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Serum Prolactin Levels in Adult Females with Telogen Effluvium: A Case Control Study

Erişkin Kadın Telogen Effluvium Hastalarında Serum Prolaktin Düzeyleri: Vaka Kontrol Çalışması

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ABSTRACT Objective: The effect of prolactin hormone on hair follicle is complicated and the relationship between prolactin and hair loss is still controversial. The aim of this study is to evaluate the serum prolactin levels in female patients with telogen effluvium and to discuss its role in hair loss. **Material and methods:** Forty-seven adult female patients diagnosed with telogen effluvium and forty-two age matched healthy female controls were included in this retrospective study. Serum prolactin levels were statistically compared between telogen effluvium patients and healthy controls (Mann-Whitney U test). **Results:** The median age of patient group was 29 (19-46) years and the median duration of symptoms was 12 (1-156) months. Neither patients nor the controls had hyperprolactinemia. The median serum prolactin level of patients was 10.47 ng/mL (2.75-23.53) which is statistically significantly lower than controls (p=0.033). No statistically significant difference was detected in prolactin levels between acute and chronic telogen effluvium patients (p=0.444). **Conclusion:** In contrast to most studies mentioning the catagen inducing effect of prolactin, in this study lower prolactin levels were found in patients diagnosed with telogen effluvium compared to the control group. However the majority of these studies associating hyperprolactinemia and hair loss include hyperandrogenemic cases and the catagen inducing effect of prolactin is mostly reported with high doses. In this study, absence of patients with hyperprolactinemia and hyperandrogenism may explain the contrast findings with the literature. As a result, it may be useful to consider the dose and gender dependent effects of prolactin in hair loss.

Keywords: Prolactin; alopecia; hair loss

ÖZET Amaç: Prolaktin hormonunun saç folikülü üzerindeki etkisi karmaşıktır ve saç dökülmesi ile ilişkisi hala tartışmalıdır. Bu çalışmanın amacı, telogen effluvium tanısı alan kadın hastalarda serum prolaktin düzeylerini değerlendirmek ve saç dökülmesindeki rolünü tartışmaktır. **Gereç ve Yöntemler:** Bu retrospektif çalışmaya telogen effluvium tanısı almış 47 yetişkin kadın hasta ve yaş uyumlu 42 kadın sağlıklı kontrol dahil edildi. Serum prolaktin düzeyleri telogen effluvium hastaları ve sağlıklı kontrol grubu arasında istatistiksel olarak karşılaştırıldı (Mann-Whitney U testi). **Bulgular:** Hasta grubunun ortanca yaşı 29 (19-46) ve ortanca semptom süresi 12 (1-156) aydı. Hasta ve kontrol grubunda hiperprolaktinemi yoktu. Hasta grubunun ortanca serum prolaktin düzeyi 10,47 ng / mL (2,75-23,53) olup, kontrol grubuna göre istatistiksel olarak anlamlı derecede düşüktü (p=0,033). Akut ve kronik telogen effluvium hastaları arasında prolaktin düzeylerinde istatistiksel olarak anlamlı fark saptanmadı (p=0,444). **Sonuç:** Prolaktinin katajen indükleyici etkisinden bahseden çoğu çalışmanın aksine, bu çalışmada telogen effluvium tanısı alan hastalarda kontrol grubuna göre daha düşük prolaktin seviyeleri bulunmuştur. Bununla birlikte, hiperprolaktinemi ve saç dökülmesini ilişkilendiren bu çalışmaların çoğu hiperandrojenemik vakaları içermektedir ve prolaktinin katajen indükleyici etkisi çoğunlukla yüksek dozlarda bildirilmektedir. Bu çalışmada hiperprolaktinemi ve hiperandrojenizmi olan hastaların yokluğu literatürle kontrast bulgularını açıklayabilir. Sonuç olarak saç dökülmesinde prolaktinin doz ve cinsiyete bağlı etkilerinin dikkate alınması faydalı olabilir.

Anahtar Kelimeler: Prolaktin; alopesi; saç dökülmesi

The human hair follicle is a target of various neurohormones that regulate the hair growth including the prolactin (PRL).[1,2] PRL is defined as an epithelial stem cell modulator.[2,3] Although limited number of studies indicated hyperprolactinemia as a possible cause of hair loss, the role of PRL on human hair growth is still controversial.[1,2,4,5] Androgenic and diffuse types of hair loss are defined as the most common types of hair loss associated with hyperprolactinemia.[4] Telogen effluvium (TE) is the most common type of diffuse hair loss and may be triggered with various factors such as febrile illness, major surgery and stress.[6] Whereas in one third of patients, no triggering factor can be detected.[6]

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The aim of this study is to evaluate the serum levels of PRL in patients with TE and to investigate its possible role in TE.

MATERIAL AND METHODS

This single-centered, retrospective study included 47 adult female patients, diagnosed with telogen effluvium and 42 aged matched healthy female controls. Ethical approval was received from Institutional Review Board (approval number: 2020-08/739 date: 26.08.20). Informed consent was obtained from all participants. Medical records of patients who admitted to dermatology outpatients clinics between January 2017 and December 2018 and diagnosed as TE were reviewed retrospectively.

Hair pull test is a quick clinical test to monitor hair loss disorders in our clinics and which is strongly positive in TE.[7] It is performed by grasping 50 to 60 hairs with thumb and index finger and gentle traction is applied. Less than 5% of hairs pulled from a bundle of 60 hairs, test is considered positive.[8] Patients who applied with a symptom of generalised shedding of hair and positive hair pull test were diagnosed as TE in the dermatology outpatient clinics by the same dermatologist. Patients diagnosed with female pattern hair loss, androgenetic alopecia, alopecia areata and scarring alopecia were not included in the study.

Only the patients with normal laboratory test results including complete blood count, routine urine, serum ferritin, serum vitamin B_{12}, serum zinc, serum free T3, T4 and thyroid stimulating hormone were included in the study. Patients under the age of 18, patients who had systemic diseases (such as thyroid disorders, renal and/or hepatic failure, malignancy, anemia or endocrine disorders such as polycystic ovarian disease and hyperandrogenism) and who use drug for at least one year (which could alter serum prolactin levels and which may trigger TE) were excluded from the study. Patients who were in lactation and menapause periods were also excluded from the study.

The control group included 42 healthy women who applied to the dermatology outpatient clinic for check-up without no history of systemic diseases and drug use. Participant's medical history, demographic features and serum PRL (**Siemens, ADVIA Centaur XPT Immunoassay System**) levels were recorded. The reference values for serum PRL were 1.2-30 ng/mL in females older than 18 years. Hyperprolactinemia was defined as concentrations of serum PRL levels higher than 30 ng/mL.

Serum PRL levels were compared between patients with TE and healthy control group. Patients with TE are also splitted in 2 groups as acute (lasts for about 3-6 months) and chronic (persist beyond 6 months or more).[9] Serum PRL levels were also compared between acute and chronic TE subgroups.

STATISTICAL ANALYSIS

The data were statistically analysed using SPSS 25.0 software (IBM Corp, Armonk, NY, USA). The distribution pattern of the data was determined by using the Kolmogorov-Smirnov normality test. Test results were presented as median (minimum-maximum) for continous variables and as a number (%) for categorical variables. Since the age and the levels of PRL parameters were not distributed normally, Mann-Whitney U nonparametric test was used to compare these parameters between the patients and the control groups. Additionally PRL levels between acute and chronic TE groups were compared with Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

RESULTS

The study consisted of 47 female patients diagnosed with TE and 42 healthy female controls. The median age of patient group and control group were 29 (19-46) and 26.5 (18-42) years respectively. The median duration of symptoms was 12 (1-156) months in patients with telogen effluvium. Of the 47 telogen effluvium cases, 61.7% (n=29) were chronic and 38.3% (n=18) were acute. Neither patients nor the controls had hyperprolactinemia. Median level of PRL in patients with acute TE was 10.92 ng/mL (2.75-19.56) and in patients with chronic TE was 10.47 ng/mL (3.42-23.53). No statistically significant difference was found in PRL levels between acute and chronic TE patients (p=0.444).The median serum PRL level of patient group was 10.47 ng/mL (2.75-23.53) and mean value was 12.31±5.52 ng/mL which is statistically significantly lower than control group (p=0.033) (Table 1).

TABLE 1: Comparison of age and serum prolactin levels between patient and control group, and comparison of duration of telegon effluvium symptoms between patients.

	Patients with TE (n=47) Median (minimum-maximum)	Control group (n=42) Median (minimum-maximum)	p value
Age (year)	29 (19-46)	26.5 (18-42)	0.574
Duration of TE (month)	12 (1-156)	-	
Serum levels of PRL (ng/mL)	10.47 (2.75-23.53)	14.61 (4.91-29.17)	0.033
	Acute TE (n=18) Median (minimum-maximum)	**Chronic TE (n=29) Median (minimum-maximum)**	**p value**
Serum levels of PRL (ng/mL)	10.92 (2.75-19.56)	10.47 (3.42-23.53)	0.444

PRL: Prolactin; TE: Telogen effluvium.

DISCUSSION

In the present study, serum levels of PRL in female patients with TE were significantly lower than healthy controls. Nevertheless, when the duration of TE was compared, there was no difference in serum levels of PRL between acute and chronic groups. The role of PRL on hair loss was discussed in various studies however, the hypothesis are contradictory.

Although the regulation of intracutaneous PRL is not fully understood yet, it is known that PRL exists in human hair follicle (HF) epithelium in hair cycle dependent levels.[1] Ex vivo studies report that PRL has effects on human HF growth, cycling and epithelial stem cell function.[1,10,11] The effect of PRL on hair growth has been reported differently according to the species as seasonally dependent or independent. PRL regulates seasonally dependent cycles in mammals, on the other hand, it regulates seasonally independent hair cycles in men and mice.[2] It is reported that, PRL leads the induction of both anagen and catagen hair follicules in mammals. But treatment of murine anagen HFs with PRL led to catagen.[12-16] Also, treatment of organ cultured human scalp HFs from male donors with high dose PRL significantly inhibits hair shaft elongation and hair bulb keratinocyte apoptosis.[1]

The studies linking hyperprolactinemia with hair loss report the hyperandrogenic conditions especially.[5,17] In literature, the well known androgen stimulating effect of PRL has been mentioned in female androgenic alopecia.[17] Orfanos and Hertel suggest to examine PRL levels together with androgens and thyroid function tests in patients with hyperandrogenism symptoms.[18] Similarly, Schmidt et al. state that PRL supports the suprarenal cortisol and androgen production.[19] So thyroxin and PRL may lead to female pattern hair loss (FPHL). It is stated that relationship between high prolactin and FPHL is unclear and increased prolactin levels may be secondary to hypothyroidism or hyperestrogenism.[20] Carmina et al. report that it is useful to measure serum levels of PRL to rule out and treat other conditions that may affect hair regrowth in FPHL.[21]

On the other hand, TE is a distinct form of diffuse alopecia with various other triggers. So it is matter of debate whether routine PRL measurement is necessary in all forms of diffuse alopecia. In studies that report high PRL levels in patients with hair loss, the presence of hyperandrogenism or other endocrinopathies that usually accompany hyperprolactinemia suggest that existing alopecia may also be due to concominant endocrinopathy. In this respect, we think that this study may contribute to the literature in terms of not including patients with hyperandrogenism or other endocrinopathies.

In contrast to all studies which report hair growth inhibitory effects of PRL in mice and humans;[1,2,15,16] in this study we found relatively lower PRL levels in patients diagnosed with TE compared to the control group. There are some reports supporting our findings. Girolomoni et al. report stimulatory effect of PRL on the proliferation of cultured epidermal human keratinocytes in vitro.[22] Similarly, an in-situ study supports this finding which reports that PRL has proliferative effects on hair matrix keratinocytes.[23] The same dose of PRL (400 ng/mL) was applied to HFs derived from fe-

male frontotemporal scalp skin and resulted significant HF shaft elongation with quantitative immunohistomorphometry technique in this study.[23] Based on this study results, low PRL levels may cause a low stimulating effect on hair growth and affect hair loss. This could explain the results of the current study.

Langan et al. also report that hair-growth-promoting effect of PRL is reversed by treatment with a PRL receptor (PRLR) antagonist in the study. This catagen-promoting effect of the used PRLR antagonist suggests that endogenous, intrafollicular PRL production actually maintains human female frontotemporal scalp HFs in anagen. They explain this differential response of the HFs to PRL due to the gender/location specific differences in the key target genes whose expression is up-or downregulated after PRLR stimulation.[23] We found lower levels of PRL in female patients with TE, supporting the hypothesis of gender differences in the response of the HFs to PRL.

Also some studies report that in women, TE may develop as a side effect of dopamin agonists that inhibit pituitary PRL secretion.[24-26] Katz et al. suggest that dopamin agonists decrease serum PRL levels and this may effect the shedding phase of the HF cycle.[24] Langan et al. argue for the possibility that PRL may be a hairgrowth promoting and anagen maintaining hormone in women.[23]

In addition, a study has reported subnormal serum PRL levels in men presenting with premature balding.[27] In vitro investigations report that PRL is an autocrine hair growth modulator and supraphysiologic doses of PRL has an inhibiting effect on human HF.[15] Although we found lower PRL levels in patients with TE compared to control group, changes were within the normal reference range and there was not any patient with hyperprolactinemia. The absence of patients with high PRL levels in this study may explain the contrast findings with the literature.

Lutz states that moderately elevated PRL levels in diffuse hair loss may be a negligible cause of hair loss.[4] Because there is no confirmed data which supports the effect of PRL on the pattern or duration of the hair loss. There was no difference in PRL levels of acute and chronic TE patients in the current study supporting Lutz's discussion.

STUDY LIMITATIONS

Retrospective design and the fact that the diagnosis of TE is only based on the clinical findings (instead of biopsy or trichogram)are considered as limitations of this study. However, recent studies argue that average levels of PRL do not vary substantially between the phases of the menstrual cycle, evaluation of PRL levels due to menstrual phases in hair loss may be another topic for future studies.[28] Via restrospective design of the study, it could not be detected.

CONCLUSION

According to the studies, PRL is defined as an hair growth inhibitory hormone mostly in men and at high levels.[1,2,15] We found lower physiologic serum levels of PRL in female patients diagnosed with TE regardless of the duration. We suggest that it is better to consider the role of PRL on hair loss minding the gender and dose dependent effects. Also based on the study findings, the deficiency of PRL in TE may be considered in patients with normal androgen levels inverse to hyperprolactinemia that may detected in androgen dependent hair loss.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Burcu Tuğrul;* ***Design:*** *Burcu Tuğrul, Gül Aslıhan Çakır Akay;* ***Control/Supervision:*** *Burcu Tuğrul, Gül Aslıhan Çakır Akay;* ***Data Collection and/or Processing:*** *Burcu Tuğrul;* ***Analysis and/or Interpretation:*** *Burcu Tuğrul, Gül Aslıhan Çakır Akay;* ***Literature Review:*** *Burcu Tuğrul, Gül Aslıhan Çakır Akay;* ***Writing the Article:*** *Burcu Tuğrul, Gül Aslıhan Çakır Akay;* ***Critical Review:*** *Burcu Tuğrul, Gül Aslıhan Çakır Akay;* ***References and Fundings:*** *Burcu Tuğrul;* ***Materials:****Burcu Tuğrul.*

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