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Serum preptin and amylin levels in acne vulgaris patients

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Abstract
Acne vulgaris is a common disease with multi-factorial etiology that occupies the pilosebaceous unit. Several recent studies demonstrated that insulin and insulin resistance can play a role in acne pathogenesis. In the present study, the roles of preptin and amylin, which are directly associated with insulin secretion and released from pancreas beta cells, in acne vulgaris pathogenesis were investigated. The study was conducted with 40 cases with acne vulgaris and the control group that included 40 healthy subjects with similar body mass index. Serum preptin and amylin levels and fasting blood glucose, triglyceride, total cholesterol, LDL, VLDL, HDL, C-peptide, insulin and HbA1c levels were examined in the study group. HOMA-IR values were calculated. Although patient group serum preptin and amylin levels were higher when compared to the control group, however the difference was not statistically significant ($p > 0.05$). It was determined that there was a positive correlation between severity of the disease and amylin levels. In the patient group, it was found that the glucose level was significantly higher when compared to the control group ($p < 0.001$). Serum insulin and C-peptide levels and HOMA-IR index were higher in the patient group when compared to the control group, however the difference was not statistically significant ($p > 0.05$). It is considered that increased preptin and amylin levels in acne vulgaris patients may be associated with the etiopathogenesis of the disease. We also considered that decreasing the elevated levels of these two peptides to normal levels may be helpful for the treatment of the disease.

Keywords: Acne vulgaris, insulin resistance, preptin, amylin

Introduction

Acne vulgaris is a common, chronic, inflammatory disease with multifactorial etiology that affects the pilosebaceous unit. Often observed in adolescence and in facial, bust, dorsal and shoulder areas where sebaceous glands are concentrated. Ductal hyperkeratinization, increase in sebum production, microorganisms (such as Propionibacterium acnes (P. acnes)) and inflammation are the most important factors playing a role in etiopathogenesis [1]. Furthermore, genetic factors, hormones, nutritional habits, physical factors, emotional status and drugs are the other responsible factors [1,2]. The skin, especially the pilosebaceous unit, is considered an endocrine organ where numerous hormones and receptors are synthesized. Several recent studies demonstrated the effects of various hormones on the pilosebaceous unit [3]. A number of studies showed that insulin and insulin like growth factor-1 (IGF-1) levels and insulin resistance are effective in the pathogenesis of acne. In the abovementioned studies, it was reported that insulin could directly affect the pilosebaceous unit, induce sebum production and sebocyte proliferation, and further suppress sex hormone binding globulin (SHBG) concentrations, increasing the free androgen levels [4,5]. Furthermore, it was also reported that hyperinsulinemia may play a role in acne pathogenesis by increasing serum IGF-1 levels and decreasing insulin like growth factor binding protein (IGFBP)-3, a potent pro-apoptotic factor for keratinocytes and thus, stimulating the proliferation of basal keratinocytes [6,7]. Again, studies demonstrated that hyperinsulinemia plays an important role in ovary disfunction in patients with polycystic ovarian syndrome (PCOS) where the risk of acne is increased. Previous studies determined that hyperinsulinemia and hyperandrogenism can ameliorate with weight loss and treatment in these patients [8]. Furthermore, certain studies reported that antidiabetic agents such as insulin sensitizers such as metformin and thiazolidinedione reduced insulin levels and consequently decrease androgen levels and improve ovarian functions [9,10].

Preptin and amylin are polypeptide hormones that are synthesized with insulin in 34 and 37 amino acid pancreatic beta cells,

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respectively, in response to glucose and known to have effects on insulin and glucose metabolism. Preptin physiologically increases the insulin secretion that occurs as a response to glucose, while amylin inhibits insulin secretion, and acts directly on pancreatic β-cell products to inhibit glucose-induced insulin secretion and insulin-mediated glucose uptake. Peripheral insulin resistance results in chronic stimulation of pancreatic beta cells, leading to an increase in insulin and amylin released with insulin. Abnormal accumulation of amylin and pro-amylin in pancreatic β-cells leads to β-cell loss in patients. This results in secretion of insulin and an impaired glucose metabolism. Increased amylin levels were indicated in individuals with impaired glucose tolerance and obese individuals with insulin resistance [11-17].

In the present study, we aimed to investigate the variations in preptin and amylin hormone levels in patients with acne, their role in acne pathogenesis and the relationship between preptin and amylin hormone levels and acne severity.

Material and Methods

Forty patients between 14 and 30 years of age who were admitted to Fırat University Hospital, Dermatological and Venereal Diseases Policlinic and who were clinically diagnosed with acne vulgaris as described in 'Acne vulgaris: review and guidelines 2009' and 40 healthy volunteers, who applied to the hospital for annual check-up and were similar in age and body mass index (BMI) with the patient group, were included in the patient and control groups in the present study. Ethics approval was obtained from Fırat University Human Research Ethics Committee and informed consent forms were obtained from the study participants. The study was sponsored by the Firat University Scientific Research Projects Coordination Unit (project number: TF.11.72). Patients and individuals with diabetes mellitus (DM) or known endocrinological disorders or with a family member with DM or known endocrinological disorders, tobacco and alcohol users, individuals in diet or pregnant, or with over the limit BMI, individuals who are on medicine for chronic systemic diseases or medicine that could cause acneiform rash were excluded from both patient and control groups in the study. The lipid profile, which includes triglyceride, LDL, VLDL, HDL, and total cholesterol, and HbA1c, insulin, C-peptide, fasting blood sugar, values were checked, and BMI measurements were conducted in both patient and control groups. BMI was calculated with the following formula: (kg) / (height) m^2 [18]. The Global Acne Grading System (GAGS) was used to assess acne severity [19]. In calculating insulin resistance, homeostasis model assessment of insulin resistance (HOMA-IR) (glucose mg / dl x insulin mU / ml) / 405 formula was used. Cased with HOMA-IR> 3.2 was diagnosed with insulin resistance cases [20].

Preptin and Amylin Hormone Measurements

Since preptin and amylin are peptide structured hormones and could be disintegrated by proteases, 500 kallikrein units aprotinin per ml was added to simple biochemical tubes before blood was drawn from the participants to prevent proteolysis. 5 ml fasting blood sample was obtained from each participant and after the sample was centrifuged for 5 min at 3000 g, the obtained serum was transferred to Eppendorf tubes and stored at -80 ° C until the day of the study. Serum preptin levels were studied with the human preptin ELISA (enzyme-linked immunosorbent assays) kit (ELISA CK-E10788 kit, Hangzhou Eastbiopharm, China). Serum amylin levels were studied with human IAPP (Islet Amyloid Polypeptide) ELISA kit (Human IAPP ELISA B831510HU kit, Bioabb, China).

Statistical Analysis

Study data were analyzed with "SPSS for Windows 18.0" software. The t-test was used to analyze the difference between the numerical data for the groups, Pearson's correlation test was used for correlation analysis. The results were presented with mean and standard deviation values. The results were analyzed with a 95% confidence interval and a significance level of $p < 0.05$.

Results

The age, gender, and body mass index values for the patient and control group participants were similar and there was no statistically significant difference between these values ($p > 0.05$) (Table 1).

Table 1. Patient and control group demographics

	Acne Vulgaris	Control	p value
n	40	40	
Sex (F/ M)	20/20	27/13	p>0.05
Mean duration of disease	3.65±1.83	-	
BMI	21.72±1.80	21.62±2.83	p>0.05

The study group and control group laboratory test values were measured and compared between the groups. The laboratory test results for the patient and control groups are presented in Table 2.

Table 2. Preptin and amylin values and laboratory test findings for the patient and control groups

	Acne	Control	P
Preptin (ng/ml)	6.36±3.43	5.37±3.13	p>0.05
Amylin(pg/ml)	148.52±109.37	131.46±80.82	p>0.05
Glucose(mg/dl)	88.12±12.21	78.77±10.67	P<0.001a
Triglycerides(mg/dl)	81.30±33.30	76.77±40.50	p>0.05
LDL (mg/dl)	87.58±23.49	91.71±44.90	p>0.05
HDL (mg/dl)	53.47±12.92	49.77±15.32	p>0.05
VLDL (mg/dl)	6.72±6.03	14.95±7.70	p>0.05
Total cholesterol(mg/dl)	154.30±29.28	157.50±41.96	p>0.05
HbA1c (%)	4.72±0.34	4.60±0.39	p>0.05
Insulin (ng/ml)	6.64±6.14	6.34±2.47	p>0.05
C-peptide (ng/ml)	1.84±0.75	1.70±0.72	p>0.05
HOMA-IR*	1.43±1.26	1.29±0.56	p>0.05

*(Mean Standard Deviation)
a There was a statistically significant difference between the patient and control groups (p<0.001)

Analysis of the preptin and amylin levels of the individuals in patient and control groups demonstrated that serum preptin and amylin levels were higher in the patient group when compared to the control, however the difference was not statistically significant ($p > 0.05$). Serum preptin levels in the patient and control groups are presented in Figure 1, and serum amylin levels are presented in Figure 2.

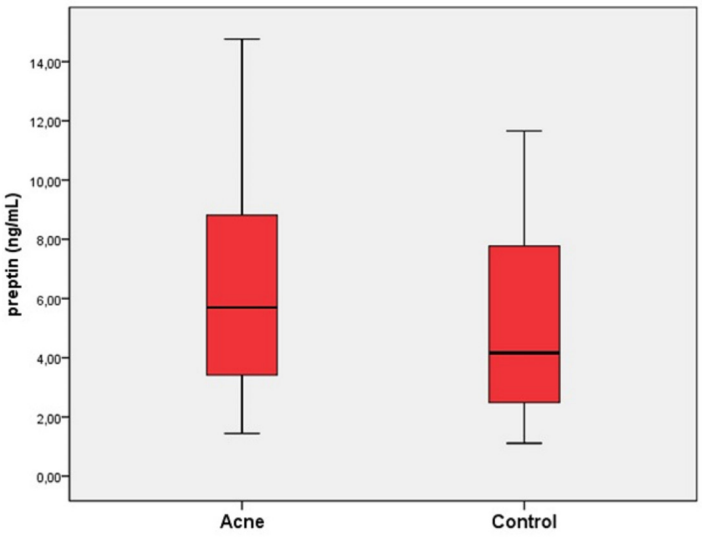

Figure 1. Serum preptin levels in the patient and control groups are presented

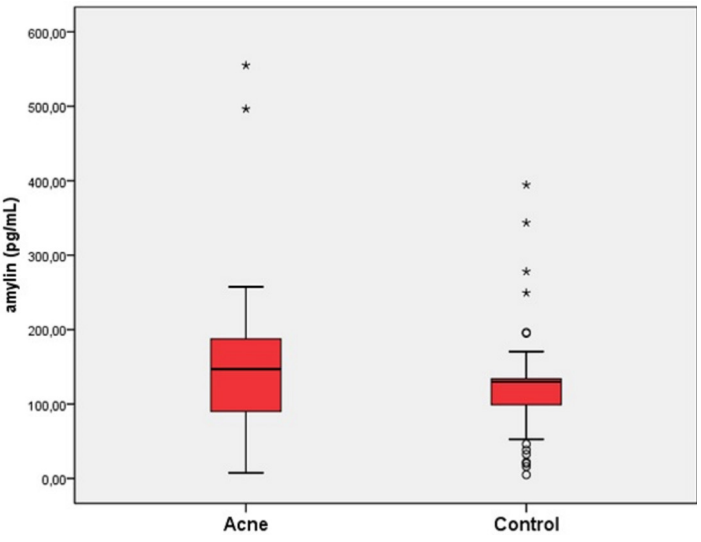

Figure 2. Serum amylin levels

It was determined that the glucose levels were significantly higher in the patient group when compared to the control group ($p < 0.001$). Serum insulin, C-peptide levels and HOMA-IR index were higher in the patient group when compared to the control group, but the difference was not statistically significant ($p > 0.05$). Similarly, there was no statistically significant difference between the patient and control groups based on the lipid parameters ($p > 0.05$).

The severity of the patients, which was graded based on the GAGS, was analyzed to determine whether there was a correlation between disease severity and serum preptin and amylin levels, and it was determined that there was a positive correlation between disease severity and serum amylin levels ($r = 0.327$). There was no correlation between serum preptin and disease severity ($r = 0.152$).

Discussion

Acne is a common dermatological disease and its incidence could rise up to 85% in adolescence [21]. Ductal hyperkeratinization, increased sebum production, microorganisms (such as P.acnes) and inflammation are the most important factors that play a role in etiopathogenesis [1]. The androgens, which play an important role in etiopathogenesis, directly or indirectly stimulate keratinocyte proliferation, increase in the volume of sebaceous glands and sebum secretion. Androgens also play a role in the acne pathogenesis by causing proliferation and alteration in sebocytes and infundibular keratinocytes [22]. Insulin can directly stimulate androgen-sensitive pilosebaceous units [4]. Increase in serum insulin concentration stimulates sebum production and sebocyte proliferation, additionally inhibits SHBG concentrations, leading to an increase in free androgen amounts [5]. It was emphasized that hyperinsulinemia resulting from nutrition with foods with high glycemic index that is associated with insulin levels and acne pathogenesis is effective in acne pathogenesis [5]. Several recent studies demonstrated that insulin resistance can play a role in the pathogenesis of acne [23-26].

Despite the fact that steroid hormones were studied in the pathogenesis of acne in previous years, current studies mostly scrutinize whether peptide and protein structured hormones play a role in acne etiopathogenesis. To date, there are only a few studies published on the significance of preptin in humans. There are no previous studies on preptin and amylin levels in acne patients. The present study is the first research that investigated the roles of two new peptide hormones, namely preptin and amylin, which play a role in glucose homeostasis, in the etiopathology of the disease.

Çelik et al. found that plasma preptin concentration was significantly higher in patients with PCOS with increased risk of acne and insulin resistance when compared to the healthy control group with similar age and BMI [27]. In this study, they determined that BMI, plasma preptin and insulin levels and HOMA-IR index were significantly higher in PCOS patients when compared to healthy controls.

In another study conducted to investigate preptin levels in PCOS patients, Bu et al. suggested that elevated serum preptin levels were associated with impaired glucose tolerance [28]. Although Çelik et al. claimed that the reason for elevated serum preptin levels in PCOS patients might be due to insulin resistance, Bu et al. suggested that this might be related to glucose intolerance rather than insulin resistance. In another study conducted with Type-2 DM patients by Yang et al. it was suggested that preptin could play a role in the pathogenesis of insulin resistance. Similar to these studies, we found elevated preptin levels in acne patients, albeit insignificant [29]. In the present study, we considered that elevated preptin levels in acne patient group when compared to healthy controls could contribute to acne etiopathogenesis via insulin resistance and impaired glucose tolerance.

Amylin, another hormone, stimulates basal insulin secretion, while inhibiting stimulated insulin secretion. In animal experiments, amylin was shown to inhibit insulin secretion by stimulating β-cell apoptosis and increase insulin resistance [30].

In a study conducted by Reinehr et al. on obese children, it was found that serum amylin, insulin and triglyceride levels were higher in obese children when compared to the control group, and when children who lost weight were reassessed, significant decreases were indicated in amylin, insulin and triglyceride levels [17]. James et al. found high amylin levels in a study conducted with patients with PCOS, where the prevalence of acne increases [31].

Although the amylin, insulin, and triglyceride levels in the patient group were not statistically significant, it was found that the glucose level was significantly high in the patient group. The high insulin levels in the patient group, albeit insignificant, could be an indicator of an early stage insulin resistance. Again, a positive correlation was determined between serum amylin levels and triglyceride and VLDL. In the present study, a positive correlation was also identified between amylin levels and disease severity. The said positive correlation between amylin and disease severity led us consider that the elevated amylin levels increased the hyperinsulinemia and thus, the development of acne in individuals. This relationship shows that amylin levels may be indicative of disease severity.

In several previous studies, the relationship between peptide-protein molecules in glucose homeostasis and acne was investigated [32, 33]. However, there is no previous study on preprint and amylin levels. Although the findings of the present study demonstrated higher preptin and amylin levels in the patient group when compared to the control, the differences were not statistically significant. It was found that glucose levels were higher in the patient group when compared to the control group. We considered that the reason for the increase in glucose was elevated insulin level and HOMA-IR values. Because, high glucose levels despite the increase in insulin levels reflect the presence of insulin resistance, which is in the etiopathology of this disease. As a result, glucose levels are measured high in the circulation. Furthermore, these two parameters, which we studied with glucose concentrations, are directly correlated and their increase or decrease directly affect the glucose levels. For example, preptin and amylin levels were higher in the patient group in parallel to the high glucose levels. However, the preptin and amylin levels were partially lower in the control group when compared to the patient group, indicating that the glucose levels changed based on the concentrations of the said two hormones.

Conclusion

The present study findings suggested that the increased amounts of preptin and amylin in acne patients, which is directly associated with insulin secretion, might be related to the etiopathogenesis of the disease. Furthermore, the results of the present study suggested that amylin is more significant in the etiopathology of acne, because the amylin levels were increased more as the severity of the disease increased when compared to preptin. Although links between several abovementioned hormones and acne have been established, we believe that the results of the present study would contribute to the literature, since this study is the first in the literature.

Competing interests
The authors declare that they have no competing interest.

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Ethical approval
Ethics approval was obtained from Fırat University Human Research Ethics Committee.

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