Serum Leptin Levels in Patients with Psoriasis Vulgaris

PSORİAZİS VULGARİSLİ HASTALARDA SERUM LEPTİN DÜZEYLERİ

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Abstract

Objective: Psoriasis is a complex, multifactorial chronic hyperproliferative skin disease. T-cells are responsible for initiation and maintenance of psoriasis. Leptin plays an important role the T-cell immunity. In this study, we aimed to investigate in association between psoriasis and leptin whether leptin plays a role in the immunopathogenesis of psoriasis or not.

Material and Methods: Thirty-eight patients with psoriasis (15 male, 23 female; mean age 40.8 $\pm$ 15.4 years) and 38 age-and sex-matched healthy control subjects (15 male, 23 females; mean age 38.6 $\pm$ 9.2 years) were recruited in this study. The body mass index (BMI) was calculated for subjects at study enrolment. The severity of psoriasis was estimated by means of the Psoriasis Area and Severity Index. Leptin was determined with a human leptin radioimmunoassay kit.

Results: The mean serum leptin concentration was not statistically different in patients with psoriasis (22.2 $\pm$ 19.5 ng mL^{-1}) when compared with that in healthy control subjects (15.9 $\pm$ 11.4 ng mL^{-1}) ($p > 0.05$). Leptin was not correlated with PASI score, positive or negative family history of psoriasis and early or late onset and duration of the disease.

Conclusions: Leptin may not play a significant role in the immunopathogenesis of psoriasis.

Key Words: Leptin, psoriasis

Özet

Amaç: Psoriazis kompleks ve nedeni tam olarak bilinmeyen kronik hiperproliferatif bir deri hastalığıdır. T lenfositler hastalığın başlamasında ve devam etmesinde görev alırlar. Leptin T hücre immünitesi üzerinde önemli rol oynadığı için psoriazis immünopatogenezinde de yeri olabilir. Bu çalışmada leptin ile psoriazis arasındaki olası ilişkinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya 38 psoriazisli hasta (15 erkek, 23 kadın; yaş 40.8 $\pm$ 15.4 yıl/SD) ile yaş ve cinsiyet uyumlu sağlıklı 38 kişi (15 erkek, 23 kadın; yaş 38.6 $\pm$ 9.2 yıl/SD) dahil edildi. Çalışmaya katılan bütün bireylerin vücut kitle indeksleri [body mass index (BMI)] hesaplandı. Psoriazisin şiddeti PASI (Psoriasis Area and Severity Index) skoru ile ölçüldü. Leptin ölçümünde insan leptin radioimmunoassay kit kullanıldı.

Bulgular: Psoriazisli hastaların ortalama serum leptin konsantrasyonu (22.2 $\pm$ 19.5 ng mL^{-1}) ile sağlıklı kontrol grubunun serum leptin konsantrasyonları (15.9 $\pm$ 11.4 ng mL^{-1}) karşılaştırıldığında istatistiksel olarak aralarında anlamlı fark yoktu ($p > 0.05$). Serum leptin düzeyi ile PASI skoru, pozitif veya negatif aile hikayesi, hastalığın erken veya geç başlaması ve hastalık süresi arasında korelasyon saptanmadı.

Sonuç: Elde ettiğimiz sonuçlar psoriazis immünopatogenezinde leptin'in önemli bir rol oynamadığını düşündürmektedir.

Anahtar Kelimeler: Leptin, psoriazis

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Psoriasis is a chronic hyperproliferative and T-cell-mediated inflammatory skin disorder. Infiltrations of T-cells are followed by the keratinocyte hyperproliferation. T-cells are responsible for initiation and maintenance of psoriasis. The precise mechanism of how activated T-cells trigger psoriasis is yet unknown.[1,2]

Leptin is a 16-kDa nonglycosylated peptide hormone synthesized exclusively in adipocyte cells to regulate weight control in a central manner. Endothelial effects of leptin are responsible for angiogenesis in retinopathy and atherosclerosis. Leptin also acts on reproduction, hematopoiesis, blood pressure, bone mass, lymphoid organ homeostasis, and T lymphocyte systems.[3,4] Leptin links the pro-inflammatory T helper (Th)1 immune response to the nutritional status and the energy

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balance. Both CD4+ and CD8+ T-lymphocytes express leptin receptors. Moreover, several reports have shown that stimulus through the leptin receptor leads to a T1-type inflammatory response with enhanced production of TNF-α and IL-6 by monocytes and IL-2 and IFN-γ by T lymphocytes.[5-7]

Due to the effects on T-cell-dependent-immunity we considered leptin could play a role in the immunopathogenesis of psoriasis. Therefore, the purposes of this study were: (i) to investigate serum leptin concentrations in patients with psoriasis; and (ii) to explore whether disease severity has an effect on the blood leptin concentration.

Material and Methods

Patients and Controls

The patients presented to our dermatology department with plaque-type psoriasis aged from 18 to 69 years between January 2005 and September 2005 were included into the study (n= 38). These patients fulfilled including criteria of the study. As a control group, healthy hospital staff volunteers aged 18-58 years were recruited in the study (n= 38). The patients who received oral acitretin, methotrexat, cyclosporin and any form of phototherapy treatment within the last 2 months were excluded. Subjects in both groups with a history of eating disorders, acute or neurological disorders, hypertension, ischemic heart disease, diabetes or amenorrhea, and smokers were not included in the present study. Also excluded were subjects who used any topical or other systemic medication within the last 2 weeks. Subjects were matched for age, sex and weight.

The body mass index (BMI) [weight (kg) height^{-1} (m^2)] was calculated for subjects at study enrolment. The severity of psoriasis was estimated by means of the Psoriasis Area and Severity Index (PASI). Family history of psoriasis, age at onset of psoriasis, duration of the disease and joint involvement were recorded. We accepted early-onset psoriasis if it had started before 30 years. The association of these parameters with serum leptin concentration was investigated.

All participants gave a written informed consent after full explanation of the purpose and nature of all procedures used. A permission of Ethic Committee was taken. Blood samples were taken from the subjects for the analysis of leptin levels at the same hours (10 am). Following centrifugation of the blood sample, serum was collected and kept at -70 ^{0}C until use.

Serum Leptin Analysis

Leptin was determined with IRMA DSL 23100 (Diagnostic System Laboratories, Inc, Webster, TX) using human leptin radioimmunoassay kit. The lower limit of sensitivity for leptin was 0.5 ng/ml. The intraassay coefficient of variation of the assay at 30 μg/L was 3.9%, and at 12 μg/L it was 1.7%. Body weight and percent body fat of the subjects were measured by bioimpedance meter (Tanita).

Statistical analysis

The data were summarized by median (minimum-maximum), mean $\pm$ standard deviation and percentages. Because parametric distributions of each group and subgroups were not normal according to Kolmogorov-Smirnov and Shapiro-Wilk ($p> 0.05$), Mann-Whitney U test was used in comparison of the groups**.** Gender distribution was evaluated by chi-square test. Correlations were performed by Spearman's correlation analysis.

Results

The gender ratio, age and BMI were not substantially different for each variable ($p> 0.05$) between patients with psoriasis (15 male, 23 female; mean age 40.8 $\pm$ 15.4 years; BMI: 32.3 $\pm$ 10.5) and healthy volunteers (15 male, 23 females; mean age 38.6 $\pm$ 9.2 years; BMI: 29.1 $\pm$ 7.1). The mean serum leptin concentration was not statistically different ($p> 0.05$) in patients with psoriasis (22.2 $\pm$ 19.5 ng mL^{-1}) when compared with that in healthy control subjects (15.9 $\pm$ 11.4 ng mL^{-1}). Females in the two groups had significantly higher ($p< 0.001$) serum leptin levels and BMI than males (Table I).

There were 7 patients (18.4%) with family history of psoriasis and 19 patients (50%) had early onset of the disease. Only 1 patient (2.6%) had

Table 1. Serum leptin concentrations in patients with psoriasis and healthy controls.

	n	Age, years (mean ± SD)	Median age (years) (Min-Max)	Serum leptin ($ng\ mL^{-1}$) (mean ± SD)	Median leptin ($ng\ mL^{-1}$) (Min-Max)
Healthy controls	38	38.6 ± 9.2	40 (19-61)	15.9 ± 11.4	15.4 (1-62.8)
Psoriatic cases	38	40.8 ± 15.4	37 (18-69)	22.2 ± 19.5	17 (1.4-82.8)
Male	15	44 ± 15.8	43 (21-69)	9.07 ± 6.7	7.5 (1.4-22.4)
Female	23	38.7 ± 15	36 (18-65)	30.9 ± 20.3	28.8 (5.5-82.8)*
Family history	7	34.8 ± 13.8	30 (21-60)	20.3 ± 9.9	25.3 (2.5-29.3)
Family history	31	42.1 ± 15.6	42 (18-69)	9.07 ± 6.7	16.3 (1.4-82.8)
Early onset	19	28.8 ± 6.4	28 (18-43)	17.3 ± 15.4	11 (1.4-59.7)
Late onset	19	53.7 ± 9.5	54 (37-69)	27.7 ± 22.1	26.7 (1.8-82.8)

* Compared to males in psoriatic cases P< 0.001

psoriatic arthritis. The mean PASI score was 15.6 ± 13.6 and the mean duration of the disease 10 ± 9.9 years. There were no statistically differences (p> 0.05) between serum leptin levels and positive or negative family history of psoriasis and early or late onset of the disease. Leptin was not correlated (r= 0.062, p= 0.71) with PASI score (Figure I) and duration of the disease in patients with psoriasis.

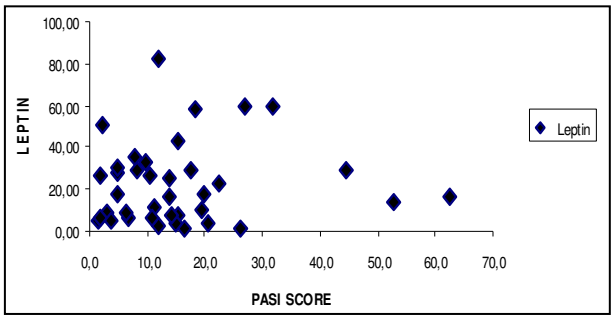

Figure I. Leptin level and PASI score (r_s=0.062, p=0.710).

Discussion

Leptin is an adipocyte-secreted hormone that centrally regulates weight control. Moreover, leptin exhibitis a variety of other effects, including the regulation of endocrine functions, reproduction, and immunity.[8] Defectiveness in leptin and its receptor impair cell-mediated immunity in *ob/ob* and *db/db* mice.[9,10] Lord et al reported that leptin increases the proliferative response of T lymphocytes and regulates the T helper type 1 (Th1)/Th2 balance in mixed lymphocyte cultures.[11] Congenital leptin deficiency is associated with a decreased number of circulating CD4+ T cells and impaired T cell proliferation and cytokine release in human.[12]

T cells play an important role in the immunopathogenesis of psoriasis. It has been shown that both CD4+ and CD8+ T-lymphocytes are detected in the papillary dermis and the epidermis of the psoriatic lesions. CD4+ T cells migrate into skin with aggravation of the disease as new lesions develop.[13] We did not detect a significant association between psoriasis and leptin but, in the light of these immunological findings we think that leptin must play a role especially in the association among the disease and obesity and food intake.

Decreasing body fat mass or reducing food intake cause hipoleptinemi that lead to immune defection and increasing of infection and this immune deficiency may be protective against development of autoimmune conditions.[14] This hypothesis may support the epidemiological studies which demonstrate that psoriasis is more extensive in over-weight people.[15] Psoriatic patients are more obese compared with non-psoriatic patients but onset of the disease is not associated with obesity. However obesity is morbid condition in psoriatic patients.[16] In this study, the percentage of overweight and obese patients were increased in ratio as in the literature but there was no association between BMI and PASI score and there was no relationship between serum leptin level and severity of the disease.

In the present study, we aimed to investigate serum leptin concentration in patients with psoria-

sis and to explore whether there was an association among leptin levels and severity, duration or onset of the disease. We have detected that serum leptin level in patients with psoriasis was not different from that of healthy control groups. In addition, leptin has no an effect on severity, duration or onset of the disease. We hope that these results will make a substantial contribution to further studies investigating the pathophysiological mechanisms responsible for psoriasis and leptin.

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