Assessment of Heavy Metal and Trace Element Levels in Patients with Telogen Effluvium

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Abstract

Background: Despite a multitude of studies, etiology of primary chronic telogen effluvium (TE) remains incompletely understood. Essential heavy metals are associated with beneficial effects in humans as well as in other living organisms. However, they may lead to toxic effects when the exposure exceeds the higher tolerable limits. We wanted to assess the heavy metal and trace element levels in patients with chronic TE. Materials and Methods: A total of 40 subjects with chronic TE were included in the study, and 30 healthy women served as control. General and dermatological examinations were taken up in all individuals. Those patients with positive hair pull test were evaluated with the help of a trichogram. The presence of >20% telogen hair as documented by trichogram was a requirement for the study inclusion. UNICAM-929 spectrophotometry device was used for determining serum trace element and heavy metal concentrations. Results: In spite of an absence of significant differences in terms of average Zn concentration, weight, or height between patients and controls, significant differences were noted for Cd, Fe, Mg, Mn, Pb, Co, and Cu (P<0.05). Conclusion: Our results suggest that heavy metals may play a causative role in the development of chronic TE. However, contrary to previous reports, zinc did not appear to play an important etiological role, while these patients had elevated serum iron levels.

Key Words: Heavy metals, telogen effluvium, trace elements

What was known?
Telogen effluvium is the most frequent cause of hair loss and is associated with diffuse and nonscarring hair loss. Essential heavy metals are associated with beneficial effects in humans as well as in other living organisms. However, they may lead to toxic effects when the exposure exceeds the higher tolerable limits.

Introduction

Hair is a structure with utmost cosmetic importance that derives from ectoderm. It provides a significant contribution in terms of the maintenance of the self-image as well as healthy and productive social interactions.¹ As compared to men, hair loss has a deeper impact in women on social interactions relative to the alterations in quality of life. Despite these differences, hair loss is a significant source of concern for all individuals regardless of the age and gender.²

Telogen effluvium (TE) is the most frequent cause of hair loss and is associated with diffuse and nonscarring hair loss. In general, it occurs approximately 3 months after the primary insult, affecting <50% of the scalp.¹ Hair loss extending beyond 6 months is considered as chronic TE (CTE) and occurs most commonly in women in their 4th or 5th decade of life. It can be primary or secondary. In the former case, no triggering factors can be identified and the hair pull test is usually strongly positive.³,⁴

Heavy metals are elements that have a density at least five times greater than that of water and that have high atomic numbers.⁵ They are categorized into two groups as essential and nonessential heavy metals. Essential heavy metals are associated with beneficial effects in humans as well as in other living organisms. However, they may lead to toxic effects when the exposure exceeds the higher tolerable limits.⁶ The potential routes of entry of heavy metals into the body include either natural environmental exposure or other means such as mining, soil erosion, industrial waste, air pollution, or pesticides. Although occupational exposure is possible.
in some individuals, diet represents the major source of exposure. Copper (Cu) is a trace element that plays an important role in oxygen transport by red blood cells and in the production of hemoglobin. Its deficiency may be particularly associated with weakening and loss of hair. Zinc (Zn) is a metal with essential roles in cellular division, tissue growth, and tissue repair. In hereditary or acquired Zn deficiency thinning, breaks, and loss of hair may be seen. Cobalt (Co) is an important component of vitamin B12. On the other hand, cadmium (Cd), and lead (Pb) concentrations were determined using a UNICAM-929 spectrophotometer (Unicam Ltd, York Street, Cambridge, UK).

Materials and Methods

A total of 40 patients with CTE attending to the dermatology outpatient unit of Dursun Odabaş Medical Center, Yüzüncü Yıl University were included in the study. The control group included 30 women who presented to the Dermatology department for routine examination of various diseases such as contact dermatitis, tinea pedis, and itching other than any hair problem. The study protocol was approved by the Ethics Committee of Yüzüncü Yıl University for Clinical Research. Age, occupational status, and marital status were recorded, and general and dermatological examinations were performed. Patients with strongly positive pull tests were included in this study. Among those with suspicious positive hair pull test, approximately 60 hair were pulled from the root and assessed using a trichogram. This test was repeated on two sites of the scalp (vertex and occipital areas). Using adhesive bands, the hair samples were placed between the microscopic slides and cover-glass for microscopic examination of the hair shaft and root at ×40 magnification. Patients in whom telogen hair samples comprised more than 20% of the total pulled hair were considered eligible for the study. All patients had a disease history of more than 6 months. Before hair pull test, patients were instructed not to wash or use any treatment on the hair. Complete blood count, fasting blood glucose, liver and kidney function tests, and thyroid hormone levels were determined in all participants. Only those with normal results were included. Patients with conditions such as recent history of abortion, pregnancy, lactation, anemia, hyperandrogenemia, thyroid dysfunction, chronic disorders (diabetes, hypertension, renal disease, and rheumatologic disorders), strict diets, nutritional deficiencies, history of hair dying, use of hair heating, surgery, drug use (chemotherapy, antidepressants, anticonvulsants, hormone intake, anti-gout medicines, anti-hypertensive, use of iron, zinc, or vitamin supplementation, etc.), and with female pattern hair loss were excluded from the study. Blood samples were obtained into empty tubes in both groups, and the sera were separated with centrifugation at 3000 rpm for 10 min. The samples were stored at −80°C in plastic tubes until the time of analysis. Serum Fe, Mg, Mn, Zn, Pb, Co, Cd, and Cu concentrations were determined using a UNICAM-929 spectrophotometer (Unicam Ltd, York Street, Cambridge, UK).

Statistical analyses

Descriptive statistics were expressed as mean and standard deviation for the parameters examined in our study. Pair-wise group comparisons were performed with the t-test for samples with normal distribution, while Mann Whitney U test was used for variables without normal distribution. The level of statistical significance was set at 5% and SPSS statistical software version 19.0 (SPSS Inc, Chicago, III, USA) pack was used for analyses.

Results

Table 1 presents the descriptive statistics and comparisons for Cd, Fe, Mg, Mn, Bp, Zn, Co, Cu, weight, and age. It shows that the differences for Zn, weight, and age were not significant between the groups, while significant differences were noted for Cd, Fe, Mg, Mn, Pb, Co, and Cu between controls and patients (P<0.05).

Discussion

Our results suggest that heavy metals might play a pathological role in the occurrence of CTE. However, contrary to previously held belief, zinc did not appear to be an important etiological factor, and serum iron levels were elevated in this group of patients. Zinc is one of the most extensively studied elements in the etiology of TE. In studies done by Hamad et al., Prasad, and Sinclair, low zinc levels were associated with hair loss. On the other hand, Rushto and Yacoub et al. found normal zinc levels in subjects with TE. Despite the demonstration of low serum zinc levels in multiple studies, others have found normal levels in line with our observations. Thus, zinc replacement that has traditionally been used for the treatment of TE may not be that significant clinically.

Karm et al., Kantor et al., Obaidat et al. observed low serum ferritin levels in patients with TE, proposing that iron deficiency anemia may have an important role in the development of TE. Contrary to previous publications, our patients had elevated iron levels, which may be due to the exclusion of patients with iron deficiency anemia. However, this significant
increase as compared to controls seems to imply that iron supplementation may actually be counterproductive rather than providing benefit.

Cadmium not only inhibits the enzymes responsible for deoxyribonucleic acid repair but also initiates an inflammatory reaction by stimulating the production of free oxygen radicals from polymorphonuclear cells. Cadmium has been classified as a Group 1 human carcinogen by the International Agency for Cancer, with particular association with lung, kidney, and prostate cancers.[6,19] Cigarette smoking represents the most common means of exposure include soil, dyes, gasoline, insecticides, cosmetics, batteries, and lead pipes leading to water contamination.[24] Lead binds to hemoglobin in erythrocytes and is gradually released in soft tissues. Its elimination half-life in the human body is 27 years.[17,18] Lead is involved in redox reactions and leads to free radical formation by being incorporated into electron transport. Although most cases of lead toxicity are multifactorial, the most frequent manifestations of toxicity include the production of free radical species, enzyme inhibition, and prevention of the absorption of important trace elements.[29] As emphasized by Shah et al. lead may play a significant role particularly in the gastrointestinal system. Excessive exposure may lead to delayed puberty, neurological disorders, mental retardation, fainting, and even coma.[29,30] Rossi reported decline in renal functions, hypertension, and peripheral arterial disease even with low blood concentrations of lead.[31] Abdel Aziz et al. suggested that increased blood cadmium levels in the presence of elevated lead concentrations may represent a cause of hair loss and that effective antioxidant therapy may assist in reducing this toxic effect.[42] Studies until now have generally failed to find an association between lead exposure and hair loss. In our study, the patient group had significantly higher Pb levels as compared to controls. This observation suggests that lead may play an etiologic role in the development of chronic TE, even without toxic exposure levels.

Pyo et al. reported that copper plays an essential role in the proliferation and differentiation of dermal papillary cells, which have significant function in the development of the hair follicle.[32] On the other hand, Trüeb proposed that heavy metals including copper may impair the ability of the body to form hair shafts through covalent bond formation with the sulfhydryl groups in keratin.[33] In a study by Dastgheib et al. examining the serum and hair copper levels in 16 patients with alopecia areata and 27 healthy volunteers, no significant differences were found.[34] Ozturk et al. reported reduced serum and
Contrary to previous studies, our patients had no significant differences in serum copper levels among of 312 patients with hair loss and 30 controls, proposing that serum copper levels had no association with hair loss. In contrast with previous studies, our patients had higher serum Cu levels than controls; this may indicate a need to re-assess the role of copper supplementation used for hair loss treatment. Further studies are warranted to better elucidate this issue.

Manganese is an activator for many enzymes such as hydroxylase, transferase, kinase, and decarboxylase, which are mainly located in the mitochondria. Its best-characterized property is the role it plays as a coenzyme, responsible for the incorporation of metals into metalloproteins. It also has an effect on arginase enzyme. In particular, it plays significant role in the mitochondrial function, fatty acid metabolism, and protein synthesis. Furthermore, it is important for the proper functioning of thyroid hormones and adrenal hormones. Manganese toxicity is relatively rare and mostly occurs in workers in iron, copper, and steel industry. Several studies have shown that it may lead to neurological disorders as a result of accumulation in the central nervous system. In particular, hearing loss has been reported. To the best of our knowledge, until now no previous studies have examined the association between chronic TE and serum manganese levels. According to our results, patients with TE had significant elevation in their manganese levels. Further studies need to be undertaken to establish the relation of serum manganese level with chronic TE.

Cobalt compounds have been used as a colorant for centuries in the production of jewelry, glass, and earthenware pots owing to their dark blue color. Cobalt contamination of air, water, and soil generally occurs in industrial areas. Recently, we have witnessed increased cobalt exposure due to increased use of cellular phone batteries, plasma televisions, and liquid crystal displays. Other sources of cobalt exposure include food items such as chocolate, butter, fish, and hazelnuts. Following cobalt exposure cardiovascular system, nervous system, hematological system, respiratory system, and skin are mostly affected. Furthermore, cobalt represents a major cause of occupational contact dermatitis. Furthermore, although it has been previously linked with acne or maculopapular rashes, no studies have examined cobalt levels in patients with TE. Recent advances in technology have resulted in increased levels of cobalt exposure. Significantly higher cobalt levels in our patients as compared to controls suggest that it may be involved in the pathogenesis of chronic TE.

Not only the number of previous studies examining the association between chronic TE and heavy metals but also the number of specific heavy metals measured in this context is low in number. In this regard, a major difference between our study and previous works is the fact that measurements were performed for a wide array of heavy metals, including those that have been measured for the first time in patients with chronic TE in the current study.

However, the small sample size is one major limitation of our study. The main reason for that is the lower prevalence of chronic TE as compared to acute TE. In addition, the initial target to include more male patients could not be met, leading to a predominance of female participants.

**Conclusion**

Despite numerous previous studies reporting on the health effects of heavy metals, the impact of certain heavy metals and trace elements on the hair remain obscure. In this regard, studies have generally attempted to quantify the heavy metal accumulation in the body. Our objective was to investigate the effects of heavy metals in chronic TE, a disorder with unknown etiology that occurs more commonly in females. Further studies are required to better delineate the association between hair loss and trace elements as well as heavy metals.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**What is new?**

- Heavy metals may play a causative role in the occurrence of chronic telogen effluvium (TE)
- Contrary to previously held belief, zinc did not appear to be an important etiological factor of chronic TE.

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