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The Role of Micronutrients in Young Men Presenting with Hair Loss

Genç Erkeklerde Saç Dökülmesinde Mikrobesinlerin Rolü

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ABSTRACT Objective: Vitamins and minerals, micronutrients, play a role in the cellular structure of the normal hair follicle cycle, essential for the growth and function of matrix cells in the hair follicle. They can cause hair loss when they are insufficient. We aimed to investigate the potential role of deficiencies of micronutrients in the etiology of male hair loss. **Material and Methods:** A total of 116 male patients aged 18-30 years, who were admitted between November 2018 and October 2019, were included in the study. Male patients with a diagnosis of androgenetic alopecia (AGA) and telogen effluvium (TE) were included. The factors that may play a role in the etiology, were investigated with the following tests; hemogram, fasting blood glucose, serum iron, ferritin, folate, vitamin B_{12} and D levels, zinc levels and thyroid function tests. **Results:** The mean age of the patients with TE was 23.18±3.6 years, and the mean age of the patients with AGA was 24.43±3.59 years. AGA was found to be 62.06% and TE was found to be 37.93% in the study group. In general, the deficiencies of vitamin D, vitamin B_{12} and low ferritin levels were found as 54.3 (n=63), 45.6 (n=53) and 15.5% (n=18) respectively. The mean time of hair loss was 37.7±35 months. Family history was positive 69.44% (n=50) in AGA, 45.5% (n=20) in TE. **Conclusion:** Especially vitamins D and B_{12} levels were found to be lower. Therefore, we recommend that these tests should be requested in male patients with hair loss and we think this will contribute to the treatment.

Keywords: Androgenic alopecia; hair loss; men; micronutrients; telogen effluvium

ÖZET Amaç: Vitaminler ve mineraller, yani mikro besinler, normal saç folikülü döngüsünde hücresel yapıda rol oynarlar, kıl folikülünde matriks hücrelerinin büyümesi ve işlevi için gereklidir. Yetersiz olduklarında saç dökülmesine neden olabilirler. Bu çalışmada, saç dökülmesi ve seyrelmesi ile başvuran erkek hastalarda etiyolojinin olası rolünü araştırmayı amaçladık. **Gereç ve Yöntemler:** Kasım 2018 ile Ekim 2019 arasında saç dökülmesi şikâyeti ile başvuran toplam 116 hasta çalışmaya alındı. Androgenetik alopesi (AGA) ve telogen effluvium (TE) tanısı alan 18-30 yaş arası genç yetişkin erkekler araştırmaya dâhil edildi. Hemogram, açlık kan şekeri, serum demir, ferritin, folat, vitamin B_{12} ve D düzeyleri, çinko düzeyleri ve tiroid fonksiyon testleri incelenerek etiyolojide rol oynayabilen faktörler araştırıldı. **Bulgular:** TE'li hastaların ortalama yaşı 23,18±3,6 yıl, AGA'lı hastaların ortalama yaşı 24,43±3,59 yıldı. Hastaların %62,06'sında AGA, %37,93'ünde TE saptandı. Tüm hastalarda D vitamini eksikliği %54,3 (n=63), B_{12} vitamini eksikliği %45,6 (n=53), ferritin değerinde düşüklük %15,5 (n=18) olarak bulundu. Saç dökülmesinin ortalama süresi 37,7±35 aydı. Aile öyküsü AGA'da %69,44 (n=50), TE'de %45,5 (n=20) pozitif idi. **Sonuç:** Çalışmamızda özellikle vitamin D ve B_{12} düzeyleri daha düşük bulundu. Bu nedenle saç dökülmesi olan erkek hastalarda bu testlerin istenmesini öneriyoruz, bunun tedaviye de katkıda bulunacağını düşünüyoruz.

Anahtar Kelimeler: Androjenik alopesi; saç dökülmesi; erkekler; mikrobesinler; telogen effluvium

In terms of appearance, hair is important for both men and women. Hair loss particularly affects the psychological health of the person. Male hair loss was once seen as a physiological event, but today it is considered as a disease and studies are carried out on its causes.[1]

Hair loss in men can be due to androgenic reasons, as well as non-hormonal reasons. Many factors, such as nutritional deficiencies, use of medication, and psychological stress are blamed.[1]

Vitamins and minerals, i.e. micronutrients, are the main elements that play a role in the normal

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hair follicle cycle, and are essential for the growth and function of matrix cells in the hair follicle.[2-4] Therefore, these micronutrients can be considered as a modifiable risk factor for the development, prevention and treatment of hair loss.[5]

As a result, it can be thought that hair loss can be improved with vitamin and mineral supplements. Despite the fact that they are accessible and that their supplementation is easy, it is important to know which vitamins and minerals are more effective in hair loss. It may be beneficial to include micronutrients such as iron, zinc, folic acid or vitamin B_{12} (vit B_{12}) in the treatment of hair loss. Micronutrients, including vitamins and trace elements, are therefore very important components of our diet.[2]

Several publications are available in the literature which separately investigate serum iron, ferritin, vit B_{12}, folate, zinc, vitamin D (vit D) levels in young adult male patients.[6-8] However, as far as we know, there are no publications which investigate these factors collectively. Thus, we aimed to investigate whether micronutrient factors such as vitamins and minerals have a potential role in the etiology of the disease by reviewing the results of the tests administered to the male patients presented with the complaint of hair loss and thinning.

MATERIAL AND METHODS

The files of young men between the ages of 18-30 that presented with a diagnosis of androgenetic alopecia (AGA) and telogen effluvium (TE) to the dermatology outpatient clinic between November 2018 and October 2019, were reviewed retrospectively. The study was performed according to the rules expressed in the Declaration of Helsinki. The approval was obtained from Ankara City Hospital local ethics committee (protocol no: E1/1351/2020 date: 23.12.2020). A total of 116 medical records of male patients with a diagnosis of AGA or TE were reached. Information with respect to patients' age, gender, disease duration, family history, comorbid systemic and skin diseases, use of medication, trauma and operation history, exposure to environmental agents such as heavy metals, nutritional habits and presence of stress were reviewed along with all the results of the laboratory tests, which were performed in order to investigate the etiology. Factors that may play a role in the etiology were searched by reviewing the complete blood counts, fasting blood glucose, serum iron, ferritin, folate, vit B_{12}, vit D, and

TABLE 1: Laboratory test results of the patients.

	Telogen Effluvium (n=44)	Androgenetic Alopecia (n=72)	Total (n=116)
Vit D levels	26	37	63
(<30 ng/mL)	(59.1%)	(51.38%)	(54.3%)
Vit B12 levels	14	39	53
(<300 pg/mL)	(31.8%)	(54.16%)	(45.6%)
Ferritin levels	6	12	18
(<40 ng/mL)	(13.6%)	(27.2%)	(15.5%)
Folate levels		2	2
(<4 ng/mL)	-	(2.7%)	(1.7%)
ft3 levels (2,3-4,2 pg/mL)	1 (2.27%)	1 (38%)	14
ft4 levels (0,83-1,43 ng/mL)	8 (18.1%)	2 (2.77%)	(12%)
TSH levels (0,51-4,94)	-	2 (2.77%)	
AntiTPO levels	7	4	11
(>60 iu/mL)	(15.9%)	(5.55%)	(9.48%)
Anti TG levels	4	3	7
(>60 iu/mL)	(9.09%)	(4.16%)	(6.03%)
Fasting glucose (>100 mg/dL)	-	1	1
		(1.38%)	(0.86%)
Zinc levels (<70 µg/dL)	-	-	-

AntiTPO: Anti-thyroid auto-antibody; Anti TG: Anti-thyroglobulin.

zinc levels, and results of the thyroid function tests. Laboratory test results of the patients are shown in Table 1.

The results of hair pull tests and the presence of any scar, which was investigated by hair dermoscopy, were also recorded from the patient medical files.

The patients were divided into two groups as patients with AGA and patients with TE on the basis of the clinical findings. Hamilton-Norwood classification was used to classify patients with AGA.[9]

RESULTS

The mean age of the patients with TE was 23.18±3.6 years and it was 24.43±3.59 years (18-30 years) in patients with AGA. AGA was detected in 62% (n=72) of the patients, whereas TE was detected in 38% (n=44) of the patients. The demographic characteristics of the patients are shown in Table 2. Vit D deficiency was detected in more than half of the both AGA and TE cases (54.3%). Low Vit D level was found to be 51.3% in AGA group and it was 59% in TE group. Vit B_{12} deficiency was 54.16% in AGA group, while it was 31.8% in the TE group. Folate deficiency, which was 2.7%, was detected only in AGA patients. The ratio of low ferritin level was 15.5% (n=18) in the all study participants (13.6% in TE group and 27.2% in AGA group). There was no difference in terms of zinc deficiency between two groups.

Family history was positive in 69.44% of AGA group and 45.5% of TE group. There were 14 cases (12%) with at least one hormonal disorder, when free T3, free T4 and TSH hormones were taken into account. There were 18 cases (15%) with autoimmune thyroiditis, of whom thyroid function tests were normal. The majority of these patients (n=11) were in the TE group. Laboratory test results of the patients are shown in Table 1.

In terms of comorbid systemic diseases, two patients had thyroid pathology. Diabetes mellitus, bipolar disorder, depression, migraine, asthma, hyperlipidemia, myasthenia gravis, lung and liver sarcoidosis, and vertigo were present in one patient each. Comorbid diseases and the medication used for the treatment of these diseases are shown in Table 3.

STATISTICAL ANALYSIS

"Statistical Programme for Social Sciences 21" (SPSS 21) program was used for statistical analyses. Mean and standard deviation values were used in the descriptive statistics of the data. Percentage ratios were used to summarize the data.

DISCUSSION

Hair loss is a common symptom and can be observed along with a wide spectrum of diseases. Therefore, it is important to first determine the etiology and then decide on the treatment accordingly. Hair loss in men

TABLE 2: Demographic characteristics of the patients.

	Telogen Effluvium	Androgenetic Alopecia	Total Number of Cases
Number of cases	44 (37.93%)	72 (62.06%) Type 2=54 Type 3=15 Type 5=1 Type 7=2	116
Mean age* (18-30 years)	23.18±3.6 years	24.43±3.59 years	23.95±3.6 years
Mean duration* (1-156 months)	23.22±22.57	46.63±37.57	37.7±3.5 months 0-6 months=15 6 months-1 year=12 1 year-5years=63 More than 5 years=26
Family history n (%)	20 (45.5%)	50 (69.44%)	70 (60.34%)

TABLE 3: Comorbid diseases and the medication used.

Comorbid Diseases	Telogen Effluvium	Androgenetic Alopecia
Systemic diseases	1-Thyroid pathology (hyperthyroidism) 1-Gastritis 1-Myasthenia gravis	1-Diabetes mellitus 1-Thyroid pathology (hyperthyroidism) 1-Bipolar disorder 1-Depression 1-Migraine and asthma 1-Hyperlipidemia 1-Lung and liver sarcoidosis 1-Vertigo 1-Myasthenia gravis
Skin diseases	3-Seborrheic dermatitis 1-Acne 1-Alopecia areata 1-Premature graying of hair 1-Hyperhidrosis 1-Verruca	3-Seborrheic dermatitis and acne 1-Psoriasis 1-Nummular dermatitis 1-Pityriasis rosea 1-Urticaria 1-Hyperhidrosis 1-Folliculitis
Medication used	Metimazole Propranolol Lansoprazole	Thyroid drug (levotiroxin), insulin, anti-asthma (salbutamol), antidepressant (escitalopram), antipsychotic (risperidone), azathioprine betahistine dihydrochloride

can be induced by androgen. Apart from androgens, many other factors play a role on hair growth. These are hereditary or nutritional factors or factors associated with stress, lifestyle, medications, metabolic diseases, smoking, alcohol, and long-term exposure to diseases, which all affect the hair cycle resulting in the thinning and weak growth of the hair. These factors directly affect the hair growth and render the hair follicles more sensitive to the impact of androgens.[1,10]

Some researchers have suggested that oxidative stress plays a role in hair diseases.[1,11-14] These researchers have shown that androgens increase the levels of reactive oxygen species (ROS) in dermal papilla cells and this mechanism increases the secretion of transforming growth factor (TGF ß) 1, which inhibits hair growth.[10] Researchers have shown that the use of antioxidants inhibits the release of TGF ß1, which increases hair growth.[14] Trueb has shown that nutritional deficiencies in androgenic alopecia can also lead to apoptosis in hair follicle cells.[1] It has been shown that antioxidants alone can increase hair growth, even without the use of antiandrogens, and that the unaccompanied use of antiandrogens does not produce a good clinical response in those with hair loss.[10] For this reason, it is also suggested to encourage the use of antioxidants, vitamins and minerals in order to prevent hair loss and increase hair growth.[10]

Based on the information given above, we investigated the levels of micronutrients in young adult male patients. The most striking finding of this study is that vit D deficiency has been detected in more than half of the both AGA and TE cases (53.7%). Vit D is known to have an anti-inflammatory and immunoregulation effect, apart from maintaining serum calcium and phosphorus levels.[15-17] Some researchers have shown that vit D_3 promotes hair growth by inducing dermal papilla cells.[18-20] Vit D binds to the nuclear vit D receptor (VDR) in order to regulate the growth and differentiation of keratinocytes.[17] Mouse hair follicle keratinocytes are immunoreactive for VDR and are most active in the anagen phase.[21] The role of this vitamin in hair follicle is also proven by hair loss in rickets type 2 patients.[22] Most authors agree that the patients with hair loss and vit D deficiency should be supplemented with this vitamin.[5,20,23]

Vit B_{12} is required for DNA synthesis.[5,16,23] Its role in nucleic acid production shows that it can lead to an increase in hair follicle proliferation. In case of its deficiency, hair loss and greying occur because the

hair follicles can't get enough oxygen and nutrients from the blood.[24] There are few studies that demonstrates the relationship between hair loss and vit B_{12} deficiency, and the data provided in these studies are contradictory.[25,26] In our study, while vit B_{12} deficiency was 54.16% in AGA group, it was 31.8% in the TE group. These rates indicate that vit B_{12} can be effective in hair loss.

Folate is a type of vitamin B, which functions as a coenzyme in the synthesis of water-soluble nucleic acids and in amino acid metabolism, and can be effective on hair follicles as vit B_{12}.[16] We detected folate deficiency in only 1.7% of our cases. In a retrospective study, vit B_{12} deficiency was reported in 2.6% of the patients with acute and chronic TE, but there was no folate deficiency.[27] Although there are several studies on the relationship of folate and vit B_{12} with hair loss, vit B_{12} and folate are not recommended per se, as these studies were not comprehensive enough.

In our study, we also detected low ferritin levels. Iron deficiency is the most commonly encountered nutritional deficiency in the world. Although its role in hair loss is controversial, it is one of the most blamed factors. Iron deficiency is thought to cause diffuse hair loss even in the absence of anemia.[28] It is not known how low iron storages induce hair loss.[29] Iron is the cofactor of ribonucleotide reductase enzyme, which plays a role in DNA synthesis; therefore, low levels of iron in the serum impedes DNA synthesis in proliferating cells, and this is thought to be the reason of hair loss.[4,28] It is recommended to check for iron deficiency in patients presented with hair loss. Iron deficiency is more common in women presented with hair loss than in men.[30] In many studies, the criterion for low ferritin levels is accepted as any level below 40 ng/mL.[30] In our study, we used the same criterion and based on this criterion, we have found low ferritin levels in 15.5% (n=18) of the patients. Most authors agree on the benefits of iron supplements in patients with low ferritin levels and hair loss.[28] In our study, we found that male cases may have iron deficiency, although small in amount.

Despite the fact that many authors suggest that iron deficiency may be associated with different types of hair loss, Olsen et al. have shown that iron deficiency is more common in women but does not increase compared to controls.[28,30-33] Gowda et al. suggested that iron deficiency is associated with gender and not with the type of hair loss, whereas Sinclair suggested that there is no clear relationship between low ferritin levels and hair loss.[31,34]

Iron, vit D, folate, vit B_{12} are the types of vitamins and minerals that can cause premature hair greying in childhood or in early adulthood. If deficient, supplementing these micronutrients can prevent premature greying. A study conducted in India demonstrated the possible role of low serum calcium, serum ferritin, and vit D levels in premature hair graying.[35] In our study, one patient who presented with premature hair greying, did not have any deficiency with respect to any micronutrients.

Zinc is an essential trace element, has antioxidant activity, stabilizes the cell membrane, and prevents oxidative radical damage.[16,29] Alopecia is a known symptom in zinc deficiency.[16,36,37] Orally supplemented zinc is frequently used in the treatment of hair loss, even when there is no zinc deficiency. However, its efficacy is controversial. In some studies, zinc levels were found low in patients presented with hair loss, whereas in other studies no difference was observed.[27,37] Ozturk et al. found low levels of zinc and copper in the urine and serum of male patients with AGA.[6] In some studies, intake of zinc in high doses has been shown to affect the hair development.[38,39]

Jin et al. confirmed that the male pattern alopecia patients had lower levels of zinc, copper, iron and manganese in hair compared to those of healthy men.[7] However, in our study, we did not find any difference between the cases in terms of serum zinc levels. Rojas et al. examined zinc, iron, copper, selenium deficiencies as possible causes of the hair loss following bariatric surgery and demonstrated that the hair loss was in fact due to the deficiencies of these elements.[8]

Recently and Broadley demonstrated as a result of their 2-year long study that there is an improvement in hair loss with adequate nutrition, both in men and women.[40] When a good nutritional balance is achieved, vitamins, micronutrients and antioxidants can neutralize ROS, protect the immune system, pre-

vent phagocytosis, autophagy, and apoptosis.[3,41] In addition, endocrine disrupting effects of chemicals that induce cell growth can also be prevented. Thus, it has been shown that hair loss can be treated even without antiandrogens.[10] Kondrakhina et al. has shown that all patients with AGA have a deficiency of elements (Zn, Cu, Mg, Se) and vitamins (B_{12}, E, D, folic acid).[42] All these studies emphasize the role of micronutrients in the treatment of hair loss.[42]

Patients presenting with AGA commonly have a family history of the disease. In particular, AGA is thought to be inherited through a polygenetic, autosomal dominant transition.[43] Bilgiç et al. reported that 85% of the patients included in their study had a family history.[44] In our study, 69.44% of the patients included in the AGA group had a family history, whereas 45.5% of the patients included in the TE group had a family history. This result indicates that besides genetic factors, nutrition plays a major role in the etiology as well.

Diffuse telogen hair loss was observed in 55% of the patients with hyperthyroidism and in 33% of patients with hypothyroidism.[45-47] If the euthyroid condition is achieved, hair loss is reversible. In cases of long-term hypothyroidism, hair loss is irreversible due to the atrophy of the hair follicle.[45] In our study, there were 14 cases (12%) with at least one hormonal disorder with respect to ft_3, ft_4, and TSH hormones; on the other hand there were 18 cases (15%) with autoimmune thyroiditis, the thyroid tests of whom were normal. The majority of these patients (n=11) were in the TE group. This finding suggests that thyroid pathologies may also be blamed for hair loss.

Many medications may cause hair loss. In our study, 2 patients were using antithyroid and thyroid medications. It could not be understood whether the other medications used led to alopecia. Psychological stress is considered as a common cause of hair loss. Many patients complain of increased hair loss after a stressful situation. Hair loss itself is also a source of stress for the person, so it is often difficult to determine which of the two in fact is the cause of the other.[48] The patients with a family history in particular have increased stress factors. In our study, 2 patients had depression and 1 patient had bipolar disorder.

CONCLUSION

In this study, the causes of hair loss in young adult men were investigated. Apart from hormones, we have observed that deficiencies in some of the vitamins and minerals, such as vit B_{12}, vit D, iron and folic acid, may also play a role in hair loss. Therefore, we think that complete blood count, serum iron, ferritin, vitamin levels and thyroid function tests may be requested in the male patients presenting with hair loss, in order to identify the underlying cause.

In this study, patients' vit D and vit B_{12} levels were lower than their ferritin levels. Patients had low levels of folate, while low levels of zinc were not observed.

The limitations of this study are that it was a retrospective study, there was no control group without hair loss and the number of patients were low. Another limitation of the study was the lack of the post-treatment follow-ups of the patients, which could not be fully assessed.

Considering the role of vitamins and minerals in normal hair follicle development and in immune cell function, large double-blind placebo-controlled prospective studies are required to be carried out in order to determine the efficacy of vitamins and minerals in patients with 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: *Ayşe Akbaş;* ***Design:*** *Ayşe Akbaş, Fadime Kılınç;* ***Control/Supervision:*** *Ayşe Akbaş, Fadime Kılınç;* ***Data Collection and/or Processing:*** *Ayşe Akbaş, Fadime Kılınç;* ***Analysis and/or Interpretation:****Ayşe Akbaş, Fadime Kılınç;* ***Literature Review:*** *Ayşe Akbaş;* ***Writing the Article:*** *Ayşe Akbaş;* ***Critical Review:*** *Ayşe Akbaş, Fadime Kılınç;* ***References and Fundings:*** *Ayşe Akbaş.*

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