

ABSTRACT

Title: Acipimox during Short-Term Exercise Exerts A Negative Feedback of Growth Hormone on Ghrelin Secretion in Patients with Bulimia Nervosa and in Healthy Women: The Role of Lipolysis

Objective: Eating disorders, such as bulimia nervosa (BN) and anorexia nervosa (AN), are characterized by abnormal eating behavior. The main features of BN are binge-eating and inappropriate compensatory methods to prevent weight gain. The appetite-modulating peptide ghrelin is secreted by the stomach and shows a strong release of growth hormone (GH). A potential GH-ghrelin feedback loop between stomach and the pituitary has been recently reported. Acipimox (Aci), an analogue of nicotinic acid, inhibits lipolysis in adipose tissue (AT) and reduces plasma glycerol and free fatty acids (FFA) levels. Exercise and Aci are stimulators of GH secretion. We suppose that a negative feedback from increased GH levels during exercise may play a role in reducing plasma ghrelin levels. We surmised that altered baseline activity and exercise-induced activation of the sympathetic nervous system (SNS) results in excessive stimulation of lipolysis associated with negative energy balance and may lead to abnormal AT metabolism in patients with BN. Disruption of the gut-brain-AT axis might be involved in the pathogenesis of BN. **The Aims:** The aim of this study was to evaluate plasma GH and plasma ghrelin levels under resting conditions and in response to exercise alone or together with Aci administration in patients with BN and healthy women. Simultaneously, we measured plasma FFA and plasma glycerol levels in circulation and subcutaneous (sc) abdominal AT glycerol levels using a microdialysis technique *in situ* and *in vivo* under basal conditions and after exercise alone or together with systemic administration of Aci. **Study Design and Methods:** We investigated responses of plasma GH, ghrelin, FFA, glycerol and AT glycerol concentrations to exercise in BN patients and healthy women (C) given the anti-lipolytic drug Aci or placebo. Seven BN and seven C women were recruited for this randomized, placebo-controlled, single-blind study. Aci or placebo was given 60 minutes before the exercise (45 min, 2 W/kg of lean body mass [LBM]). GH, ghrelin, FFA, glycerol plasma concentrations and microdialysate glycerol concentrations were measured using commercial kits. Glycerol was measured *in vivo* in sc abdominal AT using microdialysis. **Results:** The exercise induced an increase in plasma GH and FFA in both groups and a decrease in plasma ghrelin only in BN patients. Exercise with Aci administration resulted in plasma GH increase, and in plasma ghrelin and FFA decrease in both groups. The exercise induced a higher increase of extracellular glycerol concentrations in sc abdominal AT of BN patients, while exercise with Aci administration induced a higher decrease of extracellular glycerol in BN patients compared to the C group. The exercise induced similar increases in plasma glycerol levels in both groups. The exercise with Aci administration resulted in plasma glycerol decrease more in BN patients. **Conclusions:** In conclusion, we confirm the results of a randomized, placebo-controlled, single-blind, microdialysis study, *i.e.* that the Aci-induced suppression in plasma ghrelin levels during short-term exercise in both groups suggests an inhibitory feedback of GH on ghrelin secretion in both groups. The post-exercise rise (45 minute) in AT glycerol is much more attenuated by acute Aci treatment in BN patients and that hypersensitivity of SNS in sc abdominal AT may exist in patients with BN. Simultaneously, we found facilitated turnover of plasma glycerol after short-term exercise together with Aci administration in BN. Aci effects a FFA-independent mechanism. Lower basal lipolysis in AT in BN patients may be due to the protective mechanism that prevents the exhaustion of energy reserves. **Key Words:** Bulimia nervosa • Acipimox • Growth hormone • Ghrelin • Free fatty acids • Glycerol • Exercise • Microdialysis • Adipose tissue