

TRACE ELEMENTS STATUS IN CHILDREN WITH BRONCHIAL ASTHMA

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Zinc, copper and magnesium are important elements in the preservation of immune resistance. Zinc and copper are both required for numerous biochemical functions and for optimal activity of the immune system. They are also involved in cell and tissue growth. We aimed to define the relation between bronchial asthma and serum levels of these three trace elements. Zinc levels were significantly decreased in comparison to the control values ($p < 0.01$). On the other hand, Copper and ceruloplasmin levels were significantly higher in comparison to the control values ($p < 0.01$). Our study showed relatively low blood levels of zinc in subject with asthma. Chronic inflammation causes a characteristic decline in serum zinc levels in experimental studies. It is well known that zinc deficiency affects the regulation of T-cell lymphocytes, which may play some part in the development of allergies. These findings suggest a different zinc and copper nutritional status between asthmatic and healthy subjects. Asthmatic children, in particular, seem to be at a risk of zinc deficiency. The changes in trace element status may be the effect of chronic disease state and do not associate with the cause of disease.

Key words: Trace elements, bronchial asthma, ceruloplasmin

INTRODUCTION

Bronchial asthma is a chronic inflammatory disease of the respiratory tract. Different genetic and environmental factors are involved in the pathogenesis of asthma (1). The rise in asthma and allergic disease among children is a matter of worldwide concern (2,3). Many authors have argued that the changes in diet may have been an important determinant of increased susceptibility to asthma (4,5). We believe that a reduction in antioxidant intake, reflected in the diet of pregnant women, would increase the susceptibility of the newborn baby to allergens (4).

Our particular interest was to test the hypothesis that a low trace element levels is a risk factor for asthmatic symptoms in childhood. In this study, we aimed to define the relation between bronchial asthma and serum levels of trace elements (zinc, copper and magnesium) and ceruloplasmin.

MATERIAL AND METHOD

The study group consisted of 41 asthmatic children who were followed at Zonguldak Karaelmas University Faculty of Medicine Departments of Pediatrics and Pulmonology and 30 control group children who attend the pediatric outpatient clinics by the complaints of nonspecific non-chronic disorder(s) (acute upper respiratory system infection, urinary tract infection e.t.c.).

The control group consisted of non-allergic volunteers with normal IgE plasma levels without any particular health problems. They had never had any episode of breathlessness and/or wheezing and had never used asthma medication. The children are from middle-income socioeconomic status families.

A total 41 stable allergic or non-allergic asthma patients were selected for this study according to criteria of the American Thoracic Society Statement (6). The diagnosis of bronchial asthma depends on the special history, family history and physical examination and laboratory results. Mean duration of asthma was 22.4 ± 8.1 months.

RAST tests were performed to all bronchial asthma patients to detect the atopy with the allergens, which were met frequently in their daily lives.

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Table 1. Demographic characteristics of patients and control group.

	Cases	Control	p value
Mean (SD) age in years	7.6±1.8	7.6±1.8	p>0.05
Number (%) female	22 (56.0%)	17 (56.6%)	p>0.05
BMI mean (SD) kg/m ²	16.0±6.2	17.5±4.3	p>0.05
Weight mean (SD) kg	23.4±9.8	28.2±8.4	p>0.05

Table 2. Levels of copper, zinc, ceruloplasmin and magnesium in asthmatic and control

	Cases	Control	p value
Copper mean (SD) µg/dl	143±20.8	130±22.7	p<0.01
Zinc mean (SD) µg/dl	70.6±8.3	78.3±9.2	p<0.01
Ceruloplasmin mean (SD) mg/dl	0.32±0.01	0.28±0.01	p<0.01
Magnesium mean (SD) mg/dl	2.17±0.10	2.23±0.15	p<0.01

Chest x-ray, Water's x-ray, complete blood count and eosinophil count were performed for all patients. Cromalin or nedocromil sodium for prophylaxis was given to all patients who had the diagnosis of bronchial asthma. None of the patients and control groups in the study used inhaled steroid or systemic steroids and acetyl salicylic acid for the last 2 weeks or other nonsteroidal antiinflammatory drugs. Bronchial asthma patients were allowed to take beta-2 agonist drugs when needed.

Blood samples were taken at least 12 hours after the last dose of beta-2 agonists. All of the patients who were followed up had stable asthma. Serum of peripheral venous blood samples was determined from the patients and control group and samples were preserved at -70 °C.

The zinc and copper concentrations in serum were measured by means of an Atomic Absorption Spectrometer (Varian spectr AA 250 Plus, Australia), with a deuterium background correction. The zinc and copper concentrations in the samples diluted 1:5 with ultra deionised water and values were expressed in µg/dl. Each measurement was performed twice and averages were taken (7). Magnesium and ceruloplasmin levels were measured using colorimetric and immunoturbidimetric methods by Cobas Integra 800 analyser (Roche Diagnostic). Assays were conducted blind to clinical information.

Statistical analysis

All results were given as the mean ± standard deviation value and data analysis were performed by SPSS 9.0 statistical programme. The data were coded into a database and analyzed by SPSS.

Differences between cases and controls were tested by *t* test and χ^2 test as relevant and p<0.05 value was accepted as statistically significant. Linear correlation coefficients for element concentrations were calculated with respect to their mutual relations in sera.

RESULTS

The main analyses were restricted to 71 children. (41 patient cases, 30 control). Table-1 shows the distribution of demographic data of cases and controls. Demographic characteristics were similar in patients with asthma and control subjects.

There were statistical differences in serum zinc, copper and ceruloplasmin levels between control and cases. Magnesium levels were not statistically different (Table 2). The prevalence of atopy in asthmatic group defined according to the results of the RAST test was 75%. In the intra-correlation any statistical difference was not found between serum copper and zinc levels in asthmatic patient ($r=0.202$, $p>0.05$)

DISCUSSION

The results of this study confirm previous observations that there is low serum zinc level in asthmatic children. Also when the copper and ceruloplasmin levels were higher than control group, magnesium level was similar. Our results are in agreement with the data found in the literature (8,9).

It is clear that profound variations in copper and zinc status occur during the course of acute and chronic inflammation. Zinc and magnesium are important elements in the preservation of immune resistance and both zinc and copper are required for numerous biochemical functions and for optimal

activity of the immune system. Zinc plays an important role in DNA and protein synthesis and is intimately involved with copper as cofactors in several important enzyme systems (10,11). Significant higher levels of serum ceruloplasmin were observed in the asthmatic children compared to the controls and were correlated with the hypercupremia.

Zinc and copper are involved in cell and tissue growth. Changes in patterns of dietary consumption, associated with development of a more affluent lifestyle, may have contributed to the rise in asthma over the past few decades (4,12). Plausible mechanisms have been proposed for the influence of dietary factors such as sodium, magnesium, antioxidants, selenium and fats on respiratory symptoms and lung function (13).

Ceruloplasmin significantly increased IL-8 secretion and activation of NF-kappa B. These findings suggest that copper ions may cause some of the biologic effects of inhaled particulate air pollution (14). Proinflammatory interleukins IL-1 induce synthesis of ceruloplasmin and are considered to be responsible for copper release in to plasma (15,16).

There is now some epidemiological support for dietary antioxidant vitamins being risk factors for asthma in adults (17,18). There are some defense mechanisms to escape from the effects of oxidant radicals. These defense systems prevent the production of free radicals, decrease their activities or destroy them. The most important antioxidant endogen systems are mitochondrial cytochrome oxidize, superoxide dismutase (SOD), catalase and glutathione peroxidase (GSH-Px) systems.

Also albumin, ceruloplasmin, ferritin and hemoglobin which are found in the extra cellular space have antioxidant properties (19). Glutathione peroxidase has selenium and Cu/Zn, and superoxide dismutase system has copper and zinc in their structure which diminishes the harmful effects of free oxygen radicals. Decreasing these trace elements causes the effects of antioxidant systems to be lower and this leads to hyperactivity and inflammation in the respiratory tract (20,21).

Our study was showed relatively low blood levels of zinc in subject with asthma. Chronic inflammation causes a characteristic decline in serum zinc levels in experimental studies (22). It is well known that zinc deficiency affects the regulation of T-cell lymphocytes, which may play some part in the development of allergies (23). T cell derived inflammatory mediator IL-2 is also involved in the cellular control of copper levels (24).

On the other hand copper levels were higher than normal subjects. In another study, serum copper has been found to be elevated while serum zinc levels were found to be low (25). It is debatable whether an increase in the copper level has an impact upon SOD absorption; however, it is clear that a decrease in this element impairs the enzyme activity. Such a condition may cause oxidative stress or may further increase the existing stress.

An additional hypothetical explanation of a rise in susceptibility to asthma is that the change from Th2 to Th1 phenotype now occurs less frequently since, in wealthier societies, children no longer suffer the infections that used to promote this change (26,27). There is epidemiological support for this hypothesis with respect to atrophy but little so far with respect to asthma (28).

Increased dietary magnesium has been shown to be associated with an independent beneficial effect on lung function, airway responsiveness, and wheezing in the United Kingdom population (29). Another study has shown that a low intake of magnesium, which is involved in the relaxation of smooth muscle, is associated with reduced lung function, bronchial hyper-reactivity and self reported wheezing (30).

On the other hand, epidemiologic studies showed that diet should be considered in the potential effect of both the severity of the disease and its treatment on the clinical picture of asthma cases. Diminution or change of dietary intake in asthmatic patients can be followed by a low intake of micronutrients. Therefore in order to evaluate the role of dietary factors in asthma, it is necessary to perform studies on patients with diagnosis of asthma.

Although a number of studies have examined the possible role of dietary micronutrients and antioxidants in asthma, little data is present about the influence of either the severity of the disease or its treatment on intake and on the plasma levels of these micronutrients. However, Picado et al. did not mention any zinc deficiency in asthmatics with respect to non asthmatics. These data suggest that study on the association between micronutrient and asthma is necessary to support the information (31).

Our study showed that a risk of development of zinc deficiency in asthmatic children. This knowledge emphasizes the need of more accurate assessment of the intake of trace elements in asthmatic children. Additionally our results are not specific and reflect the inflammatory state in general.

The changes in trace element status may be the effect of chronic disease state and do not associate with the cause of disease. Further studies on the relations between the allergic diseases and trace elements are needed to understand the details of these conditions.

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