Evaluation of the levels of trace elements in the blood and hair of patients with seborrheic dermatitis

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Abstract. Background: Seborrheic dermatitis is a chronic inflammatory disease. Structure and amount of lipids in skin, immunological reaction against Malassezia, lipase activity, genetics, environmental factors and stress contribute to the development of the disease, but the pathogenesis is not known precisely. Trace elements play a role in many important functions of organisms. However, the effects of trace elements on skin and adnexal structures are not fully understood. In this study, we aimed to determine the serum zinc, copper, and iron levels as well as the hair zinc, copper, iron, and manganese levels in patients with seborrheic dermatitis and to reveal the relationship between these parameters and seborrheic dermatitis. Materials and methods: 35 female patients with seborrheic dermatitis, aged over 18 years, and 34 healthy females with no known dermatologic or systemic diseases at similar ages were included in the study. Groups were compared in terms of serum and hair trace element levels. Results: When the serum samples of the groups were compared in terms of trace element levels, copper was statistically significantly higher in the seborrheic dermatitis group, but there was no statistically significant difference between zinc and iron levels. Zinc, copper, iron, and manganese levels in the hair samples of the seborrheic dermatitis group were significantly higher than in the control group. Conclusion: Results have shown that trace elements can contribute to the pathophysiology of seborrheic dermatitis. Malassezia colonization seen in seborrheic dermatitis, irritation, and inflammation may affect the passage and distribution of trace elements.

Introduction

Seborrheic dermatitis (SD) is a chronic inflammatory dermatitis characterized by greasy yellow flakes covering erythematous lesions, affecting seborrheic areas such as scalp, face, and chest front and back. The disease, seen at all ages, affects ~1 – 3% of adults [1]. Although the pathogenesis of the disease is not completely known, it has been suggested that structure and amount of lipids in skin, various types of Malassezia found in normal skin flora, lipase activity, specific immune reactions against Malassezia, genetics, environmental factors, and stress will trigger the disease [2].

Zinc (Zn), copper (Cu), iron (Fe), and manganese (Mn) are important trace elements for human health. They play a role in many important functions of organisms such as oxygen transport, elimination of free radicals, immunological response, and inflammatory events. Zn and Cu are present in the structures of numerous metalloenzymes necessary for growth and development. Fe and Zn play a role in mitotic processes and affect widespread epithelial changes in iron deficiency. Mn is essential for development, metabolism, and the antioxidant system [3].

Among biological samples, hair is the best bio-indicator in metal analysis. Hair mineral analysis shows the mineral composition that accumulates over a long time in proportion to the level of elements in the body. Concentration of trace elements found in hair is not subject to rapid fluctuation due to diet,
air, and water; thus, hair is advantageous compared to other diagnostic samples [4].

In this study, we aimed to determine serum Zn, Cu, and Fe levels as well as hair Zn, Cu, Fe, and Mn levels in SD patients and to reveal the relationship between these parameters and SD.

Materials and methods

A total of 35 female patients with infiltrating erythematous squamous plaques on scalp, aged over 18 years, diagnosed with SD by dermatological examination and 34 healthy females with no known dermatologic or systemic diseases at similar ages were included in the study. The Firat University ethics committee approved the study. Participants were informed about the study; all provided consent forms. Lichen planopilaris and discoid lupus erythematosus were excluded for absence of alopecia in patients. It was distinguished from psoriasis based on the fact that it did not exceed the scalp margin of the plaques and due to pale erythema and absence of accompanying psoriatic lesions. Not included in the study were patients who received topical and/or systemic corticosteroid therapy within 3 weeks, those who received topical calcineurin inhibitors, hair dye users, those who received vitamin or trace element supplementation, and obese individuals. Hair samples of the healthy control group were taken from the occipital area, while hair samples of the patient group were taken over infiltrating, erythematous scaly plaques. The hair samples were collected by cutting a bunch 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 in a length of ~ 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, 0.25 g of hair samples were washed with ultrapure water (Human Power I, Seoul, Korea), then washed with demineralized shampoo. Washed hair was vortexed with 2 mL methanol for 5 minutes and then left in ultrasonic bath for 10 minutes, then left to dry at 80 °C and kept in desiccator until time of analysis.

Samples were incubated in a microwave oven (CEM Mars 6, USA) in Teflon containers with nitric acid and hydrogen peroxide for 2 minutes at 85 °C. In compliance with the program of the microwave oven, temperature was increased by 4 °C per minute to 135 °C, then increased by 5 °C per minute to 230 °C and held at this temperature for 15 minutes. Finally, samples were burned to be made ready for analysis. Zn, Cu, Fe, and Mn levels were calculated from analysis of the obtained solutions using an atomic absorption spectrometer (AAS) (Perkin Elmer Analyst800, Waltham, MA, USA; in flame mode) (hallow cathode lamps). According to study protocol, blood samples taken from forearm and at least 18 hours after fasting in the morning were centrifuged at 1,800 rpm for 30 minutes. Obtained serum samples were stored at –80 °C until use. For determination of Zn and Cu levels in serum, samples were diluted 10 times with ultrapure water without preliminary preparation and read against a standard chart using the method mentioned above, according to Mogaddam et al. [5] and Michalska-Mosiej et al. [6]. Each serum sample was measured at least 3 times.

For determination of serum Fe level, serum obtained from participants was prepared by diluting 1 mL of equal volume of 20% (w/v) TCA in polyethylene tubes. The lid was tightly closed, and the mixture was stirred and left at 90 °C for 15 minutes. Samples were left to cool to room temperature and centrifuged for 30 minutes at 1,800 rpm when temperature reached room temperature. The supernatant fraction obtained after centrifugation was read against a standard chart using the method mentioned above, according to Klimczak et al. [7]. All standards were prepared by diluting 1,000 µg/mL stock solution daily and samples were read against standard graph. When the correlation coefficient of the standard graph was at least 99%, it started to work, otherwise the graph was refreshed.

Statistics

SPSS v.17.0 package program was used for statistical evaluation of obtained data in the study (SPSS Inc., Chicago, IL, USA). Student’s t-test was used to compare the trace element levels of cases in control and SD groups. Pearson’s correlation test was used to evaluate the relationship between
Trace elements in patients with seborrheic dermatitis

**Results**

A total of 69 cases were included in the study, 35 (50.7%) cases were SD patients and 34 (49.3%) were healthy controls. The mean age of the SD group was 29.5 ± 7.9 years (min – max: 18 – 48 years), and the mean age of the control group was 28.9 ± 7.1 years (min – max: 18 – 45 years). There was no statistically significant difference between the groups (p = 0.922).

Serum samples of the two groups were compared in terms of trace elements: in the SD group, Cu value was higher (p = 0.041) than in the control group, but there was no statistically significant difference between the groups in terms of Zn and Fe values (p-values: 0.374 and 0.667, respectively). Serum trace element levels of the groups are presented in the Table 1.

According to the evaluation of hair samples of the two groups, Zn, Cu, Fe, and Mn levels were significantly higher in the SD group than in the control group (p-values: 0.016, 0.013, 0.001, and 0.000, respectively). Hair elements content in the examined groups are presented in Table 2. When the two continuous variables, p-value below 0.05 was considered statistically significant.

**Discussion**

SD is a common, chronic inflammatory disease of the skin, characterized by scaly, itchy, reddish brown plaques in seborrheic areas such as scalp, face, and chest. Although the disease is seen at all ages, incidence of the disease increases in the infantile period and between ages of 30 – 60 [8]. *Malassezia*, which is accused in the pathogenesis of the disease, is present in normal skin flora. Since this microorganism requires lipid for growth, it colonizes in seborrheic areas. Sebum is hydrolyzed to lipases, glycerin, and fatty acids secreted from *Malassezia*. Resulting oleic acid is responsible for skin inflammation [9].

Zn, an essential trace element, has a number of physiological roles and is particularly necessary for the growth and functioning of the immune system. Zn deficiency can lead to frequent infection, hypogonadism, weight loss, mental disorder, eczema, alopecia, night blindness, loss of appetite, and delayed wound healing [10]. In a study conducted by Van Weyenbergh et al. [11] in patients with leishmania, patients were divided into three groups as localized cutaneous leishmania (LCL), mucosal leishmania (ML), and visceral leishmania (VL). When the LCL, ML, and VL groups were compared with the control group in terms of serum Zn level, it was statistically significantly lower in all the three groups than in the control group (p-values: < 0.01, < 0.01, < 0.001, respectively). In a study on the evaluation of serum Zn levels in patients with acne vulgaris by Özuğuz et al. [12], serum Zn levels were found to be significantly lower in the acne group than in the control group (p < 0.001). Negative correlation was found between disease severity and serum Zn level. The authors concluded that Zn, which acts as a cofactor for metalloenzymes in many cellular pathways, can be used in the treatment of acne due to its anti-inflammatory activity. In another study by Sheikh et al. [13] in patients with psoria-

<table>
<thead>
<tr>
<th>Element</th>
<th>Concentration of element in serum (µg/dL)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper</td>
<td>127.5 ± 28.3 Control group n = 34</td>
<td>156.6 ± 52.7 Seborrheic dermatitis group n = 35</td>
</tr>
<tr>
<td>Zinc</td>
<td>83.9 ± 28.9</td>
<td>79.0 ± 14.8</td>
</tr>
<tr>
<td>Iron</td>
<td>129.1 ± 10.9</td>
<td>127.9 ± 11.5</td>
</tr>
</tbody>
</table>

*Student’s t-test was used for statistical evaluation.

<table>
<thead>
<tr>
<th>Element</th>
<th>Concentration of element in hair (µg/g)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper</td>
<td>42.6 ± 25.3 Control group n = 34</td>
<td>59.1 ± 28.3 Seborrheic dermatitis group n = 35</td>
</tr>
<tr>
<td>Zinc</td>
<td>344.8 ± 100.6</td>
<td>435.8 ± 189.9</td>
</tr>
<tr>
<td>Iron</td>
<td>15.1 ± 8.4</td>
<td>26.1 ± 15.8</td>
</tr>
<tr>
<td>Manganese</td>
<td>5.6 ± 4.2</td>
<td>14.9 ± 11.0</td>
</tr>
</tbody>
</table>

*Student’s t-test was used for statistical evaluation.
sis, it was found that serum Zn levels were significantly lower in the psoriatic group than in the control group (p < 0.0001). In a study, in which serum Zn was investigated in a patient group with SD, although serum Zn level was higher in the SD group than in the control group, no statistically significant difference was found between the two groups (p = 0.507) [14]. In the literature, the data obtained from studies in which serum Zn level is investigated shows variability. There was no statistically significant difference in serum Zn values obtained in our study despite the lower concentration in patient group.

Cu is a cofactor of many metalloenzymes, like cytochrome oxidase, dopamine hydroxylase, tyrosinase, lysyl oxidase, and superoxide dismutase (SOD). Increase in serum Cu level leads to decrease in effectiveness of these enzymes. Animal experiments and clinical trials have shown that excess serum Cu causes acute coronary events by impairing cholesterol metabolism [15]. The relationship between superoxide dismutase and glutathione peroxidase activities and trace element levels was investigated in patients with critical leg ischemia, a prognostic indicator of atherosclerosis. It was found that activity of these enzymes deteriorated with a significant increase in Cu levels [16]. In a study conducted by Van Weyenbergh et al. [11] in patients with leishmaniasis, serum Cu levels were found to be significantly higher in the LCL and VL groups than in the control group (p < 0.001 and < 0.001, respectively). There was no statistically significant difference between the ML group and the control group (p < 0.05) [11]. In another study evaluating patients with psoriasis, serum Cu levels were found to be significantly higher in the psoriasis group (p < 0.0001) [13]. In a similar way, serum Cu values obtained in our study were found to be significantly higher in the SD group than in the control group.

In a study by Tisma and Poljak-Blazi [17], they aimed to explain the role of oxidative stress induced by ultraviolet (UV) light and Fe metabolism in the pathophysiology of rosacea. In this study, the number of ferritin-positive cells in skin samples of rosacea patients was significantly higher (p < 0.001) [17]. In a study by Koyuncu et al. [14] in which serum Fe levels in patients with SD were evaluated, Fe levels in the patients with SD were found to be statistically significantly lower than in the healthy controls (p = 0.002) [14]. In another study conducted by Ponikowska et al. [18], serum levels of Fe in psoriatic patients were examined. When the examined groups were compared in terms of serum Fe levels, they were lower in the psoriasis group, but no statistically significant difference (p = 0.29) was found. It has been reported that Fe deficiency tends to develop in patients with psoriasis, a chronic, immunologically mediated skin disease, which may contribute to progression of the disease. In another study conducted by Rashmi et al. [19] in patients with psoriasis, serum Fe levels were found to be significantly lower in the psoriatic group compared to the control group (p < 0.05). When serum Fe levels were examined in our study, it was seen that data we obtained was similar to the results of the study conducted by Ponikowska et al. [18].

Serum level of trace elements can vary depending on many variables such as food and even daily rhythms. Results obtained from hair are balanced and represent longer periods of time. Many biochemical functions such as immune activity, protein synthesis and effects of hormones are dependent on trace elements; however, functions of Zn, Cu, Fe, and Mn in hair follicle is unknown. Trace element analysis in hair is frequently used in search for dietary habits, exposure to toxins, drug abuse, and metabolic diseases [20]. However, in the literature, there is no study to evaluate Zn, Cu, Fe, and Mn levels in hair of patients with SD. Zn and Fe levels were found to be high in the hair of the SD group. Cu levels were found to be statistically significantly higher in both serum and hair samples of the SD group. Hair Mn level was also higher in the SD group. Kwiatek et al. [21] evaluated cancerous and intact area of kidney in terms of trace element levels in their study. It has been found that trace element levels are lower in cancerous tissues requiring more blood [21]. In this context it can be said that affected areas in the SD patients are more perfused, and the amount of trace elements in the perifollicular area is relatively increased. It can be said that transmission of Zn, Cu, Fe, and Mn as well as post-transition metal levels are increased. In a study by Üstündağ et al. [22], the levels of selenium (Se) in gastric mucosa and plasma
were evaluated in *Helicobacter pylori* (HP)-infected patients. Se level was found to be significantly higher in gastric tissue. The authors have linked the increased levels of Se in gastric tissue to inflammation resulting from HP [22]. Hair samples in the SD group were taken from hyperemic inflamed area. Similar to the literature, in this study high trace element levels detected in hair samples may be related to perifollicular hyperemia. When we look at the relationship between hair and serum levels of trace elements, hair and serum levels of all of the trace elements did not correlate. In this direction, it can be said that not only hyperemia, but also local inflammatory processes may play a role in elemental passage.

**Conclusion**

The results of our investigation have shown that trace elements can contribute to the pathophysiology of SD. *Malassezia* colonization seen in SD, irritation, and inflammation may affect passage and distribution of trace elements. Detection of trace element levels in lesional and perilesional hair and skin specimens in patients with SD may shed light on the association of trace element distribution with the disease.

**Research limitation**

Hair samples from the patient group were taken only from infiltrating, erythematous, inflammatory plaques. In addition to this process, taking hair samples from non-lesioned areas will contribute to the evaluation of hair trace element levels in the disease.

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**Conflict of interest**

The authors declare that there is no conflict of interest.

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**References**


[13] Sheikh G, Massood Q, Majeeed S, Hassan I. Comparison of levels of serum copper, zinc, albumin,


