ORIGINAL ARTICLE

Trace Element Levels in Children With Atopic Dermatitis

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Abstract

Background: Trace elements are micronutrients that are present in small amounts in the body and are essential for normal functioning of the immune and antioxidant systems. Inflammation and oxidative stress are major pathogenic mechanisms in the development of atopic dermatitis (AD). The role of micronutrients in AD has been investigated in a limited number of studies, although the results are contradictory.
Objectives: In this study, we examined the levels of iron, copper, and magnesium in serum and the level of zinc in erythrocytes in children with AD. We compared our findings with those of a healthy control group.
Method: The study population comprised 92 AD patients and 70 controls. We performed a complete blood count and measured levels of iron, copper, and magnesium in serum and levels of zinc in erythrocytes.
Results: We found that serum magnesium and erythrocyte zinc levels were lower in children with AD than in the control group; levels of copper and iron did not differ between the groups. The levels of micronutrients studied were not correlated with disease severity.
Conclusion: Evaluation of zinc and magnesium levels in children with AD could prove useful. The role of micronutrients in the pathogenesis and course of AD warrants further study.

Key words: Trace elements. Zinc. Iron. Copper. Magnesium. Atopic dermatitis. SCORAD.

Resumen

Antecedentes: Los elementos traza son micronutrientes presentes en cantidades muy bajas en el organismo que son esenciales para el funcionamiento normal de los sistemas inmune y oxidativo. La inflamación y el estrés oxidativo constituyen mecanismos patogénicos importantes en el desarrollo de la dermatitis atópica.
Se ha investigado previamente sobre el papel de los micronutrientes en la dermatitis atópica pero los resultados obtenidos no son concluyentes.
Objetivos: En este estudio se examinan los niveles de hierro, cobre y magnesio séricos y los niveles de zinc en eritrocitos de niños afectos de dermatitis atópica y se comparan los resultados con los obtenidos en una población control sana.
Métodos: Se incluyeron 92 pacientes con dermatitis atópica y 70 controles. En todos ellos se realizó un hemograma completo y se cuantificaron los niveles de hierro, cobre y magnesio en suero y el de zinc eritrocitario.
Resultados: En nuestros resultados encontramos una disminución en los valores de magnesio sérico y en los niveles de zinc en eritrocitos procedentes de niños con dermatitis atópicas, respecto a los controles. Los niveles de micronutrientes estudiados no se correlacionaban con la gravedad de la enfermedad.
Conclusión: La evaluación del Zn y Mg en los niños con dermatitis atópica puede resultar de utilidad.

Palabras clave: Elementos traza. Zinc. Hierro. Cobre. Magnesio. Dermatitis atópica. SCORAD.

Introduction

Atopic dermatitis (AD) is a common chronic inflammatory skin disease characterized by a relapsing-remitting course that usually manifests during early childhood. The frequency of the disease has increased 2 to 3-fold over the past 3 decades [1,2]. The development and phenotypic expression of AD depend on a complex interaction between genetic and environmental factors [3], inlcuding nutrition [4].

Minerals and essential elements are key to nutrition and good health [5,6]. They play a crucial role in the normal functioning of the immune system and antioxidant mechanisms [7]. Inflammation and oxidative stress are considered the main problems in patients with AD [8]. Findings on the effect of some micronutrients in AD are scarce and contradictory. However, the role of zinc, iron, magnesium, and copper in AD has been investigated [9-13].

The aim of this study was to analyze concentrations of iron, magnesium, and copper in serum and levels of zinc in erythrocytes and evaluate their effect on disease severity in children with AD.

Patients and Methods

The study population comprised children admitted to the Pediatric Allergy Clinic of Ankara Children's Hematology Oncology Education and Research Hospital with a diagnosis of AD confirmed according to consensus conference criteria [14]. Patients with asthma, allergic rhinitis, and acute and chronic diseases other than AD were excluded. Severity was graded using the SCORing Atopic Dermatitis Index (SCORAD) [15]. According to SCORAD, AD was classed as mild (SCORAD <25), moderate (SCORAD 25-50), or severe (SCORAD ≥50). The control group consisted of age-matched and sex-matched healthy children. The local ethics committee approved the study, and all parents gave their informed consent.

Body weight and height were measured using the same instrument, and the weight-to-height ratio was determined. Malnutrition status was evaluated according to standard data for Turkish children. A weight-to-height ratio of between 80% and 90% was considered mild malnutrition, while 90% and higher was considered normal.

Fasting blood samples were taken from patients and controls between 8 AM and 10 AM. A complete blood count was performed, and levels of iron, copper, and magnesium in serum and levels of zinc in erythrocytes were measured. Blood samples were mixed with 5 cc of isotonic saline and centrifuged for 3 minutes at 3000-4000 rpm. This process was repeated 3 times, and measurement was completed with spectrophotometry using the Randox kit (Randox Laboratories). Serum copper and magnesium levels were measured by spectrophotometry using the Randox kit (Randox Laboratories) and Cobas kit (Roche Diagnostics), respectively.

Complete blood counts were performed using a Coulter Max M device (Beckman Coulter). Anemia was assessed using normal hemoglobin levels for age. Serum iron levels were analyzed using the Roche/Hitachi Modular P800 Analytics System (Roche Diagnostics).

SPSS for Windows version 11.5 was used for the statistical evaluation. Continuous variables were given as mean (SD), and differences between groups were evaluated using the *t* test. The χ^2 test or Fisher exact test was used to compare dichotomous variables. The correlation of continuous variables was analyzed using the Spearman test. A 2-tailed *P* value of <.05 was considered statistically significant.

Results

The study population comprised 92 AD patients and 70 controls. Both groups were similar in terms of sex, age, and frequency of malnutrition (Table).

Patients with AD had significantly lower serum magnesium levels and erythrocyte zinc levels (*P*=.007 and *P*<.001, respectively). In the AD group, magnesium levels were lower than normal in 19 patients (20.7%); none of the controls had low magnesium levels. Zinc deficiency affected 94.6% and 55.7% of the AD and control groups, respectively (*P*<.001). Serum concentration of iron and copper did not differ significantly between the groups (*P*=.913 and *P*=.921, respectively). Serum hemoglobin levels were lower in the AD group (*P*=.011); 14 patients (15.2%) in the AD group and 3 patients (4.3%) in the control group had anemia (*P*=.025). Five patients (5.4%) in the AD group and none of control patients had copper levels higher than normal limits. Copper levels were lower than normal in 47 controls (67.1%) and 69 AD patients (76.7%) (*P*=.213). The SCORAD index did not correlate with serum concentrations of magnesium, copper, iron, and hemoglobin, and erythrocyte zinc levels (*P*=.211, *P*=.982, *P*=.957, *P*=.565, and *P*=.357 respectively) or with the frequency of anemia (*P*=.323). No differences were observed between patients with severe AD and patients with mild-to-moderate AD for serum concentrations of magnesium, copper, and iron (*P*=.688,

Table. Serum Trace Element Levels in Patients With and Without Atopic Dermatitis[a]

	Cases (n=92)	Control (n=70)	*P* Value
Age, month	27 (25.8) (median, 19.5)	22.7 (23.6) (median, 13.5)	.259
Male, No. (%)	58 (63.0%)	37 (52.9%)	.192
Frequency of malnutrition, No. (%)	6 (6.5%)	3 (4.3%)	.733
Hemoglobin, g/dL	11.8 (1.0)	12.2 (1.1)	.011
Iron, μg/dL	64.1 (29.8)	64.6 (28.3)	.913
Copper, μg/dL	76.0 (27.3)	76.3 (14.1)	.921
Magnesium, mg/dL	2.1 (0.4)	2.3 (0.4)	.007
Zinc, μg/dL	823.9 (120.9)	1040.9 (199.7)	<.001

[a] Values are expressed as mean (SD) unless otherwise indicated.

P=.783, and *P*=.295), erythrocyte zinc levels (*P*=.461), or the frequency of anemia (*P*=1.00).

Discussion

Interest in the effect of nutrition on AD and in the role of micronutrients in particular has grown in recent years; however, results are conflicting [9-13]. In this study, we showed that serum iron and copper levels did not vary, but that serum magnesium and erythrocyte zinc levels were lower in AD patients than in healthy controls.

Zinc is an essential micronutrient for the proper functioning of the more than 100 enzymes involved in human metabolism that facilitate protein folding and help regulate gene expression [16]. It plays a central role in modulating the immune system, is essential for cellular function in the immune response, and acts as an antioxidant [17]. Because of its immunomodulatory effects, zinc is increasingly studied in inflammatory diseases such as AD [18]. Animal models show that mice fed with a zinc-deficient diet developed AD-like skin lesions [19,20]. A limited number of reports compare levels of zinc in patients with AD to those of healthy individuals, and the results are contradictory: some authors reported lower levels [9,10], whereas others found no differences [11,12]. Di Toro et al [13] found no differences in serum levels, although zinc levels in hair were lower in patients with AD.

To our knowledge, the present study is the first to evaluate erythrocyte zinc levels in children with AD. Intracellular zinc levels have been reported to be a better measure of mild zinc deficiency [21], and this could be the cause of the high frequency of zinc deficiency detected in our study.

Copper is an essential trace element in the antioxidant system and protein and DNA synthesis and is necessary for an efficient immune response [22]. Even a minimal deficiency results in changes in immune status [23]. The role of copper in inflammatory diseases is complex. Although the level of copper is increased as an acute phase reactant during inflammation [24], copper itself is used in the treatment of some inflammatory diseases [25]. Studies of copper levels in adults and children with AD revealed higher levels in patients than in controls, although they did not report any association with disease severity [10-12]. The authors reported that high copper levels could be the result of increased ceruloplasmin levels during inflammation of the skin. In contrast, we found that copper levels did not differ between patients and controls. Di Toro et al [13] found no differences in serum copper levels between AD patients and controls, although they did report higher copper levels in hair among AD patients. The discrepancy between our findings and the medical literature may be the result of differences in nutritional habits, age, and study methodology.

Magnesium is an essential mineral that has a key role in the immune response. It is a cofactor for immunoglobulin synthesis, immune cell adherence, antibody dependent cytolysis, macrophage response to lymphokines, and T-cell–B-cell adhesion [26]. Animal models revealed that mice fed with a magnesium-deficient diet had increased levels of proinflammatory cytokines [27] and developed skin lesions with a pattern similar to those of AD [14]. Ertunç et al [11] studied serum magnesium levels in children and adults with AD, although they found no differences between patients and controls. In contrast, serum magnesium levels in our patients were lower than in the control group, and magnesium deficiency was more frequent in the patient group. The presence of adult patients in the study by Ertunç et al may account for the differences in the results: in early childhood, nutrition is considered to have a major effect, whereas other environmental factors become more important thereafter. The role of magnesium in the development and course of AD requires further study.

Iron has an important role in immune function. In iron deficiency, the bactericidal activity of macrophages and myeloperoxidase activity of neutrophils are reduced; T lymphocyte numbers and mitogenesis are decreased [22]. Studies on the iron status of patients with AD have shown lower serum iron levels [16] and lower ferritin but similar iron levels [17]. In our study, although serum iron levels were lower in patients than in controls, the difference was not significant. Ferritin was not studied, but hemoglobin levels were significantly lower and the frequency of anemia was higher in patients. The higher frequency of anemia detected among AD patients could be related to zinc and copper deficiency, although the frequency of anemia did not differ between groups who had low or normal zinc and copper levels. All patients with anemia had low iron levels.

To our knowledge, no previous studies have established a relationship between the SCORAD index and levels of zinc, copper, magnesium, and iron. Accordingly, we did not find a relationship between the severity of AD and levels of micronutrients. A recent study reported that the copper-to-zinc ratio was correlated with the SCORAD index [28]. We detected no such correlation, although zinc level was not measured in serum, and this may account for the difference.

One possible reason for a deficiency in trace elements is malnutrition. Our study was limited by the fact that dietary habits were not evaluated. However, the frequency of malnutrition did not differ between our study groups. Therefore, we did not associate the deficiency of zinc and magnesium with malnutrition.

Erikson and Kare [29] found that AD patients given zinc supplements, vitamin E, and ω-3 and ω-6 fatty acids had a decreased SCORAD index within 16 weeks. On the contrary, in a double-blind, placebo-controlled trial, Ewing et al [30] found no improvement in disease severity with oral zinc supplementation. Mean patient age in this study was considerably higher than that of our patients, and nutrition may have had a relatively less marked effect in older patients. Patients in this study were not examined for zinc status before receiving supplements, and to our knowledge, no studies report on the effects of giving zinc to AD patients with zinc deficiency. Administration of magnesium supplements in AD patients has not been studied, although magnesium supplements given to atopic asthmatic children had an antioxidant effect [31]. Because zinc and magnesium deficiency was frequent among AD patients, evaluation of zinc and magnesium levels could prove useful in this group, and dietary supplements should be provided in cases of deficiency. The effect of this supplementation on disease severity remains to be determined.

In the absence of nutritional differences, we found that zinc and magnesium deficiency were more common among children with AD. Therefore, it could be useful to evaluate zinc and magnesium levels in children with AD. The role of these micronutrients in the development and process of AD requires further study.

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