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Glycemic Control and Serum and Urine Levels of Zinc and Magnesium in Diabetics in Calabar, Nigeria

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Abstract: The effects of glycemic control on serum and urine concentrations of zinc and magnesium in diabetics in Calabar, Nigeria were determined. Serum and urine Zinc (Zn) and Magnesium (Mg), Fasting Plasma Glucose (FPG), Glycated Hemoglobin (HbA1c) and urine Creatinine (creat) levels were determined in sixty diabetic subjects and forty age matched non diabetic subjects in Calabar, Nigeria using colorimetric methods and atomic absorption spectrophotometry. The FPG, HbA1c, urine Zn and Mg levels were significantly ($p < 0.05$) higher and serum Zn and urine Creatinine lower in diabetics than non-diabetic subjects. No significant ($p > 0.05$) difference was observed in serum Mg levels of both groups. There were no significant ($p > 0.05$) differences in the serum and urine Zn and Mg levels in diabetics with poor glycemic control (HbA1c $> 8.0\%$) and those with good glycemic control (HbA1c $< 8.0\%$), however, significantly higher urinary Zn and Mg and lower serum Zn levels were observed in diabetic subjects with poor glycemic control when compared with the non diabetic population. Significant positive correlations were observed between serum Zn and serum Mg ($p < 0.01$, $r = 0.473$), and between urine Zn and urine Mg levels ($p < 0.01$, $r = 0.495$), while significant negative correlation was observed between serum Mg and urine Mg levels of the diabetic population of the study. Diabetes and poor glycemic control alters the metabolism of Zinc and Magnesium by increasing their urinary excretion and lowering serum Zinc levels. The clinical implications of this are discussed.

Key words: Serum, urine, zinc, magnesium, diabetes and glycemic control

Introduction

Genetic and environmental factors contribute to the pathogenesis of diabetes and acts as trigger for the disease among subjects at high risk because of inherited susceptibility (Groop and Tuomi, 1997). The composition of our diet has changed considerably during the past few decades, and these are thought to be contributing greatly to the increasing incidence of diabetes mellitus (Vessby, 2000). Diabetes is estimated to afflict about 170 million people world-wide (Wokoma, 2002) and this represents about 2% of the world's population (Unwin *et al.*, 2001). In Nigeria, about 1-7% of the population is afflicted, with over 90% of these being non-insulin dependent (Fabiya *et al.*, 2002). The prevalence rate among students of University of Calabar was 0.4% (Anwan *et al.*, 1998).

Speculations on the role of trace elements in human diseases were aroused in 1929, when Glaser and Halpern noticed that yeast extracts potentiate the action of insulin (Glaser and Halpern, 1929). Earlier works of Mertz and his associates in 1959 demonstrating the existence of glucose tolerance factor in yeast with the identification of the active component as trivalent chromium and implication of chromium deficiency in abnormalities of glucose metabolism sparked off interest on the status of other trace and macro elements in health and diseases including diabetes (Mertz, 1998).

Direct associations of trace and macro elements with diabetes mellitus have been observed in many research studies (Nouramomammadi *et al.*, 2000). Insulin action was reported to be potentiated by some trace elements as chromium, magnesium, vanadium, zinc, manganese, molybdenum and selenium (Candilish, 2000). Proposed mechanism of trace elements enhancing insulin action includes activation of insulin receptor sites (Vincent, 2000), serving as cofactors or components for enzyme systems involved in glucose metabolism (Murray *et al.*, 2000), increasing insulin sensitivity and acting as antioxidants preventing tissue per oxidation (Kruse-Jarres and Rukguaer, 2000). Zinc is required for insulin synthesis and storage and insulin is secreted as zinc crystals, it maintains the structural integrity of insulin (Chausmer, 1998). Magnesium is a cofactor in the glucose transporting mechanisms of the cell membrane and various enzymes in carbohydrate oxidation, it is also involved at multiple levels in insulin secretion, binding and enhances the ability of insulin to activate tyrosine kinase (Suarez, 1993). Magnesium deficiencies have been implicated in insulin resistance, carbohydrate intolerance, dislipidemia and complications of diabetes (Resnick *et al.*, 1991). Lower serum levels of these elements have been reported in the diabetic state. It is not known whether differences in trace elements status are a consequence of diabetes and hyperglycemia or

alternatively whether their deficiencies contribute to the expression of the disease.

It is the objective of this study to determine the serum and urine levels of zinc and magnesium in diabetics and non-diabetics and in different states of glycemic controls to know the status of these elements in diabetics in our locality.

Materials and Methods

Sixty diabetic subjects (both males and females) attending the diabetic clinic of University of Calabar Teaching Hospital were selected for the study. Informed consent was sought and obtained from each subject before recruitment into the study. Their medical history, personal data and other parameters as weight and height were obtained. Diabetes in this study was defined based on laboratory findings as fasting plasma glucose levels greater than 7.00mmol/l on two or more occasions, or a two-hour postprandial plasma glucose levels greater than 11.00mmol/l on two or more occasions (WHO, 1999). Forty age matched non diabetic apparently healthy volunteers comprising of subjects living within calabar and its environs were used as controls in the study. Their medical history and personal data were obtained via comprehensive questionnaires. Fasting venous blood samples were collected aseptically from the subjects via venepuncture for fasting plasma glucose determination, glycated hemoglobin (HbA1c) determination and serum zinc and magnesium determinations. Spot urine samples were collected into sterile, chemically clean universal containers for urine zinc, magnesium and creatinine estimations. Fasting plasma glucose was estimated using the glucose oxidase method, urine creatinine was estimated to correct for urine flow rate of the subjects, using the Jaffes reaction method, glycated hemoglobin was estimated by column chromatography method using cation exchange resin, while serum and urine zinc and magnesium were estimated using the flame atomic absorption spectrophotometry.

Statistical analysis of results was performed on an IBM compatible computer using Microsoft excel and the SPSS statistical package.

Results

Table 1: Shows the FPG, HbA1c, urine creatinine, serum and urine zinc and magnesium levels in diabetics and non-diabetics. The FPG, HbA1c, urine Zn and Mg were significantly higher and serum zinc and urine creatinine lower in diabetics than in non-diabetics.

Table 2: Shows the serum and urine zinc and magnesium levels in diabetics with good glycemic control (HbA1c 6.5-8.0%) and those with poor glycemic control (HbA1c >8.0%). No significant differences were observed in serum and urine zinc and magnesium levels of both groups.

Table 3 shows the serum and urine magnesium levels in diabetics with poor glycemic control and non-diabetic controls. The urine zinc and magnesium levels were significantly higher and serum zinc lower in diabetics with poor glycemic controls than non-diabetics. No significant difference was observed in the serum magnesium levels of both groups.

A significant positive correlation ($p < 0.01$) was observed between serum zinc and magnesium ($r = 0.473$), urine zinc and magnesium ($r = 0.495$) and a negative correlation between serum and urine magnesium ($r = -0.441$) of diabetics.

Discussion

Derangement of trace element metabolism leading to secondary or acquired deficiency states can occur in a wide range of clinical circumstance and may result in varied ailments including diabetes mellitus, anaemia, cancer depression and cardiovascular disease etc. (WHO, 1996). Numerous studies have demonstrated the essential roles of such trace elements as Chromium, Zinc, Magnesium, Selenium, Vanadium, Molybdenum and manganese in insulin action and carbohydrate metabolism. The actual role of these elements in the pathogenesis and progress of diabetes is still unclear (Tuvemo and Gebremedhim, 1983). The observed alterations in the status of these elements seen in diabetics have been attributed to hyperglycemia and increased protein glycosylation seen in this condition (Srivastava *et al.*, 1993). The serum and urine levels of zinc and magnesium in diabetics and in different states of glycemic control as determined by glycated hemoglobin levels were determined in this study.

Serum Zinc levels of diabetics were significantly lower than those of non-diabetics, also, urine zinc levels were higher in diabetics than non-diabetics studied. Hyperzincuria or decreased gastrointestinal absorption of zinc may explain the hypozincemia seen in the diabetic's population (Chausmer, 1998). While evidence for increased zinc excretion is uniform, the data supporting decreased absorption of zinc is less clear-cut. Isbir *et al.* (1994) demonstrated a 20% decrease in serum zinc levels in type 1 diabetes, apparently the result of hyperzincuria. Lower serum and plasma zinc levels in diabetics have also been reported by other studies (Anetor *et al.*, 2002, Cunningham *et al.*, 1994, Walter *et al.*, 1991, Zargar *et al.*, 2002). The serum magnesium level, though lower in diabetics than non-diabetics, was not statistically different. However, significantly lower serum magnesium levels have been demonstrated in serum and hair of diabetics (Nouramomammadi *et al.*, 2000).

Urine concentrations of magnesium and zinc were observed to be significantly higher in diabetics than in non-diabetics population studied. These findings are consistent with the reports of works on the effect of

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Table 1: Fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), urine creatinine (creat), serum and urine zinc and magnesium in diabetics and non-diabetic subjects

Subjects	FPG mmol/l	HbA1c %	Serum		Urine		
			Zn mg/l	Mg mg/l	Creat g/l	Zn mg/gcreat	Mg mg/gcreat
Diabetics N = 60	8.57±4.47	8.25±1.18	0.60±0.28	13.60±4.80	1.66±0.52	0.69±0.37	11.55±6.40
Non diabetics N = 40	4.14±1.00	6.60±1.28	0.88±0.60	14.10±4.80	1.99±0.67	0.41±0.18	5.80±4.00
p-value	p<0.05	p<0.05	p<0.05	p>0.05	p<0.05	p<0.05	p<0.05

Table 2: Serum and urine zinc and magnesium levels in different states of glycemic control in diabetic subjects

Control state	Serum		Urine	
	Zn mg/l	Mg mg/l	Zn Mg/gcreat	Mg Mg/gcreat
Good HbA1c (6.50-8.00%) n = 21	0.66±0.26	14.16±4.55	0.80±0.47	10.6±5.19
Poor HbA1c (>8.00%) n = 39	0.60±0.28	13.27±4.90	0.64±0.29	11.78±7.05
P - value	p>0.05	p>0.05	p>0.05	p>0.05

Table 3: Serum and urine zinc and magnesium levels in diabetics with poor glycemic control and non-diabetic subjects

Control state	Serum		Urine	
	Zn mg/l	Mg mg/l	Zn Mg/gcreat	Mg Mg/gcreat
Poor HbA1c (>8.00%) n = 39	0.60±0.26	13.27±4.90	0.64±0.29	11.78±7.05
Non diabetics n = 40	0.88±0.60	14.10±4.80	0.41±0.18	5.80±4.00
P - value	p<0.05	p>0.05	p<0.05	p<0.05

diabetic state and related disorders on the urinary excretion of magnesium and zinc in patients, where higher urinary magnesium and zinc was demonstrated in the diabetic state (El-Yazigi *et al.*, 1991). The hyperzincuria may be as a result of hyperglycemia than any specific effect of endogenous or exogenous insulin on the renal tubules. Hyperglycemia has been postulated to interfere with the active transport of zinc back into the tubular cells. (Chausmer, 1998). Hypermagnesuria in diabetics have been attributed to osmotic diuresis. Glycosuria, which accompanies the diabetic state, impairs renal tubular reabsorption of magnesium from the glomerular filtrate (Garland, 1992). The serum and urine zinc and magnesium concentrations in diabetics with good glycemic control and those with poor glycemic control of the study showed no significant differences between the concentrations of these elements in the different states of glycemic control. This is consistent with the works of (Ekmekcioglu *et al.*, 2001), who demonstrated that plasma trace elements concentration were not dependent on the degree of glucose control as determined by correlational analysis between glycated haemoglobin (HbA1c) and metal levels. Zargar *et al.* (2002) also demonstrated that glycemic control does not influence the plasma levels of magnesium and zinc in diabetics. No correlation was seen between HbA1c and serum and urine zinc and magnesium in the study. A similar observation was also made by (Schlienger *et al.*, 1988). No significant correlation was observed between

blood glucose levels and serum magnesium and zinc by (Anetor *et al.*, 2002). However, a positive correlation between zinc excretion and glycated hemoglobin concentration have been reported in diabetics (El-Yazigi *et al.*, 1991). A marked depletion in plasma and erythrocyte magnesium levels was particularly evident in diabetic patients with advanced retinopathy and poor diabetic control (Fijii *et al.*, 1982). On the contrary, Paolisso, (1998) observed that glycemic control in patients with type 2 diabetes may not correct low magnesium concentration, suggesting that other factors may regulate magnesium levels in diabetic patients. Higher urine zinc and magnesium and lower serum zinc levels were seen in diabetes with poor glycemic control when compared to non-diabetics. Serum magnesium level was not affected. The reason for this and the underlying mechanism is not known. Increased urinary excretions of these elements in poor glycemic control have also been attributed to hyperglycemia, glucosuria and osmotic diuresis (Swain and Kaplan, 1999). The study also observed positive correlations between serum zinc and serum magnesium, and between urine zinc and urine magnesium. The reason for this is not known but may be due to the interwoven specific relationship that exists between each of these elements and insulin action. Serum magnesium correlated negatively with urine magnesium in the diabetic population of the study. The status of body magnesium balance is determined by the renal excretion. Thus when the magnesium status is sub optimal, magnesium

receptors on the thick ascending limb of the loop of Henle, sense the need for mg retention and cause more reabsorption (Hans *et al.*, 2002). Hence the lower the urine excretion of magnesium, the higher the serum magnesium concentration and vis-versa. No correlation was observed between serum zinc and urine zinc.

From our observations, we therefore conclude that diabetes and poor glycemic control alters the metabolism of zinc and magnesium by causing hyperzincuria, hypermagnesiumuria and hypozincemia.

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