Research Article

The levels of testosterone, zinc, manganese and selenium in type 2 diabetic patient in South-Eastern Nigeria

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ABSTRACT

Background: This study is aimed at evaluating the levels of some trace elements and testosterone, and to ascertain their possible association in type 2 diabetes mellitus.
Methods: Ninety male type 2 diabetic subjects and forty five apparently healthy non-diabetic male individuals were recruited into this study. The control group was matched for age with the study subjects and they were all within the age range of 30-67 years. Fasting Plasma Glucose (FPG), testosterone, trace elements (zinc, selenium, manganese), Body Mass Index (BMI) were determined.
Results: This study showed significant decreases in the levels of trace elements (Zn, Se, and Mn) with a concomitant decrease in the levels of testosterone in type 2 diabetic patients (P <0.001). This findings were further strengthened by the strong positive correlation between testosterone and these trace elements (P <0.05).
Conclusion: This suggests that low testosterone level might be as a result of low trace elements considering their role in testosterone production. Therefore, trace elements supplementation is recommended.

Keywords: Testosterone, Trace elements, Type 2 diabetes, Hyperglycaemia

INTRODUCTION

Type 2 diabetes mellitus formerly non-insulin dependent diabetes mellitus or adult onset diabetes, is a metabolic disorder that is characterized by hyperglycemia in the context of insulin resistance and relative insulin deficiency.[1]

Over 90% of people with diabetics, have type 2 diabetes mellitus and it is associated with certain endocrine disorders, in particular hypogonadism in men.[2,3]

Testosterone is the major male androgen and is produced by the interstitial cells of the leydig. It is responsible for male secondary sexual characteristics and sperm production.[4] Studies have shown that testosterone levels are lower in diabetic men than non-diabetic men even when one carefully studies men of the same age.[5,6] Diabetic men are highly prone to erectile dysfunction and hypogonadism due to nerve damage, poor circulation and low testosterone. These conditions are difficult to treat, and many men suffer in silence because they never bring their erectile dysfunction to their doctor or because there are few treatment options available.

However, report has shown that trace elements such as zinc, manganese and selenium are implicated in sex hormone production and normal glucose metabolism.[7] Inadequate zinc levels prevent the pituitary gland from releasing Luteinizing Hormone (LH) and Follicle Stimulating Hormones (FSH), which stimulate testosterone production.[8] Zinc also inhibits the aromatase enzyme that converts testosterone into excess estrogen.[8] In the same vein, manganese facilitates the release of Luteinizing Hormone Releasing Hormone (LHRH) from the hypothalamus into capillaries of the hypophyseal portal vessels and it is carried to the hypophyseal gonadotropes where it stimulates the release of LH and FSH which further stimulate the release of testosterone. This means that reduction in the levels of these trace elements might also cause the reduction in the levels of testosterone.

Several studies have shown that the metabolism of several essential elements were altered in diabetes and that these nutrients might have specific roles in the pathogenesis, complications and progress of this disease.[9] Fortunately, previous study has shown that appropriate trace element supplementation might prove beneficial in ameliorating some physiological deficiencies associated with diabetes and prevent or retard secondary complications.[7] However, this work seeks to find if there is any possible association between testosterone and some trace elements that are important in testosterone synthesis.

METHODS

Study design

This is a cross-sectional study and a total number of 135 participants were recruited for this study. The subjects were grouped into two categories comprising 90 known type 2 diabetic male subject recruited from the medical out-patient department of NAUTH, Nnewi and 45 non-diabetic male (control group) who are laboratory workers from NAUTH, Nnewi. The two categories (subject and control group) were aged-matched, thus all respondents were within the age range of 30-67 years. Their consents were sorted and all the participants freely volunteered. Any individual (both type 2 DM and non-DM control subject) that smoke or drink alcohol regularly; that have chronic diseases (e.g. Kidney disease), or is on medication or supplements that could potentially affect levels of trace elements was excluded from the study. The study received an approval from the ethical committee of Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi.

Blood sample collection and biochemical analysis

Fasting venous blood samples were collected from all respondents for the analysis. A part was dispensed into fluoride oxalate bottles for glucose determination using standard enzymatic spectrophotometric method. The remaining part was dispensed into a plain bottle and allowed to clot, retract and the serum stored at -20ºC until analysis of trace elements (Zn, Se, and Mn) using Atomic Absorption Spectrophotometric Method and Testosterone using Enzyme Linked Immunosorbent Assay (ELISA). The body mass index was calculated from the ratio between measured height and weight (kg/m^2).

Statistical analysis

The version 20 of Statistical Package for Social Sciences (SPSS) was used in statistical analysis. The graphical presentation was done using SigmaPlot version 12. Pearson correlation analysis was used to establish possible association between male sex hormones and trace elements. Differences with P <0.05 were considered significant.

RESULTS

The results of this study showed that the mean levels of age and BMI in both type 2 diabetic subjects and non-diabetic control subjects were similar (P >0.05). However, the mean levels of testosterone, zinc, manganese, and selenium were significantly lower in type 2 diabetic subjects than in non-diabetic control subjects (P <0.001). Fasting plasma glucose was significantly higher in diabetic subjects than in non-diabetic control subjects (P <0.001) (Figure 1).
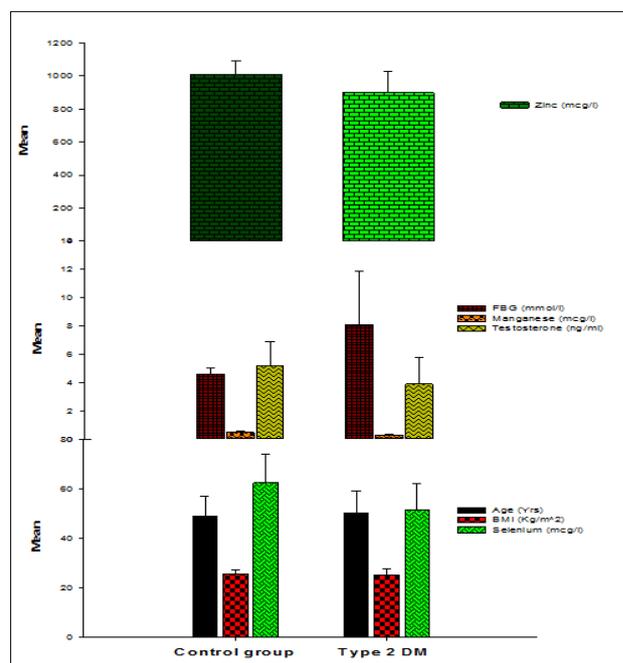

Figure 1: Levels of trace elements, testosterone, fasting plasma glucose and body mass index in type 2 diabetic and in non-diabetic subjects.

(*) that showed the levels of significance between the DM and controls did not appear on top of each type 2 DM bar for those that were significant.
*Significant when compared with control subjects (P <0.001)

The results also showed significant positive correlation between testosterone and the trace elements (Zinc, manganese, and selenium) in type 2 diabetic subjects (P <0.05). However, BMI and fasting plasma glucose did not show any significant association with the serum testosterone in the type 2 diabetic subjects (P >0.05) (Table 1).

Table 1: Correlation of testosterone levels with BMI, FBG, and trace elements (Zn, Se, and Mn) in type 2 diabetic patients.

Parameters	N	r	P value
Testosterone vs. Zinc	90	0.274	0.009
Testosterone vs. Manganese	90	0.232	0.028
Testosterone vs. Selenium	90	0.378	0.000
Testosterone vs. BMI	90	-0.095	0.371
Testosterone vs. FBS	90	0.057	0.593

All the parameters analyzed (zinc, selenium, manganese, fasting plasma glucose, and BMI) did not show any significant association with the serum testosterone in non-diabetic control subjects (P >0.05) (Table 2).

Table 2: Correlation of testosterone levels with BMI, FBG, and trace elements (Zn, Se and Mn) in non-diabetic control.

Parameters	N	r	P value
Testosterone vs. Zinc	45	0.114	0.455
Testosterone vs. Manganese	45	-0.093	0.543
Testosterone vs. Selenium	45	0.064	0.679
Testosterone vs. BMI	45	-0.063	0.679
Testosterone vs. FBS	45	0.063	0.653

DISCUSSION

This study clearly showed significant lower trace elements levels (Zn, Mn and Se) in diabetic subjects when compared with non-diabetic controls (Figure 1). Reports from several other studies, both locally and abroad, largely agree with the findings of our study.[10-13]

The low levels of trace element in type 2 diabetic subjects could be as a result of increased urinary excretion of these trace elements since it has been reported that hyperglycaemia interferes with the active transport of these elements back into the renal tubular cells. [14] El-Yazig et al. evaluated both type 1 and 2 diabetes and found that zinc and manganese excretions were significantly greater in diabetes than in matched controls.[14] They also found a positive correlation between zinc excretion and haemoglobin A_{1C} concentration.[14]

In this study, testosterone was significantly lower in men with type 2 diabetes than in non-diabetic men (Figure 1). This work agrees with other findings of some authors.[5,6] This might be as a result of low levels of trace elements such as zinc, selenium, manganese that are important in

the production of testosterone which had been shown to be low in type 2 diabetic patients.[11,14] This hypothesis is further strengthened by a strong correlation between testosterone and these trace elements in this study (Table 1). Hyperglycaemia increases urinary excretion of these trace elements which in turn may negatively affect the normal production of testosterone with attendant decrease in testosterone.

For instance, zinc is necessary to maintain normal serum testosterone. Inadequate zinc levels prevent the pituitary gland from releasing luteinizing and follicle stimulating hormones, which stimulate testosterone production.[8] Zinc also inhibits the aromatase enzyme that converts testosterone into excess estrogen.[8]

Krsnjavi et al. investigated the potential role of selenium in male infertility.[15] Blood and semen samples were collected from 18 men with low sperm counts and from 23 controls which were matched for age, smoking, alcohol and coffee consumption. The authors reported that serum selenium was significantly lower in men with oligospermia and azoospermia than in controls (fertile men). They also observed a significant difference in serum selenium levels in men with oligospermia and azoospermia, being higher in men with oligospermia than azoospermia.[15]

Manganese was found to accelerate daily sperm production and efficiency of spermatogenesis in prepubertal males.[16] These effects were explained by a hypothalamic action of the manganese that facilitates the secretion of luteinizing hormone releasing hormone (LHRH) in both sex.[16] The LHRH released from the hypothalamus into capillaries of the hypophyseal portal vessels is carried to the hypophyseal gonadotropes where it stimulates the release of LH and FSH which further stimulate the release of testosterone.

Furthermore, these trace elements (Zinc, manganese, and selenium) are important components of antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase etc. These antioxidants counteract the effect of Reactive Oxygen Species (ROS) that induce the complication of diabetes. Therefore, there low levels could lead to superoxide damage to the reproductive system which will invariably affect the testosterone level.

CONCLUSION

This suggests that low testosterone level might be as a result of low trace elements considering their role in testosterone production. Therefore, trace elements supplementation is recommended.

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