that endogenous ghrelin response to endothelin-3 (ET-3) injection stimulated growth hormone (GH) secretion through GH secretagogue receptor type 1a (GHS-R1a) (Zhao et al., 2010) and glucose and nonesterified fatty acids (NEFA) were increased by ET-3 in cattle. The present study was designed to characterize whether ET_B receptors and GH are involved in the ET-induced the production of glucose and NEFA. Eight Holstein steers (7-month-old, 209 ± 7 kg body weight, BW) were randomly assigned to receive intravenous bolus injections of 0.1% bovine serum albumin in saline (as control), bovine ET-3 (1.0 µg/kg BW), IRL1620 (selective ET_B receptor agonist, 2.0 µg/kg BW), [D-Lys³]-GHRP-6 (GHS-R1a antagonist, 20.0 µg/kg BW) and bovine ET-3 (1.0 µg /kg BW) combined with [D-Lys³]-GHRP-6 (20.0 µg/kg BW), respectively. Animals had 1 or 2 days to recover between each treatment. Blood samples were collected at -30, -15, 0, 5, 10, 15, 20, 25, 30, 35, 40, 50, 60, 90, 120 and 150 min relative to injection time. Concentrations of glucose and NEFA in plasma were analyzed by commercially available kits. The results are presented as means ± SEM. Differences in the concentrations of glucose and NEFA compared with basal levels were analyzed by repeated measure ANOVA. ET-3 produced a significant increase (P<0.001) in glucose levels at 15 min (121.8 ± 7.4 mg/dL) compared with basal levels (87.9± 1.5 mg/dL) which continued for 150 min. NEFA levels were markedly elevated (P<0.001) from 34.8 ± 2.1 µEq/L to 114.2 ± 11.0 µEq/L at 10 min after ET-3 injection which continued for 40 min. IRL 1620 mimicked the effects of ET-3 on the elevation of glucose and NEFA. Our previous results showed that ET-3-induced elevation of plasma GH was blocked by [D-Lys³]-GHRP-6. However, in this study, [D-Lys³]-GHRP-6 failed to block ET-3-induced elevation of glucose and NEFA. These results indicate that ET_B receptors are involved in ET-3-stimulated production of glucose and NEFA but in a GH-independent manner in ruminants.

Zhao H, Thanthan S, Yannaing S, Kuwayama H (2010). Involvement of endothelin B receptors in the endothelin-3-induced increase of ghrelin and growth hormone in Holstein steers. *Peptides*:31:938-943.