Relationships Between Diabetes Mellitus Type 2 and Male Testosterone Level

Afaf Khairey Esmaeel
Dept. of Biology, Faculty of Science, Babylon University, Iraq.

Abstract

The objective of the present study was to verify if there is any relation between diabetes mellitus type 2 and male testosterone concentration. Ten diabetic men in the age group (25-53) year were selected. Ten healthy men in the same age group served as control. The result show no significant changes (P>0.05) was found in testosterone level of diabetic patients when compared with testosterone level of control.

Introduction

Diabetes mellitus is a chronic disorder of the carbohydrate, lipid and protein metabolism characterized by insulin disorders, hyperglycemia and glycosuria. This condition may contribute to arteriosclerosis, microangiopathy, nephropathy and neuropathy (Camilleri, 2007).

Although most problems due to diabetes have been widely studied, the reproductive system affections are still little understood (Zarzycki & Zieniewics, 2005).

Diabetes mellitus has been associated with sexual dysfunction in both men and women. It is believed that neuropathy, vascular insufficiency and psychological problems may be involved in the pathogenesis of some phenomena such as impotence, ejaculation disorders and decreased libido, in addition to the reduced vaginal lubrication and orgasm dysfunctions (DeBerardis et al., 2007; Zarzycki and Zieniewics; 2005).

Some studies show that diabetic patients infertility caused by inappropriate synthesis of testosterone, caused by molecular changes in Leydig cells, secondary to diabetes (Dimulovic and Radonjic, 1990).

Testosterone is the principal male sex hormone and anabolic steroid. In men, testosterone plays a key role in development of male reproductive tissues such as the testes and prostate as well as promoting secondary sexual characteristics such as increased muscle and bone mass and hair growth (Tuck and Francis, 2009). Male testosterone is primarily synthesized in Leydig cells, the number of Leydig cells in turn is regulated by luteinizing hormone (LH) and follicle stimulating hormone (FSH). In addition, the amount of testosterone produced by existing Leydig cells is under the control of LH which regulates the expression of 17-B hydroxyl steroid dehydrogenase (Payne and O'shaughnessy, 1996).

Testosterone is present in three major fractions: free (2-3%), albumin-bound (20-40%), and sex hormone binding globulin (SHBG)-bound (60-80%). Non-SHBG-bound testosterone is called bioavailable testosterone because both the free and albumin-bound fractions comprise the biologically active component that is readily
available to the tissues, whereas SHBG-bound testosterone is tightly bound and thus considered inactive. A recent study has demonstrated that free testosterone levels, which are independent of SHBG, are low in one-third of diabetic men (Dhindsa, 2004).

The relation between male infertility and altered plasma levels of testosterone is still obscure (Ballester et al., 2004).

Maneesh et al. (2006) show that low serum testosterone in diabetic men was accompanied with low serum LH & FSH and suggested that the hypothalamic cells, which produce LHRH, do not function correctly to the feedback when testosterone level decreased, this inability of pituitary gland to respond appropriately to decline in testosterone implies that high serum glucose has a central effect on the interaction between the nervous system and endocrine system, the decrease in serum LH and FSH may result from impairment in its production and secretion. Obesity is associated with low testosterone levels in diabetic men, the increase in body lipids decreases serum testosterone level due to increased activity of the aromatase enzyme present in fat tissues there by converting testosterone and androstenedione to estrogens.

Consequently in diabetic men, in addition to decreased testosterone production and metabolism, higher than normal percentages of testosterone and androstenedione are converted into castradiol and estrone, respectively. This increased conversion may account for the diminished testosterone. The increased estrogens appear to exert a negative feedback effect on LH and FSH production and may thereby contribute to the alcoholic suppression of these reproductive hormones.

Also they found significantly low serum testosterone with low LH and FSH, they were suggest that the low serum testosterone levels decreased, levels of LH and FSH would increase to stimulate the production of more testosterone.

On the other hand, Miralles-Garcia et al., (2004) found that insulin-dependent diabetes is associated with reduced ejaculated semen and decreased vitality & motility of the spermatozoa, with no change in sperm viscosity.

Insulin action in motility and in the metabolism of human spermatozoa is not defined. Defects in insulin secretion may change testicular and accessory sexual glands function. Usually, the concentration of seminal insulin is higher than that in the serum (Chandrashekar & Bartke, 2005).

A recent systematic review and meta-analysis of cross-sectional studies indicated that testosterone levels were significantly lower in men with type 2 diabetes (Ding et al., 2006).

Svartberg (2007) was founded that men with type 2 diabetes have a lower serum testosterone concentration compared to men without a history of diabetes, and there is an inverse association between testosterone levels and hemoglobin A (HbA1c) concentrations.

Further, in men with low plasma testosterone the risk of diabetes mellitus is increased (Zitzmann et al., 2006). One-third to one half of men with type 2 diabetes mellitus are now recognized as testosterone deficient (Spark, 2007). A low plasma testosterone level appeared to be associated with endothelial dysfunction in men independent of other risk factors, suggesting a protective effect of endogenous testosterone on the endothelium (Akishita et al., 2007).

In addition, serum endogenous androgen concentrations were inversely associated with arterial stiffness in men with type 2 diabetes mellitus (Fukui et al., 2007).

There is an association of type 2 diabetes with low testosterone values, and therefore the effects of an intervention with testosterone are of considerable interest,
in hypogonadal men, the few studies on the effects of testosterone treatment on glycemic control were divergent (Basu, 2007).

Kalinchenko et al., (2009) were demonstrated that the beneficial effects of administration of testosterone to hypogonadal with a diabetic foot may be due to improved vascularization & to anti-inflammatory action.

**Methods**

Twenty male subjects aged 25–53 years were prospectively studied and classified as group 1 (n=10) healthy individuals, group 2 (n=10) men with diabetes mellitus type 2.

Serum testosterone was estimated for all samples by direct immunoezymatic method using reagent kit (testosterone enzymeimmunoassay test kit, catalog Number: Bc -1115, Biocheck, 837 CowanRd, Burlingame, CA, 94010).

**Collection of specimens**

Venous blood samples were obtained from all subjects by using disposable syringes and needles, samples were allowed to clot at 37 °C, then centrifuged at 3000 Xg for 15 minutes.

Sera were removed and stored at 2–8 °C.

**Assay of procedure**

1. Secure the desired number of coated wells in the holder.
2. Dispense 10 µl of standards, specimens and controls into appropriate wells.
3. Dispense 100 µl of testosterone-HRP conjugate reagent into each well.
4. Dispense 50 µl of rabbit anti-testosterone reagent to each well. Thoroughly mix for 30 seconds. It is very important to mix completely.
5. Incubate at 37 °C for 90 minutes.
6. Rinse and flick the microwells 5 times with distilled.
7. Dispense 100 µl of TMB reagent into each well. Gently mix for 5 seconds.
8. Incubate at room temperature (18-25 °C) for 20 minutes.
9. Stop the reaction by adding 100 µl of stop solution to each well.
10. Gently mix 30 seconds. It is important to make sure that all the blue color changes to yellow color completely.
11. Read absorbance at 450 nm with a microtiter well reader within 15 minutes.

**Results**

1. **Testosterone level between control and diabetic patients**

The results show no significant differences (P>0.05) in testosterone level in diabetic patients group as compared with control group as figure (1).

![Figure (1): Testosterone level (ng/ml) of control and diabetic patients.](image)
2. Relationship between testosterone (ng/ml) and duration of disease in diabetic patients

The results revealed no strong correlation between testosterone (ng/ml) and duration of diabetes mellitus type 2 in our study.

![Figure (2): The relationship between testosterone (ng/ml) and duration of disease in diabetic patients.](image)

3. Relationship between testosterone (ng/ml) and blood glucose (mg/100 ml) in diabetic patients

There is no strong correlation between testosterone (ng/ml) and blood glucose in type 2 diabetic men in our study.

![Figure (3): Relationship between blood glucose (mg/100 ml) and serum testosterone level (ng/ml).](image)

Discussion

The results show no significant differences in testosterone levels between the control group and diabetic men group. Also other studies did not demonstrate altered serum testosterone levels among diabetics, regardless of their sexual performance (Bolona et al., 2007; Ballester et al., 2005). Previous studies showed that about one-third of type 2 diabetic men have low serum testosterone levels because of a high prevalence of symptomatic hypogonadism (Kapoor et al., 2007). Other studies showed that low serum testosterone could be due to decreased synthesis or increased metabolic clearance (Cevik et al., 2004). Testosterone deficiency in diabetic men may because of the level of sex hormone binding globulin (SHBG) the major carrier protein of testosterone in circulation is low as a consequence of insulin resistance
(Andersson et al., 1994). Dhindsa et al., (2004) demonstrated that 33% (not all) of men with type 2 diabetes had significantly lower levels of free testosterone. The question thus arises as to why diabetic men have lower testosterone levels, the answer was Klinefelter's syndrome, the most frequent form of primary hypogonadism, is associated with insulin resistance and diabetes (Ota et al., 2002). Dhindsa et al., (2007) found that free testosterone was diminished in diabetic patients with organic importance. This is not found in the non-impotent diabetes. Male impotence which consists in difficulty in obtaining or maintaining full erection until the end of coitus, is a common sexual problem in diabetics (De Berardis et al., 2007; Miralles-Garcia & Garcia-Diez, 2004).

The prevalence of this complaint ranges from 20-50%, increasing with patient age and duration of the disease (Petroianu et al., 2009; Chandrashekar & Bartke, 2005). Bolona et al., (2007) stated that impotence is a multifactorial sexual disorder, secondary to endocrine, vascular, neurological and psychological disorders which act unfavorably on erection.

Petroianu et al., (2009) observed that vascular and neuronal anomalies as the causes of impotence in diabetic patients. On other hand, hormones did not significantly affect this dysfunction.

In 2005, Pitteloudet observed that the leydig cell population and testosterone metabolites were reduced, which was inversely related to the increase of insulin resistance.

Ding et al., (2006) were indicated that endogenous sex hormones may differentially modulate glycemic status and risk of type 2 diabetes in men & women. Low testosterone levels are associated with higher risk of type 2 diabetes in men but with lower risk in women.

Selvin et al., (2007) were suggested that testosterone insufficiency may be a risk factor for diabetes. So the associations of low free bioavailable testosterone levels with diabetes remained even after adjustment for age & known confounding factors including race/ethnicity & adiposity as measured by body mass index (BMI) and waist-to-hip ratio.

References
Basu R; Dalla Man C; Campini M; Basu A; Nair KS; Jensen MD; Khosla S; Klee G; Toffolo G; Cotelli C. (2007). Effects of two years of testosterone replacement on insulin secretion, insulin action, glucose effectiveness, hepatic insulin clearance and post prandial glucose turnover I elderly men.

Cevik R; Gur A; Acar S; Nas K; Sarac A. J. (2004). Hypothalamic pituitaey-gonadal axis hormones and cortisol in both menstrual phases of women with chronic fatigue syndrome and effect of depressive mood on these hormones. BMC Musculoskelet. Disord., 5: 47-51.


Kalinchenko S; Zemlyanoy A; Gooren LJ. (2009). Improvement of the diabetic foot upon testosterone administration to hypogonadal men with peripheral arterial disease-report of three cases. Cardiovascular diabetology, 8: 19, page 1 to 6.


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Selvin E; Feineib M; Zhang L; Rohrman S; Rifai N; Nelson W; Dobs A; Basaria S; Golden S. H; Platz E. A. (2007). Androgen and diabetes in men. Diabetes Care, volume 30 number 2: 234-238.


