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ORIGINAL ARTICLE

The relationship between nutritional status, vitamin A and zinc levels and oxidative stress in patients with ataxia-telangiectasia

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Abstract
Background: Ataxia-telangiectasia (A-T) is a rare and degenerative disease that leads to varying degrees of immunodeficiency, oxidative stress, and malnutrition. Vitamin A and zinc are essential for immune function and antioxidant defence.
Objective: To compare levels of retinol, beta carotene, and zinc in patients with ataxia-telangiectasia and healthy controls.
Methods: We performed a cross-sectional study with 14 AT patients and 14 healthy controls matched for age and gender. All participants underwent a nutritional and laboratory evaluation comprising concentrations of retinol, beta carotene, serum and erythrocyte zinc, malondialdehyde (MDA), T lymphocyte numbers ($CD4^+$ and $CD8^+$) and immunoglobulin (IgA).
Results: The AT patients showed high rates of malnutrition with reduced lean body mass when compared to the control group. However, the concentrations of MDA, retinol, beta carotene, and serum and erythrocyte zinc in AT patients were similar to those of the control group. The retinol levels presented a negative correlation with MDA and positive correlation with IgA serum level.
Conclusions: The AT patients assessed showed no change in nutritional status for vitamin A and zinc; however, they presented severe impairment in overall nutritional status observed and correlation between retinol with MDA and IgA.
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Introduction

Ataxia-telangiectasia (AT) is a rare degenerative disease that affects approximately 1 in 40,000 liveborn infants.[1] This disease has an autosomal recessive inheritance and progresses with neurodegeneration, immunodeficiency, sinopulmonary infections, telangiectasia, predisposition for

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malignancy, radiosensitivity, premature aging and over 50% of the patients suffer from malnutrition.[2,3]

The gene which is defective in this disease, *ATM* (ataxia-telangiectasia-mutated), codes for a protein kinase that participates in multiple signal-transduction pathways. The ATM-deficiency induces oxidative stress, which is potentiated by the constant presence of infections and leads to cell death by apoptosis.[4]

Oxidative stress results in a reduction in the plasma antioxidant defence and reduced plasma concentrations of vitamins A and E, which leads to an increase in the level of lipid peroxidation biomarkers and oxidative damage to the DNA of leucocytes.[5,6]

Some micronutrients such as vitamin A and zinc are essential for the maintenance of immune function and antioxidant defence. Zinc is essential for the development and function of neutrophils, macrophages, and natural killer cells. Thus, zinc deficiency leads to the reduction of thymulin, interleukin-2, and interferon-gamma, increases production of pro-inflammatory cytokines and is associated with a higher incidence of infections.[7,8] Zinc also participates in antioxidant defence by inhibiting NADPH oxidase, acting as a structural and catalytic component of the enzyme superoxide dismutase and inducing the synthesis of metallothionein.[7]

Vitamin A, particularly in its retinoic acid form, plays a number of roles in adaptive immunity, which include the activation and proliferation of T cells, production of interleukin 2, inhibition of B cell apoptosis, modulation of antigen presentation, regulation of the Th1−Th2 balance, differentiation of regulatory T cells and the production of immunoglobulin A (IgA). Vitamin A deficiency is associated with a decrease in the intestinal immune response and an increased risk for the development of gastrointestinal and respiratory infections.[9]

The few studies that have assessed the nutritional status of patients with AT have reported that this disease is correlated with changes in the body mass index (BMI)[10] and in the serum concentrations of retinol.[5]

The aims of the present study are to evaluate the nutritional status, to measure the concentrations of retinol, beta carotene, serum and erythrocyte zinc in the plasma of AT patients, and also to investigate the relationship between these micronutrients with malondialdehyde levels, the number of T lymphocytes ($CD4^+$ and $CD8^+$), and the serum and secretory IgA levels.

Patients and methods

The present study is a controlled cross-sectional study involving 14 AT patients, aged 3−20 years, who were diagnosed with AT according to the diagnostic criteria by the European Society for Immunodeficiencies (ESID). Nine of them (64.2%) were receiving regular infusions of intravenous immunoglobulin, and eight (57.1%) were regularly taking antibiotics. None of the patients had acute infections at the time of sample collection.

The control group consisted of 14 age- and sex-matched healthy individuals.

A questionnaire was used to assess each patient's demographic, socioeconomic, and clinical issues and the study was approved by the Research Ethics Committee.

Anthropometric evaluation and food consumption

The anthropometric evaluation included the measurement of weight, height, and skinfold thickness (tricipital and subscapular), which were measured according to the World Health Organization (1995).[11]

The patients who were unable to stand upright were weighed in their parent's arms and their recumbent height was measured on a firm, flat surface using an inextensible tape that was graduated in millimeters.

Body mass index (BMI) and height to age ratio (H/A) were expressed as Z scores. The values recommended by the World Health Organization were used as reference.[12]

The body composition was estimated using the equation based on the sum of the tricipital and subscapular skinfolds.[13] The classification of the percentage of fat body was performed according to Deurenberg et al.[14] The fat body mass and lean body mass were also calculated in kilograms (kg).

The stage of pubertal development was assessed based on the criteria proposed by Marshall and Tanner.[15]

The assessment of food consumption was performed using a 24-h dietary recall,[16] which was requested on two separate occasions with an interval of 30 days between recalls.

The calculation of the nutrients in the diet of a patient was performed with the help of the *Diet Win* program.[17] The total energy consumption, the intake of proteins per kg of body weight, and the levels of retinol, beta carotene, and zinc were assessed and compared between the patients and the controls.

Biochemical assessment

After an 8-h fast, 20 mL of blood was collected in a dimly lit room and the levels of retinol, beta carotene, serum and erythrocyte zinc, malondialdehyde (MDA), serum IgA, and $CD4^+$ and $CD8^+$ T lymphocytes were determined. Saliva samples, which were obtained in the absence of stimulation, were collected to determine the levels of secretory IgA.

- The retinol and beta carotene levels were determined by high-performance liquid chromatography (HPLC).[18,19]
- The serum and erythrocyte zinc levels were measured using atomic absorption spectrophotometry (''Perkin Elmer'' model 5.100).[20]
- The malondialdehyde level was assessed by spectrophotometry[21] using reference values of 1.0−3.5 nmol MDA/mL.

The statistical analyses were performed using the Minitab® (version 15.1) and Bioestat® (version 5.0) programs. Student's *t*-test and the Mann−Whitney test were used to assess the difference between the quantitative variables. The Chi-squared and Fisher's exact tests were used to determine the association between the qualitative variables. The Pearson's correlation coefficient and Spearman's correlation coefficient were used to determine the

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