RAPID COMMUNICATION

Increased fasting plasma ghrelin levels in patients with bulimia nervosa

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Abstract

Objective: Fasting plasma ghrelin levels play an important role in the pathophysiology of the eating disorder anorexia nervosa. Bulimia nervosa (BN) also has been associated with abnormal neuro-endocrine regulation. Thus, we examined the relationship between body mass index (BMI) and plasma ghrelin concentrations in patients with BN for the first time.

Methods: The subjects included 15 female BN patients and 11 female healthy volunteers (controls). Fasting blood samples were collected from all subjects.

Results: The plasma ghrelin concentrations in all subjects demonstrated a significantly negative correlation with BMI. Mean plasma ghrelin level in BN patients was significantly higher than that in the controls, though mean BMIs between the groups were not significantly different.

Conclusion: These findings suggest that not only BMI but also abnormal eating behaviors with habitual binge eating and purging may have some influence on circulating ghrelin level in BN.

European Journal of Endocrinology 146 1–3

Introduction

Ghrelin was originally discovered in the rat and human stomach, and stimulates growth hormone secretion in rodents (1). This peptide that antagonizes leptin action has a role in the regulation of feeding behavior and energy metabolism in the central nervous system (2). In addition, it has been reported that fasting plasma ghrelin concentrations in humans are negatively correlated with BMI (3), percentage body fat and fasting leptin and insulin concentrations (4), which play an important role in the pathophysiology of the eating disorder anorexia nervosa (3, 5).

Bulimia nervosa (BN) is characterized by habitual binge eating despite the fear of weight gain. Some studies have demonstrated impaired post-ingestive satiety associated with role of central nervous system serotonin or hypothalamic neurotransmitters (6). Plasma leptin concentrations were found to decrease and plasma neuropeptide Y concentrations to increase in normal-weight BN patients (7). We then hypothesized that fasting plasma ghrelin concentrations in BN patients may increase or show some specificity in relation to this disease. Thus, we measured the fasting plasma ghrelin concentrations in BN patients and examined the relationship between BMI and plasma ghrelin concentration before treatment.

Subjects and methods

Fifteen female BN patients meeting the criteria listed in *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (8) and eleven healthy female volunteers (the control group) were the subjects of this study. The BN patients had binge eating and purging episodes at least twice a week over the preceding 3 months. Patients were excluded if they had a history of alcohol or drug abuse, or gastrointestinal disease, and were assayed before the initiation of active treatment.

We collected fasting blood samples from all subjects at 0800 h after an overnight fast. Body weight and body fat were measured on the day when samples were obtained. Percentage body fat was obtained by bioelectrical impedance analysis (9). Blood was drawn into chilled tubes containing EDTA·2Na (1 mg/ml) and aprotinin (500 U/ml). Plasma ghrelin was measured using an RIA as described elsewhere (3). The Institutional Committee of Kagoshima University approved the protocol and all subjects provided written informed consent before participation.

Correction coefficients were calculated by linear regression analysis. The subject groups (mean $\pm$ S.E.M.) were compared using Student's *t*-test. A *P* value of <0.05 was considered statistically significant.

Results

Physiological characteristics of the subjects are shown in Table 1. The subject groups were not significantly different in age, BMI or percentage body fat.

The fasting plasma ghrelin concentration in all subjects was negatively correlated with BMI ($r = -0.50$, $P < 0.01$) (Fig. 1a) and percentage body fat ($r = -0.54$, $P < 0.005$) (data not shown). The mean plasma ghrelin level in BN (298.4 ± 135.8 pmol/l, mean $\pm$ s.d.) was significantly higher ($P < 0.0005$) than that in the control group (126.9 ± 28.2 pmol/l) (Fig. 1b).

Discussion

The plasma ghrelin concentration in subjects was negatively correlated with BMI and percentage body fat. These findings are in agreement with previous human studies (3, 4). Our results document for the first time that plasma ghrelin increased in patients with bulimia nervosa.

Ghrelin is one of the gastrointestinal peptides and when administered intracerebroventricularly, stimulates gastric acid secretion by activating the vagus system (10). As the regulation mechanism between gastrointestinal peptides and the vagus system has been reported to play a role (11), circulating ghrelin levels may act as a feedback system via the vagal system. Several lines of evidence have led us to postulate that afferent vagal hyperactivity could be an important factor in the pathophysiology of BN (12). Since BN has been reported to be due to hypervagal activity (12), afferent vagal hyperactivity may increase circulating ghrelin levels.

Table 1 Physiological characteristics of subject groups.

	BN (N = 15)		Control (N = 11)	
	Mean	SD	Mean	SD
Age (years)	23.3	5.3	24.0	1.9
Duration of illness (years)	3.2	2.9	—	—
Body mass index (kg/m ²)	20.0	2.9	21.2	1.2
Percent body fat (%)	23.4	5.2	25.8	2.7

BN, Patients with bulimia nervosa; Control, Healthy volunteers.

Recently the incidence of BN has been found to be increasing, particularly in large urban cities of western countries (13). It has been previously suggested that binge-eating behavior is associated with metabolic and leptin dynamics in normal young women (14). In line with the recent concept that binge eating and purging behavior may produce a physiological factor that promotes the binge/purge cycle (15), the habitual abnormal eating behavior in conjunction with binge eating and purging may cause hormonal dysfunction in the neuroendocrinological system components such as ghrelin and leptin. We hypothesize that habitual binge eating and purging behavior may cause an increase in circulating ghrelin levels. Moreover, we speculate that increased circulating ghrelin levels may induce hyperphagia through the appetite control system.

In conclusion, we found that not only BMI but also abnormal eating behaviors with habitual binge eating and purging may have some influence on circulating ghrelin levels in BN.

Figure 1 (a) Relationship of plasma ghrelin concentration and body mass index (BMI) for patients with bulimia nervosa (BN), healthy volunteers (controls). (b) Comparison of plasma ghrelin concentrations in patients with BN and controls.

Acknowledgements

This study was supported by a research grant from the Japanese Ministry of Health, Labor and Welfare.

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Received 3 April 2002

Accepted 18 April 2002