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RESEARCH ARTICLE

"EVALUATION OF SERUM ZINC, COPPER, MAGNESIUM AND IRON LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS"

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Abstract

Background: Type 2 diabetes mellitus (DM) is supposed to be associated with fluctuations in the serum levels of trace elements. Conversely, research also suggests that early imbalances of specific elements may play an important role in upsetting of normal glucose and insulin metabolism.

Aim: In the present study, our aim was to evaluate the essential trace elements like Zinc (Zn), Copper (Cu), Magnesium (Mg) and Iron (Fe) in diabetic patients.

Materials and methods: The study was conducted in 47 patients with type 2 DM along with 58 age and sex matched healthy controls. Various biochemical parameters like Fasting blood sugar, post prandial blood sugar, glycosylated hemoglobin and trace elements like Zn, Cu, Mg and Fe levels were measured and compared. This study was conducted in Al- Quwayiyah Government General Hospital, Saudi Arabia.

Results: The significantly decreased levels of Zn and Mg, whereas increased levels of Cu and Fe (P<0.001) in type 2 DM patients when compared to control groups.

Conclusion: The hypothesis of the current study indicates that impaired trace element metabolism to be an additional risk factor for the development and progress of disease. We suggest that evaluate the above trace elements in early stage of diabetes, otherwise it may contribute in the development of further vascular complications in diabetes mellitus.

1. INTRODUCTION

Type 2 Diabetes mellitus (DM) is an endocrinological disease associated with hyperglycemia characterized by both insulin resistance and defective insulin secretion. The resulting chronic hyperglycemia damages blood vessels and nerve cells through the body, producing micro-vascular diseases. The clinical research suggests that the homeostasis of trace element can be disrupted by DM. Conversely, research also suggests that early imbalances of

specific elements may play an important role in upsetting normal glucose and insulin metabolism (Sarkar et al., 2010; Zargar et al., 2002).

Trace elements are accepted as essential for optimum health, because of their diverse metabolic characteristic and function. Trace element deficiencies are frequently associated to chronic diseases or to problems with its absorption. Chronic hyperglycemia may cause significant alternations in the status of some micronutrients, and on other hand, some of these nutrients can directly modulate glucose homeostasis (Bhanot et al., 1994). Oxidative stress contributes to the pathogenesis of many diseases including DM. So many studies shown that copper (Cu) causes oxidative stress and acts as a pro oxidant and may participate in metal catalyzed formation of free radicals. The increased production of free radicals is likely to be associated with development of type 2 DM (Viktorinova et al., 2009).

Zinc (Zn) is one of the essential trace elements which are involved in the synthesis, storage, secretion and conformational integrity of insulin. Zn deficiency is associated with many chronic illnesses. Magnesium (Mg) is another essential trace elements, is a cofactor in both glucose transporting mechanism of cell membranes and various enzymes important in carbohydrate oxidation. In humans, some (Chaudhary et al., 2010) but not all (Valk et al., 1998) experimental studies have shown that benefits of Mg supplementation on glucose metabolism or/ and insulin sensitivity. Several studies have suggested a possible role of Iron (Fe) in insulin resistance or diabetes (Swapnil et al., 2006). Keeping in mind the above facts, the aim of the present study was to evaluate the serum levels of Zinc, Copper, Magnesium, Iron and glycated hemoglobin in patients with type 2 DM and compared with normal healthy controls.

2. MATERIAL AND METHODS

The study was case controlled in design. The patients included in the present study were all admitted to medicine unit or attending the Outpatient department (OPD) of medicine of the Al- Quwayiyah Government General Hospital, Shaqra University, KSA.

The study group consisted of 47 patients with type 2 diabetic subjects of both the sexes they were between 40—60 years. Type 2 diabetic patients were diagnosed based on the history, biochemical investigation and according to the biochemical criteria laid down by WHO. Those patients whose body mass index (BMI) was >30 were considered as obese. Age and sex matched 58 healthy controls were recruited after clinical and biochemical evaluation. Subjects suffering from other known case of liver disease, viral hepatitis B and C, cardiovascular diseases, rheumatoid arthritis, hemochromatosis, wilson disease, strokes, cerebrovascular accidents, any chronic or acute inflammatory illness, pregnancy and lactating mothers, alcoholics, and chronic drug consumption were excluded from the study. All diabetes patients selected for this study were on irregular treatment. All participants gave written informed consent and this study protocol was approved by the institutional ethical and human research committee.

Blood samples were obtained after an overnight fast. 5 ml of plain blood was collected from each subject, the serum was carefully separated by centrifugation at 3000 x g RPM for 10 minutes and transferred to micro tubes and stored at + 4^0 C before analysis. The biochemical parameters such as fasting glucose and post prandial glucose levels were estimated by enzymatic methods (Hayvarinen and Nikkila., 1962). HbA1c was assessed by the resin- ion exchange method (Jeppsson 2002). Serum Zn, Mg, Cu and Fe were determined by flame atomic absorption spectrophotometer with deuterium background correction (Perkin – Elmer model 5000) (Elmer and Conn., 1975).

3. STASTISTICAL ANALYSIS

The statistical analysis of data was performed by using SPSS version 17.0 software. All values are expressed as mean ±SD. For the comparison of values between the groups, student t- test was used, represented by 'p' value. Statistical significance was considered at a 'p' value of < 0.05.

4. RESULTS

The clinical and biochemical characteristic of the diabetic patients and normal subjects are presented in Table 1. In the present study, the biochemical parameters like serum fasting blood glucose, post prandial glucose and HbA1c levels were significantly increased in diabetic individuals when compared to controls ($p<0.001$). Trace elements like serum Zn and Mg levels were significantly decreased in diabetic patients than normal subjects, whereas increased levels of serum Cu and Fe was observed in diabetes patients when compared to healthy controls ($P<0.001$) respectively as shown in Table 2.

Table 1. Clinical and biochemical details of the study subjects

Particulars	Controls (n= 58) Mean ±SD	Diabetic patients (n= 47) Mean ±SD
Age (yrs)	48.8 ± 5.7	50.2 ± 5.1 *
Sex (male / female)	32 / 26	26 / 21 *
BMI (kg/m^2)	26.2 ± 3.0	30.5 ± 2.2*
Fasting Blood Glucose (mg/ dl)	86.2 ± 10.2	189.9 ± 19.8 *
Post Prandial Blood Glucose (mg/dl)	120.3 ± 8.9	245.2 ± 21.2 *
HbA1c (%)	4.62 ± 1.9	8.99 ± 3.1 *

The values are mean ± Standard deviation (SD), * P<0.001, highly significantly compared to controls.
BMI= Body mass Index, HbA1c= Glycated haemoglobin.

Table 2. Serum Zinc, Magnesium, Copper and Iron levels in patients and controls

Parameters	Controls (n= 58) Mean ±SD	Diabetic patients (n= 47) Mean ±SD
Zinc (µg/ dl)	95.3 ± 10.1	70.8 ± 12.3*
Magnesium (mg/ dl)	2.02 ± 0.41	1.83 ± 0.32*
Copper (µg/ dl)	81.3 ± 11.2	138.2 ± 16.5*
Iron (µg/ dl)	102.0 ± 13.3	159.8 ± 21.1*

* P<0.001, highly significantly compared to controls.

5. DISCUSSION

Trace elements are being increasingly recognized as essential mediators of the development and progression of so many diseases. On theoretical grounds, trace elements have been identified for long time as potential candidates for improving metabolic disorders like prediabetes (insulin resistance, obesity, metabolic syndrome) or diabetes (Nicolas and Jean., 2010). Zinc (Zn) is an essential trace element and it is important in glucose metabolism. It is component of many enzymes and it plays an important role in the maintenance of several tissue functions. It has been suggested that Zn metallothionine complexes in the islet cells provide protection against immune – mediated free radical attack and at specific sites where it can compete for iron and copper. Zn could also aid in protecting sulfhydryl, groups against oxidation and participate in the inhibition of the free radical in Haber-Weiss cycle by competing with transition metals (Jansen et al., 2009). In the present study, serum Zn levels were found to be significantly lowered in diabetic patients compared to controls. Similar finding was observed in Parveeena S et al (2013) and Mohan Lal et al (2013), whereas other investigators like D'Ocon (1987) found that Zn levels increased in diabetes patients. Some researchers have indicated that diabetics may loss in Zn by excreting more Zn into the intestine during the digestive processes and may be increase in urinary loss. Several modes of action have been described to explain the improved action of insulin by Zn. It appears that Zn can have direct insulin – like effects, which may be due to inhibition of the important glycogen- regulating enzyme GSK3, stimulation of the postreceptor proteins Akt and PI3 – kinase, decrease in cytokines such as IL- 1β as well as NFkB (Wijesekara et al., 2009).

It is well know that Copper (Cu) plays vital role in oxidative stress. Cu in its free form is a potent cytotoxic element because of its redox chemistry. It readily participates in Fenton and Haber - Weiss reactions to generate reactive species. Increase in Cu ion levels in patients with DM might be due to hyperglycemia that may stimulate glycation and release of Cu ions and this accelerate the oxidative stress and can result in the formation of AGEs (Nicolas and Jean 2010). Supriya et al (2013) and Sarkar A et al (2010) revealed that increased of Cu levels in type 2 DM. Similarly, we also observed significant elevated levels of Cu in diabetic patients as compared to controls. Increases in Cu ion concentrations as been linked to disorders in the structure of arterial walls, stress, infections and DM. The relationship between an increase in Cu concentrations and the oxidation of LDL-C has been confirmed (Tasneem et al., 2008).

Magnesium (Mg) is an essential ion which is involved in glucose homeostasis at multiple levels. A complex interplay exists between Mg and glucose metabolism. It plays an important role in the activities of various enzymes which are involved in glucose oxidation, and it may play a role in the release of insulin. It is mainly intracellular and its uptake is stimulated by insulin (Yajnick et al., 1984). Several authors reported that decrease in serum Mg levels in diabetic patients as compared to controls (Ankush et al., 2009). We also observed same findings low levels of Mg in type 2 DM. Hypomagnesaemia can increase the platelet reactivity, increase vascular and adrenal responses to angiotensin II enhanced thromboxane A2 release and lead to organ damage from free radicals. It has been suggested that hypomagnesaemia may induce altered cellular glucose transport, reduced pancreatic insulin secretion, defective post receptor insulin signalling, and / or altered insulin- insulin receptor interactions (Nadler et al., 1992).

Free Iron (Fe) serves as a catalyst for lipid and protein oxidation and the formation of reactive oxygen species. Epidemiological studies have reported an association between high iron stores and type 2 diabetes (Thomas et al., 2004). In the present study, Serum Fe significantly increased in type 2 diabetes as compared to control group and this finding consistent with the Swaminthan et al (2007). Iron is strong pro-oxidant that catalyzed the formation of hydroxyl radicals, and the increase in oxidative stress may be associated with the risk of diabetes. A link has been established between increased dietary Fe intakes; increase intestinal absorption particularly eating red meat, increased body iron stores. The concept of iron contributing to diabetes is supported by a few important recent animal studies (Cooksey et al., 2010).

6. CONCLUSION

The present findings demonstrate that impaired trace element metabolism to be an additional risk factor in the development and progress of disease and they contribute to the pathogenesis of type 2 DM. Increased levels of Cu and Fe together deceased Zn and Mg levels may disturb the antioxidants and enhance the lipid peroxidation in diabetic patients. We suggest that evaluate the above trace elements in early stage of diabetes, otherwise it may contribute in the development of further vascular complications in diabetes mellitus.

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