

Relationship Between Obesity with Galanin and Vaspin Levels

Obezitenin Galanin ve Vaspin Düzeyleri ile İlişkisi

Murat TAKMET¹, Dilek TUZUN², Murat SAHİN², Adem DOĞANER³, Metin KILINC⁴

¹ Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Internal Medicine, Kahramanmaraş, Turkey

² Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Endocrinology and Metabolism, Kahramanmaraş, Turkey

³ Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Bioistatistic, Kahramanmaraş, Turkey

⁴ Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Biochemistry, Kahramanmaraş, Turkey

Özet

Amaç: Amacımız obez ve normal kilolu bireylerde vaspin ve galanin düzeylerini karşılaştırmak, bu parametrelerin obezite ve diğer ilişkili parametrelerle ilişkili olup olmadığını ortaya çıkarmak.

Gereç ve Yöntemler: Çalışmaya obezitesi olan 40 hasta ve 40 kontrol alındı. Biyokimyasal parametreler hasta dosyalarından kaydedildi. Hastalardan alınan kan örneklerinin santrifüjlenmesi sonucu elde edilen örnekten galanin ve vaspin düzeyleri çalışıldı.

Bulgular: Gruplar cinsiyet ve yaş açısından birbirine benzerdi ($p>0.05$). Obezitesi olan grupta galanin düzeyleri kontrol grubuna göre daha yüksekti ($p<0.001$). Vaspin düzeyleri obezitesi olan grupta kontrol grubuna göre daha yüksekti ancak istatistiksel olarak anlamlı değildi ($p>0.05$). Hasta grubunda glukoz, insülin, trigliserit ve LDL-C düzeyleri kontrol grubuna göre istatistiksel olarak anlamlı derecede yüksekti ($p<0.001$). TSH açısından istatistiksel olarak anlamlı fark yoktu ($p>0.05$). Sırasıyla galanin ve glukoz, insülin ve BMI ile istatistiksel olarak anlamlı bir pozitif korelasyon bulundu ($p<0.001$, $r=0.401$; $p<0.001$, $r=0.519$; $p<0.001$, $r=0.714$). Ayrıca vaspin ile insülin, vücut kitle indeksi (VKİ) arasında sırasıyla istatistiksel olarak anlamlı pozitif korelasyon vardı ($p=0.05$, $r=0.222$; $p=0.03$, $r=0.238$).

Sonuçlar: Sonuçlarımız, obez kişilerde yüksek serum galanin ve vaspin konsantrasyonlarının kilo alımının bir sonucu olabileceğini veya obezitenin patogenezinde rol oynayan birçok faktörden biri olabileceğini göstermektedir.

Anahtar Kelimeler: Galanin, Vaspin, Obezite, Adipositokinler

Abstract

Objective: Our aim was to compare vaspin and galanin in obese and normal weight individuals, to reveal whether these parameters are related to obesity and other related parameters.

Material and Methods: Forty patients with obesity and 40 control subjects were included in the study. Biochemical parameters were recorded from patient's files. Galanin and vaspin levels were studied from the sample obtained as a result of centrifugation of blood samples taken from the patients.

Results: The groups were similar to each other in terms of gender and age ($p>0.05$). Galanine levels were higher in the group with obesity compared to the control group ($p<0.001$). Vaspin levels were higher in the group with obesity compared to the control group, but it was not statistically significant ($p>0.05$). Glucose, insulin, triglyceride and low-density lipoprotein cholesterol (LDL-C) levels were statistically significantly higher in the patient group than in the control group ($p<0.001$). There was no statistically significant difference in terms of thyroid stimulating hormone (TSH) ($p>0.05$). A statistically significant positive correlation was found with galanin, glucose, insulin, and body mass index (BMI), respectively ($p<0.001$, $r=0.401$; $p<0.001$, $r=0.519$; $p<0.001$, $r=0.714$). Also there was statistically significant positive correlation between vaspin and insulin, BMI, respectively ($p=0.05$, $r=0.222$; $p=0.03$, $r=0.238$).

Conclusion: Our results show that high serum concentrations of galanin and vaspin in obese subjects may be the result of weight gain or may be one of many factors involved in the pathogenesis of obesity.

Keywords: Galanin, Vaspin, Obesity, Adipocytokines

Correspondence: Dilek TÜZÜN, Kahramanmaraş Sütçü İmam Üniversitesi, SUAM, Kayseri Yolu 10.km Avşar Kampüsü 46100, Kahramanmaraş, Türkiye

Phone: +90 505-318 8188 **e-mail:** tuzund@gmail.com

ORCID No (Respectively): 0000-0002-7806-4851, 0000-0002-6693-4928, 0000-0001-7969-9157, 0000-0002-0270-9350, 0000-0002-1623-0201

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INTRODUCTION

Obesity is a metabolic health problem that develops as a result of excess fat storage of excess energy due to more energy intake than the body needs and a multi-factorial health problem that ranks second among the preventable causes of death, the frequency of which is increasing all over the world. Obesity plays a role in the development of prediabetes and type 2 diabetes (T2DM), primarily by causing insulin resistance. In addition, obesity causes diseases such as hypertension (HT), hyperlipidemia, cardiovascular diseases, cerebrovascular diseases, obstructive sleep apnea syndrome, polycystic ovary syndrome, non-alcoholic fatty liver disease, osteoarthritis and depression. The changes in the structure of adipose tissue also lead to imbalances in the secretion of adipocytokines (1).

Vaspin is an adipocytokine from the serine protease inhibitor family that is secreted from visceral and cutaneous adipose tissue (2). The release of vaspin is in the form of a circadian rhythm. Studies have shown that serum vaspin concentrations increase before meals and decrease after meals. The oscillation rhythm of serum vaspin concentrations is the opposite of glucose and insulin. It is thought that this decrease in the postprandial period is due to energy intake or increased plasma insulin and glucose concentrations (3).

Galanin (GAL) is a peptide found in organs such as the intestine, pancreas, hypothalamus, pituitary, adrenal medulla, and placenta (4). GAL plays a role in neurological, endocrinological and metabolic processes such as learning, memory, addiction, appetite, and mood in the human body (5). GAL peptide has an effect on insulin secretion from the pancreas and also increases insulin sensitivity (6).

Despite extensive research to reveal the pathophysiology of obesity disease, the precise molecular mechanisms of obesity have not been fully elucidated. In some studies, it has been observed that galanin and vaspin are effective on metabolism, glucose and lipid metabolism. However, studies on obesity and metabolic parameters are few. Therefore, the aim of this study is; to reveal the level of galanin and vaspin in obesity and to contribute to new prospective treatment regimens.

MATERIAL AND METHODS

This study was conducted prospectively in University Faculty of Medicine, Department of Internal Diseases, Department of Endocrinology and Metabolism Diseases. Before the study, informed consent forms were given to the patient and control groups, which included the details of the study. Subjects with consent were included in the study as patient and control groups.

Study Design and Patients

Individuals who were followed up and treated in Faculty of Medicine, Department of Endocrinology and Metabolism Diseases outpatient clinic and clinic between 2019-2020, and filled the voluntary participation form were included into the study. Forty patients with obesity and 40 healthy normal weight individuals were included in the study. Age, gender, height, weight, body mass index and background of both obese and normal-weight individuals were questioned. Fasting plasma glucose (FPG), blood urea nitrogen (BUN), creatinine, sodium, potassium, calcium, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), insulin, hemogram, thyroid stimulating hormone (TSH), free thyroxine (fT4) were recorded. In addition to the routine blood analyzes performed during fasting, 4 ml blood samples were taken into gel tubes to study the galanin and vaspin parameters from the individuals participating in the study. Plasma samples obtained by centrifugation of these samples in the laboratory were stored at -80°C until the time of study.

Study Exclusion and Acceptance Criteria

Our patient group was consisted of patients with obesity (Body mass index (BMI) of 30 and above) between the ages of 18-60, who filled out the voluntary participation form and did not have any additional disease. Our control group consisted of normal weight (BMI 20-25) individuals between the ages of 18-60, who filled out the voluntary participation form and did not have any additional disease. Individuals who did not fill in the voluntary participation form, individuals younger than 18 years old, over 60 years old, pregnant women, those with a BMI below 20 and those with a BMI of 25-29.9 were not included in our study. Those with additional diseases (T2DM, HT, cardiovascular disease, thyroid dysfunction, liver failure, kidney failure, respiratory system disease, etc.) were not included in the study for both the control group and the patient group.

Laboratory Analysis

For routine hormonal and biochemical analyzes, blood was collected in gel, non-anticoagulant, yellow capped tubes after 8-10 hours of fasting in the morning. After the blood samples were kept at room temperature for a while, they were centrifuged at 4000 rpm for 10 minutes. Serum obtained by centrifugation were used for the evaluation of hormonal and biochemical assays. Biochemical parameters and lipid panel were studied

by spectrophotometric method in Biochemistry Laboratory. TSH, fT4 were studied with Enzyme chemiluminescent immunoassay (ELISA).

In addition to routine assays, blood collected in gel-free anticoagulant tubes for serum galanin and vaspin levels was brought to the laboratory environment, centrifuged at 4000 rpm for 10 minutes and separated into serum. The separated serum was stored at -80°C until the study. When the study time came, the serum was analyzed manually by the ELISA method by following the kit procedure. Data were obtained using the Scanfor Multiscan FC 2.5.1 computer program. Values were obtained by calculating the unknown samples by comparison according to the calibration curve obtained in this program.

Statistical Analysis

In the evaluation of the data obtained in the study, IBM SPSS for Windows 25 program was used for statistical analysis. While evaluating the study data, Student's t-test was used to compare the mean standard deviation of descriptive statistical methods (mean \pm standard deviation) and quantitative values, and to compare normally distributed parameters between groups. Pearson correlation test was used to evaluate the relationships between parameters. P value ≤ 0.05 was considered statistically significant.

The study was approved by the Ethics Committee decision (dated: 22.01.2020; number:23). and carried out in accordance with the Declaration of Helsinki. An informed consent form was taken from the participants.

RESULTS

A total of 80 individuals, including 40 individuals with obesity (20 males and 20 females) and 40 individuals with normal weight (20 males and 20 females) were included in our study. There was no statistically significant difference between the two groups in terms of mean age and gender ($p > 0.05$). Comparison of the demographic characteristics of the cases are given in **Table 1**.

Variables	Group	n	Mean \pm SD	p
Age (years)	Patient	40	31.15 \pm 6.77	0.44
	Control	40	30.10 \pm 5.23	
BMI (kg/m ²)	Patient	40	36.59 \pm 6.68	$p < 0.001^*$
	Control	40	22.49 \pm 1.36	

Abbreviations: BMI; Body mass index, Mean \pm SD; Mean \pm Standard Deviation, N;number; *Statistically significant

FPG and insulin levels was significantly higher in obese patients compared to control group ($p < 0.001$). TG and LDL-C levels are higher in the patient group compared to the control group (respectively; $p < 0.001$; $p = 0.002$). HDL-C levels were lower in patient group compared to the control group ($p < 0.001$). Comparison of biochemical and hormonal parameters of the groups are given in **Table 2**.

Galanin levels were significantly higher in the patient group compared to the control ($p < 0.001$). Vaspin levels were higher in the patient group compared to the control but not statistically significant ($p = 0.102$). In the correlation analysis, a statistically significant positive correlation was found between serum galanin level and BMI ($r = 0.714$, $p < 0.001$). Also a statistically significant positive correlation was found between serum vaspin level and BMI ($r = 0.238$, $p = 0.03$), (**Table 3**).

A statistically significant and positive correlation was found between serum galanin levels and FPG ($r = 0.401$, $p < 0.001$). A statistically significant and positive correlation was found between serum galanin levels and TG ($r = 0.229$, $p = 0.04$). A statistically significant and negative correlation was found between serum galanin level and HDL ($r = -0.482$, $p < 0.001$). A statistically significant positive correlation was found between FPG and TG ($r = 0.277$, $p = 0.01$), (**Table 4**).

A statistically significant positive correlation was found between serum galanin levels and insulin ($r = 0.519$, $p < 0.001$). A statistically positive and significant correlation was found between serum vaspin levels and insulin ($r = 0.222$, $p = 0.05$) (**Table 5**).

DISCUSSION

Adipose tissue is one of the most important and largest endocrine organs of our body, secretes a large number of bioactive substances related to neuroendocrine and immune functions in our body (7,8). Adipocytokines are associated with the pathogenesis of diseases such as metabolic syndrome, obesity, insulin resistance, hypertension, cardiovascular diseases, and dyslipidemia (9-11). Today, it is thought that there is a pathophysiological link between adipose tissue

Table 2. Comparison of Biochemical and Hormonal Parameters of the Groups

Variables	Groups	n	Mean±SD	p
APG (mg/dl)	Patient	40	93.95±9.56	p<0.001*
	Control	40	86.40±5.60	
Insulin (mU/L)	Patient	40	18.09±8.26	p<0.001*
	Control	40	7.69±3.36	
ALT (U/L)	Patient	40	24.48±11.10	0.02*
	Control	40	18.85±10.92	
T. Chol (mg/dl)	Patient	40	154.83±41.01	0.51
	Control	40	149.93±21.89	
TG (mg/dl)	Patient	40	184.90±119.37	p<0.001*
	Control	40	82.13±44.70	
LDL (mg/dl)	Patient	40	110.55±27.55	0.002*
	Control	40	93.18±20.21	
HDL (mg/dl)	Patient	40	44.78±10.89	p<0.001*
	Control	40	54.20±11.46	
Galanin (ng/ml)	Patient	40	0.89±0.16	<0.001*
	Control	40	0.72±0.18	
Vaspin (ng/ml)	Patient	40	1.22±0.17	0.10
	Control	40	1.11±0.38	

Abbreviations: FPG; Fasting plasma glucose, ALT; Alanineaminotransferase, T. Chol; Total cholesterol, LDL; Low-densitylipoprotein, HDL;High-densitylipoprotein, TG; Triglyceride, N;number; *Statistically significant, Mean± SD; Mean±Standard Deviation

Table 3. Correlation of Galanin and Vaspin Levels with BMI and Age

Variables		Galanin (ng/ml)	Vaspin (ng/ml)	BMI (kg/m ²)	Age(years)
Galanin (ng/ml)	r	-	0.006	0.714 *	-0.083
	p	-	0.95	<0.001	0.47
Vaspin (ng/ml)	r	0.006	one	0.238 *	-0.015
	p	0.95		0.03	0.89
BMI (kg/m ²)	r	0.714 *	0.238 *	one	0.026
	p	<0.001	0.03		0.82
Age (years)	r	-0.083	-0.015	0.026	-
	p	0.47	0.89	0.82	-

Abbreviations: BMI; Body Mass Index, *Statistically significant

Table 4. Correlation of Galanin and Vaspin with Biochemical Parameters

Variables		Galanin (ng/ml)	Vaspin (ng/ml)	FPG (mg/dl)	TG (mg/dl)	LDL (mg/dl)	HDL (mg/dl)
Galanin (ng/ml)	r	-	0.006	0.401*	0.229*	0.186	-0.482*
	p	-	0.95	p<0.001	0.04	0.10	p<0.001
Vaspin (ng/ml)	r	0.006	one	0.087	-0.015	0.088	0.127
	p	0.95		0.44	0.90	0.44	0.26
APG (mg/dl)	r	0.401*	0.087	-	0.277*	0.158	-0.184
	p	p<0.001	0.44	-	0.01	0.16	0.10
TG (mg/dl)	r	0.229*	-0.015	0.277*	-	0.237*	-0.547*
	p	0.04	0.90	0.01	-	0.03	p<0.001
LDL (mg/dl)	r	0.186	0.088	0.158	0.237*	-	-0.080
	p	0.10	0.44	0.16	0.03	-	0.48
HDL (mg/dl)	r	-0.482*	0.127	-0.184	-0.547*	-0.080	-
	p	p<0.001	0.26	0.10	p<0.001	0.48	-

Abbreviations: FPG; Fasting plasma glucose, LDL; low-density lipoprotein, HDL; High-densitylipoprotein, TG; triglyceride, *statistically significant

Table 5. Correlation of Galanin and Vaspin with Hormonal Parameters

Variables		Galanin (ng/ml)	Vaspin (ng/ml)	TSH (mIU/L)	fT4 (ng/dl)	Insulin (mU/L)
Galanin (ng/ml)	r	-	0.006	0.135	-0.052	0.519*
	p	-	0.95	0.23	0.65	p<0.001
Vaspin (ng/ml)	r	0.006	-	-0.097	-0.056	0.222*
	p	0.95	-	0.39	0.62	0.05
TSH (mIU/L)	r	0.135	-0.097	-	-0.288*	0.052
	p	0.23	0.39	-	0.01	0.65
fT4 (ng/dl)	r	-0.052	-0.056	-0.288*	-	-0.097
	p	0.65	0.62	0.01		0.39
Insulin (mU/L)	r	0.519*	0.222*	0.052	-0.097	-
	p	p<0.001	0.05	0.65	0.39	

Abbreviations: TSH; Thyroid stimulating hormone, fT4; free thyroxine

dysfunction, abnormal production of adipokines and obesity (12). It has been determined that neuropeptides in the hypothalamus affect food intake, body weight, body temperature and metabolic rate (13,14).

Galanin is a neuropeptide with distribution in various tissues and organs such as gastrointestinal, central nervous system, adrenal medulla and placenta (15). The galaninergic system is responsible for many physiological processes such as gastrointestinal motility, perception of pain, learning and memory, neuroendocrine

control, regulation of feeding behavior and cardiovascular contraction and related pathologies (4,16). Recent data have shown that galanin peptide increases insulin secretion from the pancreas and increases insulin sensitivity. Galanin levels were found to be high in obese and diabetic patients (6,17). An increase was reported in the levels of GAL protein in the paraventricular nucleus of mice with a diet rich in fat and suitable for obesity (18,19). In a study in rats, it was found that after injecting galanin into the paraventricular nucleus of

the mice, they ate a fat-rich meal. This situation proves to us that there is a strong relationship between obesity and galanin (20,21). Baranowska *et al.* investigated galanin, leptin and neuropeptide Y levels in women aged 26-39 and postmenopausal women aged 47-65 years and plasma galanin concentrations were found to be significantly lower in postmenopausal women compared to younger women. However, they stated that plasma galanin concentrations are high in obese postmenopausal women (22). In our study, galanin values were statistically significantly higher in obese individuals compared to the control group. Findings from this study suggest that peripheral galanin level is associated with metabolic and nutritional status in humans.

Choi *et al* found a significant positive correlation between BMI and galanin concentrations in individuals with a diagnosis of gestational diabetes mellitus (23). Sandoval-Alzate *et al.* showed a positive relationship between BMI and serum galanin levels (24). Similar results were obtained in our study. We found a statistically significant and positive correlation between serum galanin levels and BMI. This positive correlation confirms that the increase in galanin levels may occur due to the increase in adiposity.

In our study, we found a statistically significant positive correlation between serum galanin levels, FPG and insulin. In other studies in the literature, Zhang *et al.* found a positive correlation between HOMA-IR and galanin in their study (25). Sandoval-Alzate *et al.* reported that there was a significant positive correlation between serum insulin levels and insulin resistance with galanin. In the same study, Sandoval-Alzate *et al.* showed a positive relationship between serum galanin levels and BMI and triglyceride (24). However, these results conflict with the positive results of galanin on glucose homeostasis. This situation can only be explained by the formation of resistance in galanin receptors, such as a mechanism in insulin resistance (26,27). In support of this hypothesis, in the study conducted by Acar *et al.*, when compared in terms of serum galanin levels between obese children without insulin resistance and obese children with insulin resistance, it was found to be higher in obese children with insulin resistance. However, it was not statistically significant (28). One of the studies examining the relationship between galanin and hyperlipidemia in obese individuals found a significant positive correlation between serum galanin concentration and triglyceride (29). A similar result was found by Sandoval-Alzate *et al.* demonstrated in one of his studies. They showed a positive correlation between triglyceride and serum galanin in obese patients without diabetes (24). The data obtained in our study showed similar results with these studies. In our

study, we found a significant positive correlation between serum galanin level and triglyceride. In the correlation analysis between other lipid parameters and serum galanin, we did not find a statistically significant relationship between LDL and serum galanin level, but we found a statistically significant negative correlation between HDL and serum galanin level.

Vaspin is an adipocytokine secreted from visceral and subcutaneous adipose tissues. Higher vaspin serum concentrations were found to be associated with obesity, insulin resistance, and T2DM in humans. However, the mechanisms how vaspin secretion may be linked to deterioration of glucose metabolism and insulin sensitivity are not entirely understood. Administration of vaspin to obese mice improves glucose tolerance, insulin sensitivity, and reduces food intake (30,31). Yang *et al* found higher serum vaspin concentrations in obese elderly individuals compared to normal weight individuals (32). Klötting *et al* examined whether vaspin mRNA expression is a marker of visceral obesity and correlates with anthropometric and metabolic parameters, body fat distribution, insulin sensitivity, and glucose tolerance. Their data indicates that induction of human vaspin mRNA expression in adipose tissue is regulated in a fat depot-specific manner and could be associated with parameters of obesity, insulin resistance, and glucose metabolism (33). A study examining the relationship between obesity and vaspin, but with different results, was conducted by Auguet *et al.* It was determined that serum vaspin levels did not increase in morbidly obese women and that serum vaspin levels did not correlate with glucose, BMI, and lipid parameters (34).

In a study examining the relationship between obese individuals and vaspin; obese individuals who lost 2% or more of their initial weight after a 12-week diet, significant reductions in insulin, HOMA-IR, and vaspin levels were demonstrated with a decrease in BMI (35). In contrast, Akbarzadeh *et al.* on the other hand, they could not show a significant relationship between BMI value and vaspin value in their study (36). In our study, a statistically significant positive correlation was found between serum vaspin level and BMI.

In a study conducted by Lu *et al*, rats were divided into two groups on a high-fat diet (37% carbohydrates, 13% protein, 50% fat) and a normal diet (57% carbohydrates, 18% protein, 25% fat). Mice on a high-fat diet were injected vaspin. Rats receiving a high-fat diet after vaspin injection were shown to have significantly reduced fasting glucose and fasting insulin values compared to rats receiving a normal diet (37). In a similar study rats given a high-fat diet (20% carbohydrate, 21% protein, 59% fat) were compared with

rats given a standard diet (62.8% carbohydrate, 25.8% protein, 11.4% fat) and insulin, glucose, HOMA-IR and vaspin values were found significantly higher rats given a high-fat diet (38). In our study, however, we did not find a statistically significant relationship between serum vaspin level and fasting plasma glucose in the correlation analysis. However, we found a statistically significant positive correlation in the correlation analysis between serum vaspin level and insulin levels.

Saboori *et al.* found higher concentrations of vaspin in obese women aged 20-50 years. than thin women. In addition, in this study, no significant relationship was found between vaspin levels and fasting glucose, LDL, HDL and triglyceride levels (39). Sathyaseelan *et al.* showed no significant correlation between vaspin and serum lipid levels (40). Similar results were obtained in our study as well. We did not find a statistically significant relationship between serum vaspin levels and TG, LDL and HDL.

As a result, high plasma concentrations of galanin and vaspin in obese subjects may be the result of weight gain or may be one of many factors involved in the pathogenesis of obesity. White adipose tissue plays a regulatory role in many functions in the body with the mediators it secretes. Adipokines have beneficial effects on energy balance and insulin resistance. Although thousands of studies have been conducted on the subject to date, more studies are needed to clarify the complex effect network of adipokines in the body and to benefit from adipokines in the prevention and treatment of obesity. Therefore, we think that drug treatments targeting these adipose tissue-derived adipokines may increase insulin sensitivity and also have a protective effect against atherosclerosis. Further studies to fully elucidate the role of galanin and vaspin in obesity will make an important contribution to the treatment of not only obesity, but also diabetes, hypertension and cardiovascular diseases accompanying obesity.

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