MINERALS AND TYPE 2 DIABETES MELLITUS –LEVEL OF ZINC, MAGNESIUM AND CHROMIUM IN DIABETIC AND NON DIABETIC POPULATION

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ABSTRACT

Background:
Minerals play a vital role in metabolic pathways in human body. For example Zn plays a key role in the synthesis and action of insulin, both physiologically and in the pathologic state of diabetes.

Objective:
To see the levels of zinc in diabetic and non diabetic patients attending Aziz Fatimah Hospital (AFTH) in Faisalabad.

Patients and methods:
Thirty test subjects with type 2 diabetes mellitus and thirty non diabetes mellitus were selected randomly from out patients department (OPD) of AFTH. Primary end point was to see the level of zinc. We also screened them for levels of magnesium and chromium. Patients were also stratified to low, middle and high socio economic status.
Five millilitre blood sample was collected from each subject for the analysis of above mentioned elements. One millilitre serum was drawn from blood sample for wet digestion. Sample was diluted up to 50 ml by using de-ionized water. Digested sample was analyzed by atomic absorption spectrophotometer for minerals. Statistical analysis was done by using analysis of variance (ANOVA).

Results:
Serum zinc levels were significantly lower in diabetic subjects than non diabetics (p<0.05). Zinc levels ranged from 1.05-4.8 mg/dl in males and 1.7-3.5 mg/dl in females of middle socioeconomic group which was very low than normal non-diabetic population. Mg and chromium was also very low.

Conclusion:
Zinc levels are very low in diabetic than normal which may affect their diabetic control. Same is the case with Mg and Cr.

Keywords: Zn, T2DM, Insulin

INTRODUCTION

Diabetes mellitus (DM) is disorder of heterogeneous etiologies, with the common denominator of hyperglycemia. Moreover, it is one of the commonest diseases of mankind,
prevalence of which is increasing day by day to the level of becoming an epidemic globally. DM is characterized by absolute or relative deficiency of insulin which is essential to metabolism of carbohydrates, lipids and proteins. Zn is an essential trace element that is directly involved in the synthesis, storage and secretion of insulin, as well as conformational integrity of insulin. The trace element, chromium increases insulin binding to cells by increasing insulin receptors on membrane and it may lead to increased insulin sensitivity, glucose utilization and beta cell activity. Mg is an essential ion involved at multiple levels in insulin secretion, binding and activity and is a critical cofactor of many enzymes in carbohydrate metabolism.\(^1\)

Zinc is also required for normal immune function, taste acuity and enhances the in vitro effectiveness of insulin. Impaired immune function and taste abnormalities are well documented in diabetic subjects, and decreased serum zinc levels and hyperzincuria occur in some diabetic subjects and animals. A growing body of evidence suggests that Mg plays a pivotal role in reducing cardiovascular risks and may be involved in pathogenesis of diabetes itself.\(^2\)

Abnormal zinc and lipid levels occur more frequently in metabolically uncontrolled diabetic subjects. These lipid abnormalities are key factors in the emergence of cardiovascular complications. Significantly reduced total cholesterol and triglycerides concentrations and elevated HDL correlate to zinc levels.\(^3\)

Hyperglycemia from either type of diabetes mellitus causes physiologically significant losses of zinc from the body. These losses may be due to the underlying diabetes but are probably not responsible as the causal agents.

**MATERIAL AND METHODS**

**Selection and stratification of subjects**

The study was conducted at OPD of AFTH. 30 diabetic and 30 non-diabetic patients of both sexes were enrolled for the determination of serum Zn, Mg and Cr levels. Both groups were stratified according to their income in low, middle and high. 15 male, 15 female and 5 from each income group (low, middle and high) were included.

Diabetic patients with kidney and liver diseases were excluded from the study on the basis of investigation, because kidney and liver diseases affect mineral levels.

**Collection of sample and assay method**

Five millilitre of blood was taken from each patient. Serum was separated. One millilitre serum was taken in to digestion flask and 5 ml concentrated nitric acid was added into it. The flask was heated on hot plate till the volume become half. After this, 2.5 ml perchloric acid was added. The contents were heated till the volume was left 1-2 ml; the contents were diluted up to 50 ml by using de-ionized water. This digested and sample solution was used for the estimation of minerals.

**Atomic absorption spectrophotometery**

This technique is used to measure the level of various minerals. It can measure up to 70 different metals in a solution. Samples were transported to Hi-Tech Laboratory of University of Agriculture, Faisalabad, where levels were determined by this technique.

In this technique, a liquid sample is aspirated into a flame whose temperature is approximately 3140–4949\(^\text{o}\)F. The sample was atomized in flame. A selected light source emits characteristic frequencies.

**RESULTS**

Serum levels of Zn, Mg and Cr are shown and compared in Figure 1, 2, 3. These figures clearly show that serum Zn levels are very low than non diabetic and standard levels. Same is the case with Mg and Chromium. There is difference in Zn level according to income group but this is not statistically significant.

**DISCUSSION**

Minerals in addition to being a structural component of body tissues are also involved in various physiological processes, such as proper metabolism and energy production. They also play a clear role in the synthesis, storage and secretion of insulin as well as its conformational integrity. DM is a complex metabolic disorder affecting metabolism of carbohydrates, lipids and proteins.
Fig. 1. Level of Zn, Mg and Cr according to low socio economic status

Fig. 2. Level of Zn, Mg and Cr according to middle socio economic status

Fig. 3. Level of Zn, Mg & Cr according to high socioeconomic status
This study was conducted with the aim of finding the levels of Zn, Mg and Cr in diabetic and non-diabetic population. It is evident that the levels of these minerals are quite significantly lower in both sexes, all ages and various income groups.

**Zn and insulin interactions**

Long before there was any biochemical evidence for the relationship between zinc and insulin in the beta cell, it was clear that the addition of zinc to insulin would change the time course of the effect of a given dose of insulin. As early as the 1930s, when insulin was just becoming available for commercial use, zinc was being added in vitro to make (PZI) protamine zinc insulin and lente crystalline insulin which prolonged the duration of action of the insulin by delaying its absorption from the subcutaneous injection site thus requiring fewer insulin injections. Only since the 1970s have the biochemical pathways and structures for insulin been known. Insulin is produced by the beta cell of the pancreatic islets as a single chain peptide that is bent around itself and linked by two inter-chain disulfide bonds. This pro-insulin is cleaved by the removal of an intracellular chain fragment known as the “C-peptide” to form two peptide chain (alpha and beta) molecules of 51 amino acids cross-linked to each other by inter-chain disulfide bonds. This is the insulin monomer. In the presence of zinc within the cell, insulin monomers assemble to a dimeric form for storage and secretion as the zinc crystal. Zalewski in 1994 by high fluorescence analysis showed that Zn concentration in the islet cells was related to the synthesis, storage and secretion of insulin.4

In vitro, in the presence of zinc and at neutral pH, dimeric insulin assembles further into a hexamer form, which is relatively stable. Beyond the physical chemical effects of conformation changes also affect the receptor binding and antigenic properties of insulin. In vitro data suggest that insulin binds to isolated liver membranes to a greater extent and that there is less degradation when Zn is co-administered with insulin.5

**Effects of diabetes on Zn metabolism**

It is clear from the literature that the predominant effect on zinc homeostasis of diabetes is hypozincemia, which may be the result of hyperzincuria or decreased gastrointestinal absorption of Zn or both. While the evidence for increased zinc excretion is uniform, the data supporting decreased absorption of Zn is less evident. It appears that the hyperzincuria, at least, is a result of more hyperglycemia than any specific effect of endogenous or exogenous insulin in the renal tubules. In 20 age/sex matched controls and 30 diabetic patients, the serum Zn was approximately 40% lower in the diabetes group (p<0.001). No differences within the diabetes group were observed when treatment differences between insulin, oral hypoglycemic agent or combination or between Type I and Type II diabetes were evaluated.6 Isbir et al. demonstrated a 20% decrease in serum Zn (p<0.001) in Type I diabetes, apparently the result of hyperzincuria7. El Yazigi et al. evaluated both Type I and II diabetics and found the absolute and creatinine corrected excretion were greater in diabetics than in matched controls and found a positive correlation between Zn excretion and hemoglobin at all concentrations8. At least one study suggests that insulin treatment of diabetes may reduce the hyperzincuria while oral agents had no effect on the increased zinc excretion seen in Type II diabetes9. These data suggest hyperglycemia as the basis for the hyperzincuria, but since Type I and Type II patients were taking insulin or oral hypoglycemic agents which increase insulin secretion, an effect of insulin itself has not been eliminated.

The one thing that is clear from the literature, however, is that there is loss of large amount of zinc from the body via the urine. The source of the zinc that is excreted remains incompletely resolved.

**CONCLUSION AND RECOMMENDATIONS**

The relationship between diabetes, insulin and Zn is complex with no clear cause and effect realionship. In this study the levels of Zn, Mg and Cr were markedly less than normal. (See Figs. 1,2,3) Although the measurement of minerals like Zn, Mg and Cr in diabetic patients will not be cost effective, it will be interesting to see if supplemental Zn and other minerals would result in a better glycemic control. Moreover, prospective studies in high risk individuals like
with a positive family history of diabetes mellitus and obesity are needed to see whether normalization with supplemental Zn intake will prevent or delay the onset of DM.

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REFERENCES


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