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Original Article

Evaluation of cardiometabolic function with serum adropin levels in psoriasis patients

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Abstract

Aim: Psoriasis is a skin disease with metabolic and cardiac comorbidities. Adropin is a peptide hormone which is thought to play a role in metabolic diseases, energy homeostasis, endothelial function and cardiac diseases in recent years. In this study, we aimed to evaluate adropin levels in psoriasis patients

Materials and Methods: The study included 51 plaque psoriasis patients aged 18-65 years who had no systemic disease and had not received systemic treatment in the last three months and 37 healthy controls matched by sex, age and body mass index (BMI). Serum adropin, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglyceride (TG), fasting blood glucose (FBG), fasting serum insulin, BMI, systolic blood pressure (SBP) and diastolic blood pressure (DBP) values were recorded.

Results: Serum adropin level was 73.04 ± 46.21 pg / ml in the patient group. In the control group, serum adropin level was 77.26 ± 43.69 pg / ml. Serum adropin levels were lower in the patient group, but this was not statistically significant (p = 0.667). PASI value was negatively correlated with serum adropin level. There was no correlation between serum adropin level and other variables. Insulin level, Homa-IR level, systolic and diastolic pressure were significantly higher in the patient group (p <0.05).

Conclusion: In our study, although adropin levels were not significantly lower in the patient group, we concluded that this may be associated with low PASI values. The role of adropin in psoriasis vulgaris will emerge with further studies.

Keywords: Adropin; cardiometabolic function; PASI; psoriasis

INTRODUCTION

Psoriasis is an immune mediated chronic inflammatory skin disease with systemic effects (1). Inflammation in psoriasis develops with the participation of both adaptive and innate immune systems. In recent years, Th17 cells have been shown to play an important role in the pathomechanism of psoriasis. The development of Th17 is mainly mediated by interleukin (IL) -23 produced by dendritic cells. Th-17 cells produce a variety of cytokines, including IL-17A, IL-17F, and IL-22. Tumor necrosis factor (TNF) is the upstream inducer of IL-23 and acts synergistically with IL-17, which increases up-regulation of psoriasis related proinflammatory genes in keratinocytes (2). Inflammatory mediators in the pathophysiology of psoriasis are thought to trigger much comorbidity including insulin resistance, endothelial dysfunction, cardiovascular diseases and metabolic syndrome (Met S) (3).

In recent years, there are many studies investigating the role of various peptides in psoriasis that play a role in the etiopathogenesis of metabolic and cardiac diseases (4-6).

Adropin is a peptide hormone first found in 2008 by Kumar et al., which is thought to play a role in metabolic diseases, energy homeostasis, endothelial function and cardiac diseases in recent years. It is a product of energy homeostasis-associated (Enho) gene (7-11). It has been shown that adropine can significantly reduce TNF-α, IL-6 and inducible NOS (iNOS) expressions in the pancreatic tissues of diabetic rats at the level of mRNA. Also, decreased adropine levels are associated with an increase in the inflammatory marker (TNF-α) in women with PCOS (12).There are many studies in the literature on adropin in both animals and humans. Low adropin levels are associated with insulin resistance, dyslipidemia, hepatosteatosis and increased adipose tissue. Adropin overexpression or exogenous adropin administration

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improves glucose homeostasis, but there are also studies showing that adropin plays a role in endothelial protection by increasing endothelial nitric oxide synthase (e NOS) expression (8,13).

Low levels of adropin have been found in diabetes mellitus (DM), gestational DM (GDM), Met S, nonalcoholic fatty liver disease, polycystic ovary syndrome (PCOS), and coronary artery disease (CAD) (10-16). These data suggest that adropin may play a role in etiopathogenesis in many diseases associated with metabolic and cardiac diseases.

As well as new targeted therapies there are studies showing that weight control, regular exercise and smoking and alcohol withdrawal also affect cardiometabolic status and reduce the severity of psoriasis (17). Therefore, a multidisciplinary approach to the management of psoriasis contributes to the treatment of associated cardiovascular and metabolic diseases. To our knowledge, there are only a few studies investigating the level of adropin in patients with psoriasis (18-19). Therefore, we think that the role of adropin, a newly discovered substance that plays a role in many cardiac or metabolic disorders, is worth investigating in a disease with cardiac and metabolic comorbidities such as psoriasis.

MATERIALS and METHODS

After approval from the local ethics committee, the study was started. The study was designed prospectively. The study included 51 plaque psoriasis patients aged 18-65 years who had no systemic disease and had not received systemic treatment in the last three months and 37 healthy controls matched by sex, age and body mass index (BMI). Patients with any chronic inflammatory disease, metabolic and cardiovascular disease were excluded. Serum adropin, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglyceride (TG), fasting blood glucose (FBG), fasting serum insulin, BMI, systolic blood pressure (SBP) and diastolic blood pressure (DBP) values were recorded. In addition, psoriasis area and severity index (PASI) and duration of the disease were noted in patient group. PASI was used to evaluate erythema, induration and scaling of the lesions in four body areas (head, trunk, arms, and legs). BMI was evaluated as weight/ height^2 (kg/m^2). Insulin resistance was determined with the homeostasis model assessment (HOMA-IR) calculator. Serum adropin levels were measured by using commercial enzyme-linked immunosorbent assay (ELISA) kit (Elabscience kit, Houston, Texas, USA). After piping samples, 100 µl samples were loaded into each well and covered with plate sealer. It was incubated at 37° for 90 minutes. The liquid in the plate was inverted and removed from the medium. 100µl of Dilue Biotin was added to each well, and incubated at 37° for 60 minutes. Biotin was removed from the medium and 300µl was added to each well from the prepared wash buffer and washed 3 times. 100µl is added to each well from the prepared HRP, and then incubated at 37° for 30 minutes. Washing process was repeated. 90µl Subsrat Reagent was added to each well and the plate was sealed with sealer and placed in aluminum foil again incubated at 37° for 15 minutes. 50µl Stop Solution was added to each well and open reading was done with Elisa Reader device.

Statistical Analysis

In the study, clinical and biochemical data of the patient and control groups were evaluated with Kolmogorov-Smirnov test for the assumption of normality (P> 0.05). Then, the difference between the clinical and biochemical data in terms of groups and gender was evaluated with Student's t-test. Results were considered significant at P <0.05 significance level. In addition, the relationship between adropin and variables was examined by Spearman rho correlation test. All statistical calculations were performed with SPSS 21.0 V statistical package program.

RESULTS

The mean age was 42.16 ± 14.84 years in the patient group and 44.08 ± 13.61 years in the control group. The mean duration of the disease was 12.98 ± 7.22 years in patient group. The mean BMI score in the patient group was 25.50 ± 2.22 kg / m^2. In the control group, it was 24.94 ± 1.74 kg / m^2. Baseline PASI score ranged from 3 to 12, with a mean of 7.05 ± 2.47. Serum adropin level was 73.04 ± 46.21 pg / ml in the patient group. In the control group, serum adropin level was 77.26 ± 43.69 pg / ml. Serum adropin levels were lower in the patient group, but this was not statistically significant (p = 0.667). Insulin level, Homa-IR level, systolic and diastolic pressure were significantly higher in the patient group (p <0.05) (Table 1).

Table 1. Comparison of laboratory and clinical characteristics of patient and control groups

Parameters	Patients (n=51)	Controls (n=37)	p value
TC (mg/dl)	176.16±39.81	191.22±22.87	**0.042**
LDL-C (mg/dl)	104.92±34.55	106.97±19.39	0.745
HDL-C(mg/dl)	45.53±9.01	54.73±13.80	**<0.001**
TG (mg/dl)	132.02±85.97	121.30±60.89	0.518
FBG (mg/dl)	100.65±17.29	95.22±11.40	0.100
Insulin (mlU/L)	12.67±11.47	9.04±3.25	**0.036**
HOMA-IR	3.31±3.42	2.14±0.90	**0.047**
BMI (kg/m^2)	25.50±2.22	24.94±1.74	0.202
PASI	7.05±0.47		
SBP (mmHg)	128.94±10.40	119.19±7.22	**<0.001**
DBP (mmHg)	79.98±7.72	74.59±5.05	**<0.001**
Duration (year)	12.98±7.22		
Adropin (pg/ml)	73.04±46.21	77.26±43.69	0.667

In the control group, the correlation between serum adropin level and HOMA-IR, BMI was examined and no significant correlation was found. There was no significant correlation between adropin levels and other cardiometabolic variables in the control group (Table 2).

Table 2. Correlation analysis between serum adropin level and variables in the patient group

Parameters	r-value	p-value
TC	0.165	0.248
LDL-C	0.073	0.609
HDL-C	0.026	0.854
TG	0.176	0.217
FBG	0.198	0.164
HOMA-IR	0.179	0.210
BMI	0.201	0.158
PASI	-0.823	**0.0001**
SBP	0.056	0.696
DBP	0.066	0.648

R: Correlation Coefficient

DISCUSSION

As is known, psoriasis is typically a disease with metabolic and cardiac comorbidities. Therefore, it may be possible relationship with peptide levels in the etiopathogenesis of cardiac and metabolic disorders in psoriasis. There are a few studies in the literature evaluating this relationship (4-6). In our study, serum adropin levels were lower in the patient group when psoriasis patients and control group were compared, but this was not statistically significant.

In the literature, only two studies examined serum adropin levels in patients with psoriasis. In both studies, serum adropin levels were significantly lower in the patient groups. (18-19). In one study, psoriasis patients were divided into two groups as those with and without metabolic syndrome (Met S). As a result, psoriasis patients with Met S had significantly lower serum adropin levels than those without (18). In another study, serum adropin and ischemia modified albumin levels were investigated in psoriasis patients. In this study, the authors found that serum adropin levels were significantly lower in psoriasis patients compared to the control group. A more significant decrease was found in patients with PASI> 10 than patients with PASI≤10 (19). In the study of Pektas et al., 44 patients with psoriasis vulgaris were evaluated, whereas in our study 51 patients with psoriasis vulgaris were examined for adropin. In our study, although serum adropin levels were low in the patient group, no significant difference was found between the patient and control groups. The presence of these results in our study may be related to the low number of patients, but may also be due to the low PASI value in our study, unlike other studies. In our study, the mean PASI value was 7.05 ± 2.47. Only 4 of the patients had PASI> 10. As it is known, PASI shows the activity and severity of the disease. Most of our patients had mild psoriasis (PASI≤ 10). The risk of cardiac and metabolic disorders increases with increasing PASI value. Considering that low PASI is associated with low metabolic and cardiac risk, it can be considered that a strong decrease in serum adropin level cannot be detected in this case. In our study, we found a negative correlation between serum adropin level and PASI. While there was no correlation between serum adropin levels and PASI in one of the studies conducted with psoriasis, one study found a negative correlation similar to our study (18,19). This suggests that serum adropin levels may be an early predictor of endothelial, cardiac and metabolic dysfunction in patients with psoriasis. However, in order to reach clearer data, we think that studies with larger groups are needed. In our study, there was no significant correlation between serum adropin levels and FBG, insulin and HOMA-IR in both patient group.

Animal studies have shown that the Enho gene is regulated by nutrition, but this mechanism is not fully understood. Kumar et al. reported that there was increased Enho gene expression and higher serum adropin levels in mice fed a high-fat and low-carbohydrate diet. Also they found lower adropin levels in mice fed low fat and high carbohydrates. It has also been suggested that mice with the adropin knock-out gene exhibit impaired glucose tolerance, suggesting the role of adropin in the development of insulin resistance and Type 2 DM (20). In their study with diabetic rats and control rats, Aydin et al. examined adropin expression in the pancreas, liver, brain, cerebellum, and kidneys, and found higher levels of adropin in both serum and tissues in the diabetic rat group (9). However, Akcilar et al. showed a significant decrease in adropin levels in diabetic rats and showed that adropin treatment had antidiabetic effects in Type2 DM (21). Wu et al, in their study of the relationship between serum adropin levels and coronary atherosclerosis in diabetic and non-diabetic patients, found lower adropin levels in Type 2 DM patients compared to nondiabetic patients (22). Low serum adropin levels have also been shown in studies conducted in pregnant patients with GDM (23-24). However, Beigi et al. showed no correlation between adropin and fasting blood sugar in women with GDM (23). In the study of Zhang et al., type 2 DM patients and control patients were compared and serum adropin levels were found to be lower in Type 2 DM patients and a negative correlation was found between adropin level and fasting plasma glucose (25). Similarly, Butler et al. found a negative correlation between adropin levels and fasting glucose in obese patients (26). In a study conducted by Korkmaz et al. with psoriasis patients, a negative correlation was found between serum adropin level and TG and HOMA-IR (18). When Kumar and colleagues first discovered adropin, it was proposed that adropin is involved in peripheral glucose homeostasis and lipid metabolism in response to variable macronutrient consumption. They then reported that systemic administration of adropin to rats reduces hepatosteatosis (8,20). Akcilar et al. showed a decrease in TC, TG, LDL-C levels and an increase in HDL-C levels by adding parenteral adropin to mice with DM (21). In our study, no significant correlation was found between serum adropin levels and TC, TG, LDL-C, HDL-C levels in

both patient and control groups. In the literature, there are studies indicating that there is no correlation between these parameters similar to our study (23-24,27). In some studies in different patient groups, serum adropin levels showed negative correlation with TC, TG, LDL-C and positive correlation with HDL-C (10,14,25-26). The results of these studies have not always showed consistent results, but adropin appears to play a role in lipid metabolism. In this study, we did not find any relationship between serum adropin levels and BMI. Results similar to those in our study have been shown in some studies (11,23-24). In some studies with different patient groups, it has been reported that serum adropin level is negatively correlated with BMI (10,25-26,28-29). However, in another study, a positive correlation was found between serum adropin levels and BMI in heart failure patients (27). Lovren et al. in their study showed that adropin can regulate e NOS bioactivity and play a role in endothelial function. Endothelial function plays an important role in the development and progression of atherothrombosis. The authors suggested that adropin may be a new target in diseases characterized by endothelial dysfunction (7). In a study conducted with 92 patients with Type 2 diabetes, Topuz et al. found that adropin levels were lower in the endothelial dysfunction group than in the control group. With these findings, they suggested that adropin may be an effective marker in the evaluation of endothelial function (30). Zhang et al. have included 356 patients for a study to examine the correlation of serum adropin level with CAD, and found that serum adropin level is significantly lower in CAD group than that in the control group. The multivariate regression analysis revealed that low adropin levels were an independent risk factor for CAD (31). In their study, Wu et al. suggested that low adropin levels were an independent risk factor for coronary atherosclerosis in both diabetic and nondiabetic patients (22). There are many studies showing the relationship between serum adropin levels and arterial hypertension. Chen et al. suggested that adropin may have an important role in the regulation of hypertension. They thought that this effect could be related to the underlying mechanisms such as adropin reducing obesity, insulin resistance, improving endothelial dysfunction and modulating neural system activity (32). In our study, no significant correlation was found between serum adropin levels and systolic and diastolic blood pressure in psoriasis patients. In a study of 40 obese hypertensive children and 15 healthy volunteers, no correlation was found between serum adropin level and high blood pressure (28). In another study, patients with primary arterial hypertension were compared with the control group, and significantly lower adropin levels were found in patients with primary arterial hypertension (33). Serum adropin levels were found to be significantly lower in adult patients with blood pressure above 180/100 mm Hg compared to normotensive controls, but could not be used as a target organ damage marker because serum adropin levels were similar in patients with and without target organ damage (34).

CONCLUSION

In conclusion, in this study that we investigated the relationship between adropin levels and some cardiac and metabolic variables in psoriasis patients, adropin levels was lower in psoriasis patients but it wasn't significant. PASI value was negatively correlated with serum adropin level. We concluded that this may be related to the low PASI values of the patients in our study. Therefore, in order to reach more clear and detailed data, it is appropriate to investigate the serum adropin levels in psoriasis patients in further studies.

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

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