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Serum Gelsolin Levels in PCOS-Related Androgenetic Alopecia

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Abstract

Aim: To compare serum gelsolin levels of women with androgenetic alopecia with PCOS and patients with non-PCOS alopecia. **Materials and Methods:** A total of 30 PCOS patients who applied to our dermatology clinic with the complaint of hair loss and were diagnosed with androgenetic alopecia (AGA) were included in the study. Thirty patients who were not diagnosed with PCOS but were diagnosed with AGA were considered as the control group. Patients in the control group were matched with PCOS in terms of age. AGA was diagnosed in cases of widespread thinning of the hair on the scalp and preservation of the frontal hairline. All participants underwent a complete clinical examination and blood examination. Serum gelsolin levels of both groups were measured by ELISA. **Results:** The number, age, and BMI values of the participants in both groups were recorded as similar. Serum total testosterone, insulin, HOMA-IR and LH values were significantly higher in the PCOS with AGA compared to the AGA without PCOS. There is no significant difference between groups in terms of serum FSH levels. Serum gelsolin levels of the PCOS group were significantly lower than the control group (160.1 ± 34.2 ng/mL vs. 188.6 ± 46.7 ng/mL, $p < 0.03$). We found a negative and significant relationship between serum gelsolin and testosterone levels ($r = 0.68$, $p < 0.02$). **Conclusions:** Serum gelsolin levels in PCOS patients with androgenetic alopecia were found to be significantly lower than in non-PCOS alopecia patient groups.

Keywords

Androgenenetic Alopecia, PKOS, Gelsolin, Inflammation

1. Introduction

Androgenetic alopecia (AGA) is the most common hair loss disorder whose ex-

act mechanisms are not yet known. Although the clinical course of AGA is interrupted by medical treatments, it is a progressive pathology. The psychological component of the disease prevents patient compliance with treatment. It affects 80% of men and about 50% of women [1] [2]. Typical hair loss begins at the anterior hairline and bitemporal. Progressive hair thinning and loss result in complete hair loss in the vertex. At the end of the process, only hair remains in the parietal and occipital areas [3] [4]. Because alpha-reductase Types I and II are more intense in the male frontal region than in females, the disease is more sensitive to androgens in males. Because alpha-reductase Types I and II are less in the occipital and parietal areas, these areas are more resistant to hair loss [5].

AGA is a pathology with multifactorial etiology and the common result is follicle miniaturization. Inflammation and fibrosis in the follicular bulge are among the most common abnormalities. Inflammation causes fibrosis in the hair follicle, preventing adequate nutrition and causing the appearance of hairs in different developmental stages in the frontal area. Increased hypersensitivity to androgens is another etiological culprit. Insufficient stem cell production in hair follicles, an increase in sebaceous glands, and dermal thickening are other pathologies responsible for the etiology of AGA [6] [7].

Gelsolin is a calcium-activated actin-depolymerizing filament protein. It is expressed in both extracellular and intracellular fluids. Deficiency of this protein results in widespread inflammation and apoptosis [8]. Plasma gelsolin is the extracellular isoform and is the main circulating gelsolin protein. This isoform is a biomarker used to determine the severity of different diseases and the response to treatment [9]. It is mostly used in the diagnosis and treatment follow-up of inflammatory diseases. Since damage to erector pili muscles and myofibrils is also responsible for the etiology of AGA [10], gelsolin may be responsible for the etiology of AGA. Gelsolin defect was found in proteomic analyzes of mesenchyme-derived dermal papilla cells of patients suffering from baldness [11]. Polycystic ovary syndrome (PCOS) is an endocrine disease with skin and hair manifestations characterized by hyperandrogenemia and insulin resistance. Some PCOS patients exhibit hirsutism, while others have AGA [12]. Therefore, the relationship between hyperandrogenemia and AGA is not clear. Detection of hyperandrogenemia in only one-third of AGA patients suggests the role of different molecules in the etiology [13]. There are no studies investigating circulating gelsolin levels in AGA due to PCOS. This study was designed to determine serum gelsolin levels in PCOS women with androgenetic alopecia.

2. Materials and Methods

2.1. Participant Selection

A total of 30 PCOS patients who applied to our dermatology clinic with the complaint of hair loss and were diagnosed with androgenetic alopecia (AGA) were included in the study. Thirty patients who were not diagnosed with PCOS but were diagnosed with AGA were considered as the control group. Patients in

the control group were matched with PCOS in terms of age. Revised Rotterdam criteria were used for the diagnosis of PCOS. Those who met at least two of the three criteria below were considered PCOS: 1) oligo and/or anovulation, 2) clinical and/or biochemical hyperandrogenism, and 3) unilateral or bilateral polycystic ovary image on ultrasonography. In the age-matched control group, Rotterdam criteria were not met. All participants underwent a complete clinical examination and blood examination. AGA was diagnosed in cases of widespread thinning of the hair on the scalp and preservation of the frontal hairline. In the trichoscopy examination of both groups, hair miniaturization specific to AGA was detected. Cicatricial alopecia and alopecia areata were considered in the differential diagnosis. Routine scalp biopsy was not performed for the diagnosis of AGA.

2.2. Measurement of Serum Gelsolin with ELISA

Gelsolin levels in serum samples taken in the morning after an overnight fast were studied by ELISA method using the human gelsolin ELISA Kit (Catalog no: E1233Hu Bioassay Technology Laboratory, Shanghai, CHINA). The measuring range of the kit was 3 - 900 ng/mL. Its minimum measurable level was 1.58 ng/mL. The kit's Intra-Assay CV was <8%, while the Inter-Assay CV was <10%. The absorbances of the samples were read in a Bio-Tek ELx800 (BioTek Instruments, USA) device at a wavelength of 450 nanometers. The concentrations corresponding to all absorbances were calculated in ng/ml with the formula obtained with the help of the standard curve graph.

2.3. Statistical Analysis

Demographic and laboratory data were analyzed with Statistical Package for Social Sciences (SPSS) software and using Windows package software. Whether the data distributions were normal or not was determined by the Shapiro-Wilk test. To compare categorical variables, the Pearson Chi-square test was used and continuous variables were analyzed with the Mann-Whitney U test. The relationship between Gelsolin and other parameters was evaluated by Pearson correlation analysis. Categorical data were presented as both the number of cases and the percentage. Results were presented as mean ± SD. A p-value of < 0.05 was considered statistically significant.

3. Results

The number, age, and BMI values of the participants in both groups were recorded as similar. Serum total testosterone, insulin, HOMA-IR, and LH values were significantly higher in the PCOS with AGA compared to the AGA without PCOS. There is no significant difference between groups in terms of serum FSH levels. Serum gelsolin levels of the PCOS group were significantly lower than the control group (160.1 ± 34.2 ng/mL vs. 188.6 ± 46.7 ng/mL, $p < 0.03$). **Table 1** presents the demographic, hormonal and gelsolin data of both groups in detail.

Table 1. Demographic and hormonal characteristics of PCOS with AGA and control groups.

	AGA with PCOS	AGA without PCOS	p-value
N (%)	30 (50%)	30 (50%)	
Age	29.4 ± 3.55	28.7 ± 3.09	0.71
BMI (kg/m^2)	**22.8 ± 2.33**	**23.4 ± 3.08**	0.50
Testosterone (ng/mL)	**0.77 ± 0.21**	**0.49 ± 0.30**	**0.01**
LH (mIU/ml)	**9.33 ± 1.29**	**4.98 ± 2.06**	**0.01**
FSH (mIU/ml)	**5.40 ± 1.04**	**4.77 ± 1.09**	**0.47**
Insulin (mU/L)	**9.22 ± 2.45**	**5.39 ± 1.20**	**0.03**
HOMA-IR	**2.86 ± 0.11**	**0.97 ± 0.22**	**0.02**
Gelsolin (ng/mL)	**160.1 ± 34.2**	**188.6 ± 46.7**	**0.03**

In the Pearson correlation analysis, we found a negative and significant relationship between serum gelsolin and testosterone levels ($r = 0.68$, $p < 0.02$). There was no significant relationship between other parameters and gelsolin levels.

4. Discussion

Female androgenetic alopecia (FAGA) is the most common cause of non-scarring hair loss. Although its etiology is not known exactly, it is thought to occur due to endocrine pathologies. In addition to benign adrenal pathologies, the incidence of FAGA increases in ovarian, adrenal tumors and high prolactin levels, although the age of onset is variable, it often occurs after puberty and there is an increase in the incidence of FAGA with advancing age. Typical hair loss starts from the scalp and extends to the frontal area [13]. Due to the progressive nature of the disease, early diagnosis makes it easier to take the necessary preventive measures. Delays in treatment will lead to complete loss of hair and psychological problems. PCOS is an endocrine pathology with dermatological and hair manifestations in addition to hyperandrogenemia and insulin resistance. The frequent occurrence of FAGA in diseases with androgen elevation suggests that FAGA in PCOS is due to hyperandrogenemia [13]. However, the clinical spectrum is not accompanied by androgen elevation in every FAGA patient. Therefore, it comes to mind that different etiological mechanisms, other than androgen, may be responsible for FAGA due to PCOS. Since PCOS is a chronic low-grade inflammatory disease, other causes of pathological inflammation in the hair follicle may contribute to the formation of FAGA [14]. Gelsolin is an actin-depolymerizing protein and its deficiency can cause increased hair follicle inflammation and apoptosis. This study presents the first clinical data designed to determine the relationship between serum gelsolin levels and demographic and hormonal parameters in PCOS patients presenting with FAGA.

One of the mechanisms suggested in the etiology of FAGA is increased inflammation in the hair follicle bulge. Increased apoptosis secondary to inflam-

mation leads to a gradual thinning of the hair [15]. We found serum gelsolin levels in PCOS patients to be significantly lower than control FAGAs. Decreased gelsolin levels are known to be characterized by increased inflammation [8]. Pro-inflammatory cytokines that arise due to increased inflammation in hair follicles may cause follicle damage, leading to a gradual thinning of the hair and hair loss over time. Gelsolin is also a filament protein, which can cause damage to the erector pili muscles and mediate the weakening of the hair. Defective expression of genes responsible for gelsolin in dermal papillae supports the possible etiological role of this molecule in FAGA Hypersensitivity of hair follicles to high androgens in the PCOS group is another cause of hair loss [15]. The negative correlation between serum gelsolin levels and androgens suggests that androgens block the production or effect of gelsolin. However, we do not know by which mechanism androgens impair the functions or production of gelsolin. The lack of a significant relationship between serum LH, insulin levels, and HOMA-IT and gelsolin suggests that the effect of androgens on gelsolin is independent of other endocrine parameters.

While FAGA affects the vertex and parietal regions, the absence of hair loss in the anterior frontal zone cannot be explained by the effect of gelsolin and androgens. Detection of follicle miniaturization only in these regions, with less involvement of other regions, may be due to different responses of hair follicles to etiological factors rather than systemic effects [14]. Chronic inflammatory and systemic diseases such as PCOS occur through the disruption of both adaptive and innate immune reactions [16]. Thanks to its anti-inflammatory and actin-binding properties, gelsolin can play a role in the protection and function of hair follicles. Decreased serum gelsolin levels in chronic inflammatory conditions such as PCOS may cause cellular damage in hair follicles and may predispose to FAGA. Despite the small number of cases, our study is important in that it is the first to report an increase in serum gelsolin levels in FAGA due to PCOS. More comprehensive studies that analyze gelsolin in hair follicles will allow a clearer conclusion.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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