Evaluation of the levels of trace elements in the blood and hair of female patients with chronic telogen effluvium

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Introduction

Telogen effluvium (TE) is a noncicatricial alopecia, characterized by diffuse shedding of telogen hairs as a response to metabolic or psychological stresses. Telogen effluvium, the most common cause of diffuse hair loss in adult females, is considered acute when it lasts shorter than 6 months, while it is considered chronic when it lasts longer than 6 months. Acute telogen effluvium can occur 2 – 3 months following conditions including high fever, surgical trauma, blood loss, or sudden periods of hunger [1, 2]. On the other hand, chronic telogen effluvium (CTE) is associated with thyroid disorders, usually of the idiopathic type, severe iron deficiency anemia, acrodermatitis enteropathica, and malnutrition [3].

Hair loss is known to be associated with nutritional deficiencies [4]. Zinc, copper, and iron are the basic micronutrients that are important contributors to the metalloenzymatic processes of the body such as cellular functions and hair follicle cycle [5]. Hair is a more stable and less variable specimen than blood, serum, or urine [6]. Although the roles of zinc, copper, and iron are not known precisely in the pathogenesis of hair shedding, they are thought to affect hair loss. In this study, it was aimed to determine the levels of zinc, copper, iron, and ferritin in the serum as well as the levels of zinc, copper, and iron in the hair to demonstrate the association of trace elements with the disease.

Materials and methods

Local Ethics Committee approval was obtained to conduct the study. Each participant was informed about the study, and the informed consent forms were filled in. A total of 39 female patients and 30 healthy female controls older than 18 years of age were included in the study. CTE was diagnosed based on dermatological examination and medical history. A differential diagnosis of
female-type androgenetic alopecia from CTE was made with the presence of decreased hair density, in the vertex mainly, widening of the hair parting line, and increased number of vellus hairs. Diffuse alopecia areata was differentiated from CTE by the presence of trichodynia, exclamation mark hairs, and localized hair thinning. A hair pull-test was performed to evaluate the hair shedding. A strand of approximately 40 – 60 hairs from the scalp was held between the thumb and index finger. They were pulled in the direction of the hair roots to the ends by squeezing gently between the fingers. A 2- to 3-hair shed was accepted to be normal, whereas the shedding of more than 10% of the hairs in the strand was considered a positive test [7]. A general physical examination and a dermatological examination were performed in the study participants. The body mass index (BMI) values of the participants was calculated using their weights and heights. Routine laboratory tests including blood count, fasting blood glucose, albumin, liver and kidney function tests, and thyroid hormone levels were performed in all participants, and the results were within the normal ranges. In this study, the patients with CTE were excluded if they had known precipitating causes like comorbid systemic diseases, surgery, or childbirth. Individuals who dye their hair, smokers, obese individuals (BMI > 30), individuals with a history of pregnancy-breastfeeding in the last year, individuals using vitamin and mineral supplements, individuals on a diet for the purpose of losing weight, and individuals who underwent a surgical intervention were excluded from both the patient and control groups. It was preferred that the control group would consist of healthy individuals, both dermatologically and systemically.

Blood samples were collected from the participants following a fasting period of 8 – 12 hours. Those collected serum samples were analyzed in an auto-analyzer (Beckman Coulter UniCel DXI 800, CA, USA), yielding serum ferritin levels. The remaining serum samples were stored at –80 °C until the day of the analysis.

The hair samples were collected by cutting a strand of hair at the closest point to the scalp with the help of a pair of scissors made of stainless steel. The hair samples close to the scalp were cut to a length of approximately 3 – 4 cm and with a weight of 0.5 – 1 g, and they were stored at 4 °C until the day of analysis. First, a 0.25-g hair sample was washed using ultrapure water (Human Power I, Seoul, Korea) and demineralized shampoo. The washed hairs were vortexed for 5 minutes with 2 mL methanol, and then they were left in an ultrasonic bath for 10 minutes. They were dried afterwards and kept in the desiccator until the analysis. The samples were burned in accordance with the microwave oven program. The hair zinc, copper, and iron levels were analyzed using hollow cathode lamps in flame mode in an atomic absorption spectrometer (AAS) (Perkin Elmer Analyst 800, Waltham, MA, USA).

In order to determine the serum levels of zinc and copper, the samples were diluted 10 times with ultrapure water, and they were read according to a standard chart using the method described above [8, 9].

In order to determine the level of serum iron, 1 mL of serum was diluted in polyethylene tubes with an equal volume of 20% (w/v) trichloroacetic acid (TCA) and was left at 90 °C for 15 minutes. When the temperature of the samples reached room temperature, the samples were centrifuged at 1,800 rpm for 30 minutes. The elicited supernatant was analyzed in AAS [10]. All standards were prepared from the 1,000 ppm stock solution, being diluted daily, and the elicited samples were read according to a standardized graph.

Statistics

SPSS v.17.0 package program was used in the statistical evaluation of the data collected in the study (SPSS Inc, Chicago, IL, USA). The Student’s t-test was used to compare the continuous variables in independent groups, and the Pearson correlation test was used to evaluate the relationship between two continuous variables. The statistical significance level was accepted at a value of p < 0.05.

Results

A total of 69 female cases were included in the study: 39 (56.5%) cases had CTE, and 30 (43.5%) were healthy. The mean age of the control group was 24.7 ± 7.8 years,
and the mean age of patients with CTE was 26.3 ± 7.0 years. There was no statistically-significant difference between the groups (p = 0.370). The BMI was 21.7 ± 4.1 kg/m² in the control group and 23.4 ± 5.6 kg/m² in the CTE group, and there was no significant difference between the groups (p = 0.179).

The levels of serum copper and zinc were statistically significantly lower in the CTE group (p < 0.001, 0.001, respectively). The serum iron levels did not yield a statistically significant difference between the groups (p = 0.066), however, the serum ferritin levels were statistically significantly lower in CTE group (p < 0.001). The serum zinc, copper, iron, and ferritin levels of the study participants are presented in Table 1.

In regards to the levels of trace elements in the hair, the levels of iron were not significantly different between the groups (p = 0.195). However, hair zinc and copper levels were significantly lower in the CTE group (p-values 0.017, 0.001, respectively). The levels of zinc, copper, and iron in the hair of the study participants are presented in Table 2.

In regards to the serum and hair trace element levels in all study participants, there was a significantly positive correlation between the levels of zinc (p = 0.004, r = 0.341), copper (p < 0.001, r = 0.530), and iron (p < 0.001, r = 0.740).

### Discussion

Disruption of the hair growth cycle leads to hair loss, which is a major cosmetic problem [11]. Theoretically, zinc, copper, and iron are considered to be involved in the pathogenesis of hair loss, however, studies have shown conflicting results.

Growth retardation, anemia, impaired wound healing, dermatitis, and alopecia have been reported to be associated with zinc deficiency. Zinc is a potent inhibitor of hair root regression and accelerates hair follicle healing. The major pathogenesis of hair loss in acrodermatitis enteropathica is a zinc deficiency [12, 13]. In their study, Kil et al. [14] evaluated alopecia areata, male type alopecia, female type alopecia areata, and the levels of trace elements in the patients with telogen effluvium. Serum zinc levels were found to be significantly lower in all of the groups with hair loss. Furthermore, it was concluded that zinc metabolism was associated with the hair loss in alopecia areata and telogen effluvium specifically [14]. Another study conducted with patients with a new diagnosis of alopecia areata and patients with treatment-resistant alopecia areata found lower levels of serum zinc in the patient groups. Disease duration, disease severity, and treatment resistance were inversely related to serum zinc level [15]. Similar to the literature, the serum zinc level in this study was statistically significantly lower.

Currently, deficiencies in copper, which is one of the important trace elements, is suggested to be one of the major causes involved in hair loss. Despite the availability of positive results elicited by copper supplementation in the treatment for hair loss, the function of copper in the hair follicle has not been fully understood yet [16]. A study has shown that copper is mainly involved in the differentiation and proliferation of dermal papilla cells, which are the specialized fibroblasts with a major role in the development of hair follicles [17]. However, other studies are available in the literature supporting that hair loss is not affected by the serum copper levels. In the conducted studies, serum copper levels were not significantly different in the patients with telogen effluvium, alopecia areata, or male type androgenetic alopecia compared to healthy controls [6, 14, 18].

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### Table 1. Trace element levels in serum.

<table>
<thead>
<tr>
<th>Element</th>
<th>Concentration of element in serum</th>
<th>p*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Telogen effluvium group n = 39</td>
<td></td>
</tr>
<tr>
<td>Zinc (µg/dL)</td>
<td>71.05 ± 7.89</td>
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<tr>
<td>Copper (µg/dL)</td>
<td>101.68 ± 17.24</td>
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<tr>
<td>Iron (µg/dL)</td>
<td>132.47 ± 5.8</td>
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<tr>
<td>Ferritin (ng/mL)</td>
<td>12.15 ± 3.36</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control group n = 30</td>
<td></td>
</tr>
<tr>
<td>Zinc (µg/dL)</td>
<td>81.18 ± 11.79</td>
<td></td>
</tr>
<tr>
<td>Copper (µg/dL)</td>
<td>129.17 ± 16.02</td>
<td></td>
</tr>
<tr>
<td>Iron (µg/dL)</td>
<td>135.95 ± 8.8</td>
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<tr>
<td>Ferritin (ng/mL)</td>
<td>24.61 ± 10.38</td>
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</tbody>
</table>

*p*Student’s t-test was used to compare continuous variables in independent groups. Statistical significance level was *p* < 0.05.

### Table 2. Trace element levels in hair.

<table>
<thead>
<tr>
<th>Element</th>
<th>Content of element in hair (µg/g)</th>
<th>p*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Telogen effluvium group n = 39</td>
<td></td>
</tr>
<tr>
<td>Zinc (µg/g)</td>
<td>252.69 ± 138.12</td>
<td></td>
</tr>
<tr>
<td>Copper (µg/g)</td>
<td>26.39 ± 19.23</td>
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</tr>
<tr>
<td>Iron (µg/g)</td>
<td>21.95 ± 8.47</td>
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<tr>
<td></td>
<td>Control group n = 30</td>
<td></td>
</tr>
<tr>
<td>Zinc (µg/g)</td>
<td>353.91 ± 188.19</td>
<td></td>
</tr>
<tr>
<td>Copper (µg/g)</td>
<td>43.13 ± 21.22</td>
<td></td>
</tr>
<tr>
<td>Iron (µg/g)</td>
<td>25.12 ± 14.08</td>
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</tr>
</tbody>
</table>

*p*Student’s t-test was used to compare continuous variables in independent groups. Statistical significance level was *p* < 0.05.
contrast to the other reports in the literature, serum copper levels in our study were statistically significantly lower in the CTE group. Typical dermatological symptoms of iron deficiency are koilonychia, cheilitis, and glossitis, which indicate the effects of iron on epithelial cell growth, epithelial cell maturation, and cell division [19, 20]. Ferritin reflects the iron deposit in the body. While the only cause of low serum ferritin levels is iron deficiency, it is well known that serum ferritin concentrations may increase in several clinical conditions including inflammation, diabetes, chronic alcoholism, hyperthyroidism, macrophage activation syndrome, and some metabolic syndromes. Iron deficiency is observed in the general population when the ferritin levels fall below 12 – 15 ng/L [21]. In addition, the cells in the matrix of the hair follicle are among the fastest dividing cells in the body. The ferritin levels in the hair follicle matrix are low, and the free iron levels are high. These cells may exhibit a fine sensitivity to even a small decrease in the amount of iron in the body [22]. Similar to this study, serum iron levels did not differ significantly in some studies in patients with telogen effluvium [23, 24]. Another study associated reduced ferritin levels with hair loss without an established iron deficiency [22]. In a study conducted on patients with CTE, but no iron deficiency anemia, iron therapy was reported to reduce the number of telogen hair [25]. In our study, similar to the literature, serum ferritin levels were significantly lower in the telogen effluvium group, although there was not a significant difference between the groups in terms of serum iron levels.

The hair has a high affinity for metal cations due to the presence of sulfur-rich keratin in its structure. Due to its slow growth rate, it is expected to reflect long-term metal levels [26]. Despite the fact that trace element levels in the hair have been investigated in other types of noncicatricial alopecia, such as androgenetic alopecia (AGA) and alopecia areata, no studies have been reported in the literature assessing the levels of zinc, copper, and iron in the hair in patients with CTE. In our study, similar to the literature, serum ferritin levels were significantly lower in the telogen effluvium group, although there was not a significant difference between the groups in terms of serum iron levels.

When studies of hair analysis were performed in different patient groups. In a study by Skalnaya and Tkachev [27], hair copper levels were found to be significantly higher, however, the hair zinc levels were lower in women with AGA. In a study conducted by Öztürk et al. [6], zinc and copper levels were evaluated in the hair, urine, and serum samples of male patients with AGA. In that study, the hair zinc and copper levels in the patient group were significantly lower compared to the control group (p < 0.05), however, zinc and copper levels in the serum and urine did not differ statistically between the groups (p > 0.05) [4]. A study with patients having alopecia areata reported that there was not a significant difference between the serum and hair samples in terms of their zinc, copper, and iron levels. In addition, similar to the findings of the current study, it was reported that the levels of trace elements in the hair and serum were correlated [28]. Another study conducted on children with alopecia reported low levels of zinc in the blood and high levels of copper in the hair [29]. The fluctuations that occur in the serum metal levels are limited due to the operation of homeostatic mechanisms. The level of trace elements in the hair indicates a cumulative effect [30]. In relation to this, we think that hair and serum trace element levels found in this current study were correlated.

**Conclusion**

It should be kept in mind that while investigating etiology in patients with CTE, trace element deficiencies that are necessary for the maintenance of health may also be etiological factors. In this study, the low levels of serum zinc, copper, and ferritin were found to be associated with CTE. Normal serum iron levels in patients with CTE were not sufficient to prevent disease. As a result, it is recommended that iron deposits should be kept at a high level in these patients.

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Conflict of interest

All authors declare no conflict of interest.

References


