

Serum copper and zinc levels significance in type 2 diabetic patients

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Abstract

Alterations in plasma concentrations of several trace elements have been reported to occur in type 2 diabetes mellitus. These micronutrients are suspected to have a role in pathogenesis and progression of the disease. In a comparative analysis, the plasma concentration of copper and zinc was estimated in 50 patients with type 2 diabetes mellitus and 50 healthy non-diabetic subjects. Trace elements were estimated by using atomic absorption spectrophotometer. When compared to controls, cases (type 2 diabetic patients) showed significantly higher copper and lower zinc levels ($P < 0.0001$). Serum copper levels are significantly higher in type 2 diabetes mellitus patients, while serum zinc levels are significantly decreased when compared to controls.

Keywords: Type-1 diabetes mellitus, copper, zinc, magnesium.

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Introduction

Many trace elements are important for optimum human metabolic function. These micronutrients serve a variety of functions including catalytic, structural and regulatory activities in which, they interact with macromolecules such as enzymes, pro-hormones, presecretory granules and biological membranes. There is accumulating evidence that the metabolism of several trace elements are altered in type 2 diabetes mellitus and that these nutrients might

have specific roles in the pathogenesis and progression of this disease [1].

Diabetes mellitus is a disorder of carbohydrate metabolism, leading to both metabolic and oxidative stress. Type 2 diabetes is due to insulin resistance and/or insulin secretory defects, and accounts for almost 90% of all diabetic cases [2, 3]. Direct associations of trace and macro elements with diabetes have been observed in many research studies. The proposed mechanism of trace elements enhancing insulin action includes activation of insulin receptor sites and serving as co-factors or components for enzyme systems involved in glucose metabolism.

Zinc serves as an essential co-factor for more than 200 enzymes, many of which regulate the metabolism of carbohydrates, lipids, and proteins [4, 5]. Insulin itself is believed to be stored in an inactive form of zinc crystals. Zinc ions in the secretory granules of cells are known to glue insulin β molecules, creating somatically stable hexamers [6]. When the secretory granules open to the surface, the zinc ions pressure decreases rapidly and pH levels change from acid to physiological levels, which

results in free insulin monomers and zinc ions will be released from the pancreas. Thus zinc is required for insulin synthesis and storage [6 -8]. There is accumulating evidence that the metabolism of zinc is altered in type 2 diabetes and that zinc might have specific roles in the pathogenesis and progress of this disease. Copper is the third most abundant essential trace element in the body. Copper is present in the body combined with enzymes to form metalloenzymes such as caeruloplasmin and superoxide dismutase (SOD) [7, 9]. These enzymes play major roles in redox reactions, and antioxidant defence. It has been postulated that copper possesses insulin-like activity and promotes lipogenesis [6-9]. Human studies demonstrate that diabetic patients may have abnormal levels of serum copper [10 -12]. The objective of this study was to determine the serum levels of zinc and copper in type 2 diabetic patients in our locality.

Materials and methods

Subjects: About One hundred people were recruited into this cross-sectional case control study over a 6-month period. Out of 100 study subjects, 50 are known type 2 diabetic patients and another 50 are healthy controls of the same age group. Subjects were selected by a non-probability convenient sampling method. All the subjects enrolled for the study, after explaining the purpose of the study and obtained informed written consent. These patients were of both genders between the ages of 38 and 58 years. Fifty (50) age- and sex-matched non-diabetic control subjects were selected among the hospital staff and blood donors. Exclusion criteria for both groups included in this study were: obesity, pregnancy, renal disease, hypertension, and finally those taking nutritional supplements, laxatives, diuretics, or alcohol.

After an overnight fast, blood samples were collected, at a standardized time to minimize any effect of diurnal variation, via venepuncture aseptically into fluoride oxalate tubes for fasting glucose (FBS), and plain tubes for serum copper and zinc determination. Fasting glucose was estimated using the glucose-oxidase method, while serum zinc and copper were analysed by graphite furnace atomic absorption spectrometry (Schimadzu, Japan)

Statistical analysis: The SPSS 16.0 statistical package was used for data processing. Results obtained were summarized as mean (\pm standard

deviation). Differences between the groups were compared using paired Student t-test, and the level of significance was set at $p < 0.05$.

Results

Out of 50 diabetic patients selected, 36 (72%) were males (mean age of 44 ± 7 years) and 14 (28%) were female (mean age of 42 ± 10 years). Fifty (50) age- and sex-matched healthy controls included 38 males (76%) with a mean age of 45 ± 6 years, and 12 (24%) females with a mean age of 44 ± 3 years. The mean FBS was 91 ± 8 mg/dl in controls and 136 ± 20 mg/dl in the diabetic patients ($p < 0.0001$). Mean serum zinc was significantly lower in diabetic patients compared with healthy subjects (94.6 ± 21.8 vs 143.3 ± 29.5 μ g/dl, $p < 0.0001$), while serum copper levels were significantly higher compared with health subjects (98.5 ± 32.4 vs 172.5 ± 38.2 μ g/dl, $p < 0.0001$). These results are summarized in Table 1.

Table 1: Comparison of serum levels of copper, zinc in controls and cases

| Parameter | Controls (n = 50) | Cases (n = 50) |
|--------------------|----------------------|--------------------|
| Age(in years) | 48 ± 9.4 | 49 ± 8.5 |
| Gender | | |
| Male | 36 (72%) | 38 (76%) |
| Female | 14 (28 %) | 12 (24 %) |
| FBS (mg/dl) | 91 ± 8 | $136 \pm 20^*$ |
| Copper | 98.5 ± 32.4 | $172.5 \pm 38.2^*$ |
| Zinc | 143.3 ± 29.5 | $94.6 \pm 21.8^*$ |

* $p < 0.0001$ is highly significant

Discussion

Diabetes pathogenesis is considered multifactorial, and the physiological role of copper and zinc has been implicated in the development and progress of the disease [6, 13, 14]. The serum levels of zinc and copper in type 2 diabetes and control groups were determined in this study and related to the age and gender. It was observed that the mean serum zinc level was significantly lower in diabetics as compared to control subjects, an observation also reported by Anetor et al [15] and Al-Marroof [16] and Al-Sharbatti [17]. The possible explanation of the observed hypozincemia in diabetes is hyperzincuria

which occurs as a result of hyperglycaemia, disrupting the proper metabolism of trace elements.

Despite the decrease in the zinc levels in diabetes in our study group there was no correlation between this trace element and their glucose levels [6, 16]. The study also revealed that copper levels are increased in type 2 diabetes. The increased levels of copper in the diabetic patients compared with normal human subjects agrees with earlier reports. The increase in the copper levels in patients with type 2 diabetes might be attributed to hyperglycemia, stimulating glycation, which results in the formation of highly reactive oxidants that can lead to tissue damage [17].

Conclusion

Throughout this study we focused on the changes in the serum levels of copper and zinc. We found in diabetes mellitus the mean values of the blood level of copper are significantly increased, where as the zinc values were also decreased significantly, in patients with diabetes mellitus. Further studies need to be carried out to determine the molecular role of copper and zinc in the development of diabetic complications in a larger population. Also, Glycated haemoglobin would be useful to measure in such studies (financial constraints prevented its use in the present study).

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