GROWTH HORMONE, GROWTH HORMONE RECEPTOR AND INSULIN-LIKE GROWTH FACTOR SERUM LEVELS IN PATIENTS WITH OBESITY AND FOOD ADDICTION

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Obesity is a public health problem that increasingly becomes widespread and causes various complications. Food addiction is a hedonic eating behavior characterized by overconsumption of palatable foods (i.e., foods involve a high amount of salt, sugar and fat). Disturbances in the growth hormone signaling pathway were shown to be associated with increased food intake and adiposity. The study aimed to determine the growth hormone (GH), growth hormone receptor (GHR), insulin, and insulin-like growth factor 1 (IGF-1) serum levels in individuals with obesity and food addiction. The present study involved 30 adults with obesity (23 females and 7 males) and 10 healthy adults (5 females and 5 males). 18 obese adults were diagnosed with food addiction, whereas only 2 individuals with food addiction were in the control group. GH, GHR, IGF-1 and insulin values were analyzed with ELISA kits. It was revealed that the obese subjects had significantly lower serum IGF-1 levels compared to healthy individuals (144.55±22.69 ng/ml vs 338.70±61.90 ng/ml, P < 0.001)). No significant differences in the GH, GHR and insulin levels between obese and control groups were detected (P > 0.05). No significant differences between the group with food addiction and the group without food addiction in terms of gender, age, weight, BMI, GH, GHR, insulin and IGF-1 levels were observed. Our study demonstrates that normal IGF-1 levels may be protective for the development of obesity. The serum levels of GH, GHR, insulin, IGF-1 are not associated with food addiction and, therefore, can not be used as novel markers of food addiction.

K e y w o r d s: obesity, food addiction, growth hormone, growth hormone receptor, insulin-like growth factor 1.

Obesity is a public health problem that increasingly becomes widespread and causes various complications. Food intake is vital for survival and regulated by homeostatic and hedonic mechanisms. Inadequate or excessive food intake that impairs energy balance is associated with high comorbidity and causes to serious health problems [1, 2]. The increasing rate of obesity prevalence has revealed the significance of food addiction. Food addiction is a hedonic eating behavior characterized by overconsumption of palatable foods (ie, foods involve high amount of salt, sugar, and fat) [3]. The most common symptoms of food addiction are: 1. loss of control in eating, 2. continous and increased amount of food intake despite the negative consequences. Therefore, food addiction can be associated with obesity and eating disorders [4]. Food intake that depends on the balance between hedonic and metabolic pathways is mainly controlled by the brain. Food addiction may disrupt the balance and then lead to the development of obesity [5].

Growth hormone (GH) which is a single chain polypeptide composed of 191 amino acids is synthesized by somatotropic cells in the pituitary gland via hypothalamic–pituitary axis. GH that interacts with growth hormone receptor (GHR) is responsible for

numerous biological functions such as regulation of growth, metabolism of lipids, carbohydrates, and proteins, regulation of glucose uptake and insulin secretion. Ghrelin hormone which is synthesized by the stomach is involved in the regulation of GH production and elevated ghrelin levels induce GH secretion. Insulin-like growth factor 1 (IGF-1) is implicated in the inhibiton of GH secretion [6, 7].

GH stimulates lipolysis and oxidation of lipids during long-term fasting. Obesity and type 2 diabetes which have been associated with insulin resistance are correlated with low amounts of GH release [8]. Disturbances in growth hormone signaling pathway have been associated with increased food intake and adiposity [9]. Despite particularly abdominal obesity has been shown to lead to decrease in GH release and IGF-1 levels, the relationship between GH and obesity is still unclear [10]. In the literature, no studies conducted with human samples in order to determine the relationship between food addiction and growth hormone.

In the present study, we aimed to investigate the relationship between obesity, food addiction, and growth hormone, growth hormone receptor, insulin, and insulin-like growth factor 1 values in Turkish population. In this regard, GH, GHR, IGF-1, and insulin levels were analyzed in serum of human subjects with obesity and/or food addiction.

Materials and Methods

Subjects. In the present study (non-drug/non-interventional clinical research), serum levels of human growth hormone (GH), growth hormone receptor (GHR), insulin-like growth factor-1 (IGF- 1), and insulin have been investigated in 2 groups. Group 1 ($n = 30$) was composed of overweight and obese individuals, whereas group 2 ($n = 10$) con- tained healthy individuals compatable with sex and age. Inclusion criteria of the study were: a. informed consent by volunteer, b. age between 18 and 48 years, c. BMI for healthy subjects: 18.5< and <24.9; BMI for obese: ≥30; BMI for overweight: 25 ≤ and <30. Exclusion criteria were: a. having metabolic disturbances such as diabetes and thyroid problems, b. using appetizing drugs such as steroids and antip- sychotics, c. smoking, d. being chronic alcoholic, e. being pregnant, f. being breastfeeding.

The current research was conducted based on the principles of Helsinki Declaration. The research permission was approved by Clinical Research Ethics Committe of University of Health Sciences Istanbul Fatih Sultan Mehmet Education and Research Hospital (FSM EAH-KAEK 2019/21, date of approval: 28/03/2019). All volunteers were recruited at Endocrinology and Metabolic Diseases outpatient clinic of Fatih Sultan Mehmet Education and Re- search Hospital of University of Health Sciences for face-to-face interviews and blood collection. Measurement of weight and height values were carried out with standard medical equipment. The Yale Food Addiction Scale (YFAS) which was developed by Gearthardt et al. [11] in 2009 and the validation and reliability of Turkish version was secured by Bayrak- tar et al. [12] in 2012 was used for the diagnosis of food addiction in the current study.

Determination of circulating metabolic biomarkers. Serum GH, GHR, IGF-1, and insulin concentrations were determined by the enzyme-linked immunosorbent assay (Elabscience ELISA kits, USA) based on the manufacturer's instructions. All of the experiments were performed in duplicate to confirm the precision.

Statistical analysis. The statistical evaluation of the findings were done by SPSS 25.0 (SPSS Inc., Chicago, IL, USA). The ShapiroWilk and Kolmogorov-Smirnov tests were applied to determine whether the results with normal distribution or not. Quantitative parameters with normal distribution are shown as the means ± standard deviations. Student's *t*-test or one-way ANOVA were applied in order to compare the numerical data. The comparison of categorical variables were performed by chi-square test (χ^2). The *P*-value < 0.05 was considered statistically significant.

Results and Discussion

The present study involved 30 adults with obesity (23 females and 7 males) with the mean age of 29.43 ± 8.42 years. In the control group, the mean age of 10 adults (5 females and 5 males) was 28.60 ± 4.55 years. No significant differences between the control and obesity groups were observed in terms of gender and age ($P > 0.05$). The number of the subjects with food addiction was significantly higher in obese group compared to the control group ($P = 0.029$).

The weight of participants with obesity were significantly higher than the participants in the control group (96.25 ± 20.37 kg vs 68.70 ± 13.91 kg, $P < 0.001$). The subjects with obesity had statistically significant higher BMI values than healthy individuals (34.90 ± 6.67 kg/m2 vs 22.84 ± 1.66 kg/m^2, $P < 0.001$).

The mean GH levels in the control and obese groups were 421.15 ± 196.03 pg/ml and 529.38 ± 309.32 pg/ml, respectively. The mean GHR levels in the serum of the control and obese groups were 10.00 ± 1.85 ng/ml and 9.60 ± 2.01 ng/ml, respec- tively. The mean serum insulin values in the control and obese groups were 6.17 ± 1.28 mIU/l and 5.89 ± 1.90 mIU/l, respectively. There were no sta- tistically significant differences between obese and control groups in terms of GH, GHR, and insulin ($P > 0.05$).

The healthy individuals had significantly higher serum IGF-1 levels compared to the subjects with obesity (338.70 ± 61.90 ng/ml vs 144.55 ± 22.69 ng/ml, $P < 0.001$). Demographic and biochemical data of healthy and obese individuals are seen in Table 1.

In the current study, obesity group was divided into 2 subgroups (food addiction (FA) and non food addiction (NFA)). The mean age of 18 obese adults diagnosed with food addiction (16 females and 2 males) were 28.5 ± 7.54 years. The mean age of 12 adults (7 females and 5 males) of the obese adults without food addiction diagnosis was 30.83 ± 9.77 years. No significant differences between FA and NFA groups in terms of gender, age, weight, BMI, GH, GHR, insulin, and IGF-1 were observed. Demo- graphic and biochemical data of FA and NFA groups are shown in Table 2.

Obesity which is considered as both neuro- biological and metabolic disease is one of the most significant health problems in the world [13]. The complex etiology of obesity and food addiction is

T a b l e 1. Demographic and clinical features and biochemical parameters of healthy and obese participants

Variables	Control group, ($n = 10$)		Obese group, ($n = 30$)		Statistical analysis, P
Male/Female, n (%)	5(50%)/5(50%)		7(23.4%)/23(76.6%)		0.117
FA/NFA, n (%)	2(20%)/8(80%)		18(60%)/12(40%)		0.029
	Mean	SD	Mean	SD	P
Age (years)	28.60	4.55	29.43	8.42	0.695
Weight (kg)	68.70	13.91	96.25	20.37	<0.001
BMI (kg/m^2)	22.84	1.66	34.90	6.67	<0.001
GH (pg/ml)	421.15	196.03	529.38	309.32	0.308
GHR (ng/ml)	10.0	1.85	9.6	2.01	0.583
Insulin (mIU/l)	6.17	1.28	5.89	1.90	0.669
IGF-1 (ng/ml)	338.70	61.90	144.55	22.69	<0.001

FA: Food Addiction, NFA: Non Food Addiction, BMI: Body Mass Index, SD: Standard Deviation

T a b l e 2. Comparison of clinical and biochemical parameters among obesity subgroups

Variables	FA (n = 18)		NFA ($n = 12$)		Statistical analysis, P
Male/Female, n (%)	2(11.1%)/16 (88.9%)		5(41.7%)/7(58.3%)		0.055
	Mean	SD	Mean	SD	P
Age (years)	28.5	7.54	30.83	9.77	0.467
Weight (kg)	96.94	23.85	95.208	14.58	0.824
BMI (kg/m^2)	35.89	7.69	33.41	4.70	0.329
GH (pg/ml)	603.55	320.88	418.12	265.74	0.109
GHR (ng/ml)	9.55	2.33	9.66	1.49	0.885
Insulin (mIU/l)	5.77	2.08	6.06	1.68	0.686
IGF-1 (ng/ml)	140.86	24.23	150.08	19.84	0.283

FA: Food Addiction, NFA: Non Food Addiction, BMI: Body Mass Index, SD: Standard Deviation

unclear. Therefore, the factors implicated in the development of obesity and food addiction are needed to be elucidated.

Growth hormone signaling is implicated in the modulation of growth, metabolism, and various physiological functions associated with cardiovascular, reproductive, hepatobiliary, gastrointestinal, and renal systems [14]. Deficiency of GH induces increased levels of body fat mass [15]. Deficiency of growth hormone receptor has been related to increased obesity risk and percentage of body fat [16]. In growth hormone-deficient subjects, it has been reported that increased adiposity can not be reduced by GH supplementation due to the decreased GHR expression [17].

IGF-1 and GH may affect differentiation and proliferation of adipocytes and there is interaction between pituitary, liver, and adipose tissue [18]. On the other hand, GH and IGF-1 values are controversial and the molecular mechanisms are needed to be elucidated in various human populations.

In a study conducted with morbid obese individuals, plasma IGF-1 values in obese individuals were lower compared to controls [19]. Consistently, our current study shows that IGF-1 levels are significantly lower in obesity group compared to healthy controls. In a study conducted with morbidly obese individuals, it has been reported that decreased serum IGF-1 levels are related with renal lesions [20].

Despite significant correlations between plasma GH and IGF-1 levels and eating disorders such as bulimia nervosa, anorexia nervosa [21], in the literature, no studies that investigated the relationship between food addiction and GH, GHR, insulin, and IGF-1 were found. Our results shows that serum GH, GHR, insulin, and IGF-1 concentrations are not associated with food addiction in Turkish patients.

In conclusion, the current study demonstrates: i) serum IGF-1 levels are significantly decreased in obese individuals and these decreased levels may be responsible for the development of obesity; ii) GH, GHR, insulin, IGF-1 are not correlated with food addiction and therefore, can not be used as novel markers for food addiction.

Further various human populations studies are needed to fully investigate the correlation between GH, GHR, IGF-1 values and obesity and food addiction.

РІВНІ ГОРМОНУ РОСТУ, РЕЦЕПТОРА ГОРМОНУ РОСТУ ТА ІНСУЛІНОПОДІБНОГО ФАКТОРА РОСТУ В СИРОВАТЦІ КРОВІ ПАЦІЄНТІВ ІЗ ОЖИРІННЯМ ТА ХАРЧОВОЮ ЗАЛЕЖНІСТЮ

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Ожиріння є проблемою громадського здоров'я, яка стає все більш поширеною і сричиняє різні ускладнення. Харчова залежність – це гедоністична харчова поведінка, що характеризується надмірним споживанням смачних продуктів (тобто продуктів, що містять велику кількість солі, цукру та жиру). Відомо, що порушення сигнального шляху гормону росту пов'язані з підвищеним споживанням їжі та ожирінням. Метою дослідження було визначення рівня гормону росту (GH), рецептора гормону росту (GHR), інсуліну та інсуліноподібного фактора росту 1 (IGF-1) у сироватці крові осіб із ожирінням та харчовою залежністю. Досліджено 30 дорослих із ожирінням (23 жінки та 7 чоловіків) та 10 здорових дорослих (5 жінок та 5 чоловіків). У 18 дорослих із ожирінням діагностовано харчову залежність, тоді як у контрольній групі було лише 2 особи з харчовою залежністю. Показники GH, GHR, IGF-1 та інсуліну проаналізовано за допомогою ELISA.Виявлено, що у людей з ожирінням

рівень IGF-1 у сироватці крові був значно нижчим, ніж у здорових людей (144,55 ± 22,69 нг/мл проти 338,70 ± 61,90 нг/мл, $P < 0,001$). Значних відмінностей у рівнях GH, GHR та інсуліну між групами з ожирінням та контрольною групою виявлено не було ($P > 0,05$). Значних відмінностей між групою з харчовою залежністю та групою без харчової залежності щодо статі, віку, ваги, BMI, рівнів GH, GHR, інсуліну та IGF-1 не виявлено. Показано, що нормальний рівень IGF-1 може бути захисним фактором розвитку ожиріння. Рівні GH, GHR, інсуліну, IGF-1 у сироватці крові не пов'язані з харчовою залежністю і, отже, не можуть бути використані як нові маркери харчової поведінки.

К л ю ч о в і с л о в а: ожиріння, харчова залежність, GH, GHR, IGF-1.

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