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Original article

Magnesium, zinc, and chromium levels in children, adolescents, and young adults with type 1 diabetes

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SUMMARY

Background & aims: Several trace elements are involved in insulin signal transduction and glucose metabolism. Our aim for this present study was to determine the levels of three important elements—magnesium, chromium, and zinc—as well as one oxidative stress marker—malondialdehyde (MDA)—in young type 1 diabetic patients at different periods of their growth, and to realize the relationships between trace elements, oxidative stress, and growth stages.

Methods: A total of 88 patients with type 1 diabetes mellitus in different growth stages and 76 gender- and age-matched healthy subjects were included in this study. The levels of MDA were measured through HPLC using a C-18 column. Zinc, magnesium, and chromium concentrations in serum were assessed using atomic absorption spectrophotometry.

Results: We found higher levels of blood malondialdehyde (MDA; $p < 0.001$), significantly lower levels of magnesium ($p < 0.001$), and no differences in zinc and chromium levels ($p = 0.153$ and 0.515, respectively) in younger type 1 diabetic subjects relative to those of control subjects. Only 3.4% (3/88) of younger diabetic subjects exhibited hypomagnesemia; similar results were obtained when comparing different subgroups: children, adolescents, and adults. We also observed no differences in the levels of the three elements between the genders and among the growth stages ($p > 0.05$) of the diabetic subjects. There were no correlations between the three trace elements and HbA_{1C}, diabetes duration, and insulin dose/BMI (all $p > 0.05$), but there was a significant difference between zinc levels and insulin dose/BMI ($p = 0.043$) in the diabetic patients.

Conclusions: We found elevated blood MDA, decreased magnesium, and no changes in zinc and chromium levels in younger type 1 diabetic subjects relative to those of control subjects. Only 3.4% of younger diabetic subjects exhibited hypomagnesemia. Whether magnesium supplementation is suitable for improving insulin sensitivity and decreasing oxidative stress and inflammation will require confirmation through additional studies.

1. Introduction

Type 1 diabetes is a disorder involving autoimmune destruction of pancreatic beta cells. It can accelerate polyol and hexosamine pathways and protein C activation, increase the production of reactive oxygen species, and advanced glycation end products [1]. It is common for type 1 diabetic patients to display insulin resistance and even abnormal glucose metabolism during puberty, as well as increased oxidative stress, all of which are important risk factors for

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the development of microvascular and neuropathic complications [2,3].

Several trace elements are involved in insulin signal transduction and glucose metabolism. Zinc is essential for insulin processing, storage, secretion, and action. The expression of zinc transporter 8 (Znt8) can affect beta cell physiology [4]. Zinc is an important factor of many antioxidant enzymes and also helps minimize the effects of inflammatory substances, thereby preserving cell health and insulin sensitivity [5]. Zinc deficiency can lead to greater chronic inflammation and oxidative stress. These biological functions of zinc are all associated with glucose metabolism and diabetic complications in type 1 diabetic subjects.

Magnesium plays a central role as a cofactor in many enzymatic reactions involved in energy production. It is essential for both the manufacture and action of insulin, and can inhibit insulin secretion and activate insulin receptor tyrosine kinase activity [6]. Hypomagnesemia is associated with increased intracellular calcium levels, which may lead to insulin resistance [7].

Chromium is an essential nutrient involved in the metabolism of glucose. The trivalent chromium ion is a critical component of glucose tolerance factor, which has prevented diabetes and lowered plasma glucose levels in experimental animals [8]. Recent studies have suggested that chromium functions as part of a low-molecular-weight-chromium-binding substance (LMWCr), which participates in the insulin signal activation by binding to insulin-activated insulin receptors, resulting in stimulation of tyrosine kinase activity, and, thereby, allowing muscle and adipose cells to uptake more glucose and convert it into triglycerides [9]. Importantly, LMWCr without bound chromium is ineffective for such signal activation [10].

Few investigations have been made into the levels of these three diabetes-related trace elements in young subjects at different growth stages. Our aim herein was to determine the levels of three important elements—magnesium, chromium, and zinc—as well as one oxidative stress marker—malondialdehyde (MDA)—in young type 1 diabetic patients at different periods of their growth, and to realize the relationships between trace elements, oxidative stress, and growth stages.

2. Methods

2.1. Study subjects

A total of 88 patients with type 1 diabetes mellitus (45 males, 43 females; average age: 16.5 years) and 76 gender- and age-matched healthy subjects were included in this study. Among the patients, 23 were children (<12 years old), 38 were adolescents (13–19 years old), and 27 were young adults (>19 years old). All of these patients were tested in the Department of Pediatrics of Kaohsiung Medical University Hospital. The control groups comprised subjects who had visited Kaohsiung Medical University Hospital for routine medical checks. All control subjects were checked by doctors to insure no symptoms of other systemic diseases and no habits of cigarette smoking or alcohol consumption. Subjects with WBC levels higher than the age-specific upper limit of the WBC reference range were excluded from this study. The Institutional Review Board of Kaohsiung Medical University Hospital approved the study protocol (IRB no: KMUH-IRB-970326).

2.2. Sample preparation

Blood samples were obtained in the morning after an overnight fast. The serum samples obtained after suitable centrifugation and were stored at −70 °C until required for analysis of zinc, magnesium, chromium, and MDA (within 3 months). A part of each whole blood sample was used to determine the HbA_{1C} value through an NGSP-approved method based on high-performance liquid chromatography (HPLC).

2.3. Measurement of zinc, magnesium, and chromium

The zinc and magnesium concentrations in serum were assessed using a 5100 PC atomic absorption spectrophotometer (PerkinElmer, Norwalk, CT, USA), after suitable dilution with 0.2% HNO_3. The levels of chromium were assayed using graphite-furnace atomic absorption spectrophotometry, after digestion with HNO_3 for two days. Each sample was analyzed in duplicate. Quality control was performed strictly using standard reference materials (Seronorm™ Trace Elements Serum; Nycomed AS, Norway).

2.4. Measurement of MDA

Levels of MDA were measured through HPLC using a C-18 column (JASCO Model 980-PU, Tokyo, Japan). The samples containing MDA were hydrolyzed by boiling in diluted phosphoric acid; MDA was then reacted with thiobarbituric acid reactive substance (TBARS) to form MDA–TBA adducts. The mobile phase was a methanol and potassium phosphate buffer (9:11); the flow rate was 1.2 mL/min. A UV detector was used to detect the adducts at a wavelength of 532 nm.

2.5. Statistical analysis

Data are expressed herein as means ± SD Student's *t* and ANOVA tests were used to compare the differences in the continuous variables between type 1 diabetes patients and control groups; the Chi-square test was used for categorical variables. The relationship between two continuous variables was evaluated using linear regression. Pearson's correlation coefficient (r) was applied to qualify the strength of the relationship. Statistical significance was implied by a value of p of less than 0.05. All statistical analyses were performed using SPSS 18.0 software (SPSS, Chicago, IL, USA).

3. Results

The intra-day precision was tested with seven repeats of three samples of different concentrations. The average relative standard deviations (RSDs) were 1.1, 0.6, 1.9, and 1.0% for zinc, magnesium, chromium, and MDA, respectively. The inter-day precision was determined by analyzing the three samples three times every day, for five consecutive days. The average RSDs were 4.1, 0.6, 1.5, and 2.4% for zinc, magnesium, chromium, and MDA, respectively. The recoveries of all of the elements were in the range of 98–101% of certified values. Table 1 compares the levels of blood MDA, magnesium, zinc, and chromium in the 88 type 1 diabetic patients and in the 76 gender- and age-matched healthy subjects. The levels of MDA were significantly higher ($p < 0.001$) and the levels of magnesium significantly lower ($p < 0.001$) in the diabetic patients than those in the healthy subjects. Diabetic patients did not have significant differences in blood zinc and chromium levels ($p = 0.153$ and 0.515, respectively) when compared with the controls. Only three of 88 diabetic subjects (3.4%) exhibited hypomagnesemia (Table 1), with similar results observed when comparing different subgroups: children, adolescents, and young adults (Tables 2–4). In addition, there were no significant differences in any of these parameters between genders in the diabetic subjects (Table 5). When we determined these parameters at different stages of growth, we did not observe any significant differences in the levels of MDA or these trace elements. The average contents of HbA_{1c} in these patients were at suboptimal

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