Iraqi JMS

Published by Al-Nahrain College of Medicine
ISSN 1681-6579
Email: iraqijms@colmed-alnahrain.edu.iq
http://www.colmed-nahrain.edu.iq

Serum Testosterone and Postprandial Lipids in Relation to Sexual Dysfunction in Males with Cardiovascular Disease

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Abstract

Background Earlier studies have suggested that total testosterone (Testo) concentrations influence lipid metabolism. Whether these concentrations are prospectively associated with an adverse lipid profile and an increased risk of incident dyslipidemia has not yet been investigated.

Objective Test the hypothesis that increased levels of postprandial triglycerides (TG) are associated with hypogonodism in male patients with cardiovascular disease (CVD).

Methods Forty male patients with CVD aged 30-60 years and 46 normal healthy controls were studied. Postprandial blood glucose, lipid profile, urea and creatinine were measured. In addition, Total testosterone, sex hormone binding globulin (SHBG), luteinizing hormone and follicle stimulating hormone were done by Enzyme-Linked Immuno-Sorbent Assay. Body mass index was calculated.

Results Negative correlation between Testo, and postprandial TG in both CVD and control groups was found with significant differences in Testo between these two groups, while SHBG correlated negatively with postprandial TG, in control group.

Conclusion Postprandial triglyceride levels were associated with risk of CVD. These findings are particularly interesting and may contribute to an explanation for the higher cardiovascular disease risk in men with lower total testosterone concentrations.

Key words CVD, Dyslipidemia, postprandial TG, Testosterone.

Introduction:

Causes of cardiovascular disease (CVD) are diverse but atherosclerosis and/or hypertension are the most common. Although cardiovascular disease usually affects elderly, the antecedents of cardiovascular disease, notably atherosclerosis begins in early life, making primary prevention efforts necessary from childhood [(1)].

There is therefore increased emphasis on preventing atherosclerosis by modifying risk factors, such as healthy eating, exercise, and avoidance of smoking. Almost all CVD in a population can be explained in terms of a limited number of risk factors. Dyslipidemia may come at the top of the list [(2,3)]. Dyslipidemia is a disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. It may be manifested by elevation of serum total cholesterol, the low density lipoprotein cholesterol (LDL-c) and the triglyceride (TG), and a decrease in serum high density lipoprotein cholesterol (HDL- c). Definitions of dyslipidemia are based on guidelines from the World Health Organization: HDL < 0.9 mmol/l or TG ≥ 1.7 mmol/l [(4)].

The role of triglycerides as a risk factor of ischemic stroke remains controversial, however some studies reported a strong association between elevated levels of postprandial triglycerides and increased risk of myocardial infarction, ischemic heart disease, and ischemic stroke [5-7]. The atherosclerosis has long been hypothesized to be a disorder influenced by postprandial effects of TG as early as 1950, when Moreton, suggested a linkage between chylo-micronemia, fat tolerance, and atherosclerosis by affecting endothelial function and producing the atherogenic small LDL particles [8].

Thus measurement of postprandial triglycerides, particularly because they peak 3-4 h after ingestion of a fat-rich meal, might provide more relevant information on vascular risk than measurements based on fasting concentrations [9]. Recent studies found a strong association between elevated levels of postprandial triglycerides, and increased risk of ischemic heart disease [10].

Low serum testosterone levels have been associated with several components of metabolic syndrome, including CVD, hypertension, abdominal obesity, insulin resistance, and inflammatory markers in male individuals independent of age [11,12].

Also, it has been shown that low endogenous testosterone levels are associated with increased risk for both all-cause and cardiovascular mortality [13,14]. Testosterone is a muscle-building hormone, and there are many testosterone-receptor sites in the heart. The weakening of the heart muscle can sometimes be attributed to testosterone deficiency [15].

Testosterone is not only responsible for maintaining heart muscle protein synthesis; it is also a promoter of coronary artery dilation and helps to maintain healthy cholesterol levels [16-18].

The aim of the present study was to stress on the importance of postprandial lipids, in general, and triglycerides, in particular, and its relation to serum testosterone level in evaluating the risk of CVD in males.

Methods

This study included 40 male patients with CVD of age range between 30-60 years and disease duration of 2-15 months, who were attending the Coronary Care Unit (CCU) at Baghdad medical city during the period from December 2011 to June 2012 between 9.00 and 12.00 am. Patients with diabetes mellitus and thyroid disease were excluded from the study. The study also included 46 normal male volunteers of matching age and BMI, Who were non-smokers; non alcoholics and none, had dyslipidemia as revealed from previous laboratory tests.

Ten milliliters (10 ml) of venous blood were withdrawn from both patients and controls, collected in plain tube and centrifuged for 15 minutes at 3000rpm after being allowed to clot at room temperature for 30 minutes. The separated sera were divided into aliquots and stored frozen at -20 ^{o}C to be used for hormonal assays. Postprandial blood glucose, lipid profile, urea and creatinine were measured immediately after separation of the serum. In this study the determination of patients' androgen sex hormones; luteinizing hormone (LH) [19,20], follicle stimulating hormone (FSH) [21], testosterone [22], sex hormone binding globulin (SHBG) [23] were measured by enzyme linked Enzyme-Linked Immune Sorbent Assay (ELISA, Sandwich Assay). Body mass index was calculated as body weight (in Kg)/Sq. height (in meter).

Statistical study

All values were expressed as mean ± standard deviation (mean ± SD). All Statistical analysis was performed using Social process statistical system (SPSS version 15.0). Independent student t-test was performed to assess differences between two means. Pearson correlation coefficient was used to determine the correlation between quantitative data. P value < 0.05 was considered significant.

Results

As shown in table 1, there is a significant difference in total testosterone between the two

groups (P < 0.0001), while no significant differences in SHBG, LH, and FSH (P > 0.05) can be noted. All other biochemical parameters measured were significantly different (including serum lipids, glucose urea and creatinine).

Table 1. Demographic features of cardiovascular disease patients and control subjects

Parameter	CVD Patients N = 40	Control group N = 46
Age (yr)	46.43 ± 9.8	44.17 ± 8.1
BMI (kg/m^2)	30.65 ± 5.53	30.09 ± 5.27
glucose (mmol/l)	6.07 ± 1.64	5.39 ± 1.26*
TG (mmol/l)	2.5 ± 0.73	1.76 ± 0.54‡
Cholesterol (mmol/l)	5.74 ± 0.73	4.42 ± 0.73‡
HDLc (mmol/l)	0.91 ± 0.22	1.18 ± 0.21‡
LDLc (mmol/l)	3.7 ± 0.71	2.38 ± 0.7‡
VLDL c (mmol/l)	1.14 ± 0.33	0.8 ± 0.25‡
Atherogenic index	4.38 ± 1.45	2.15 ± 0.87‡
Urea (mmol/l)	7.42 ± 1.95	5.94 ± 0.71‡
Creatinine (µmol/l)	88.6 ± 25.67	74.18 ± 7.47†
FSH (IU/l)	7.3 ± 5.15	7.4 ± 5.52
LH (IU/l)	6.96 ± 2.72	5.61 ± 2.08*
TT (nmol/l)	9.34 ± 3.51	15.14 ± 5.16‡
SHBG (nmol/L)	32.43 ± 16.9	33.39 ± 15.39

TT = total testosterone, * = P < 0.05, † P = < 0.005, ‡ P = < 0000.1

In the control group, there was a significant negative correlation of BMI with each of total testosterone, and SHBG (r = - 0.263, P = 0.04) (r = - 0.259, P = 0.049) respectively, and significant negative correlations of the postprandial TG with the total testosterone, and SHBG as shown in the fig. 1 and 2, respectively.

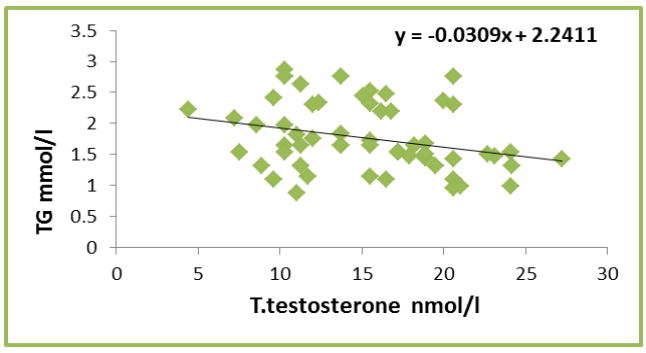

Fig. 1. Correlation between serum total testosterone and postprandial triglycerides

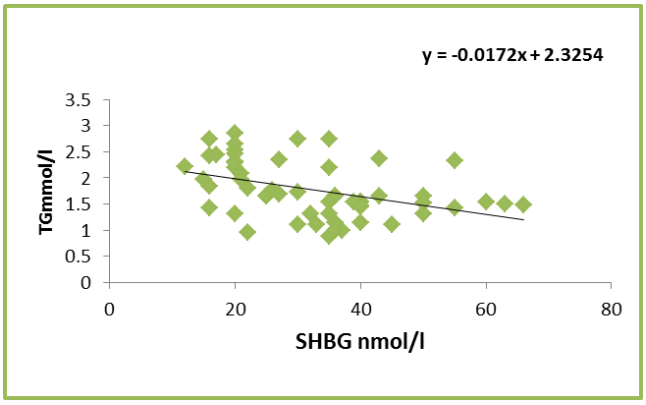

Fig. 2. Correlation between serum sex hormone and postprandial triglycerides

In the CVD patients' group serum total testosterone was negatively correlated with BMI (r = - 0.348, P = 0.028). There was also a negative correlation between total testosterone and postprandial TG as shown in fig. 3.

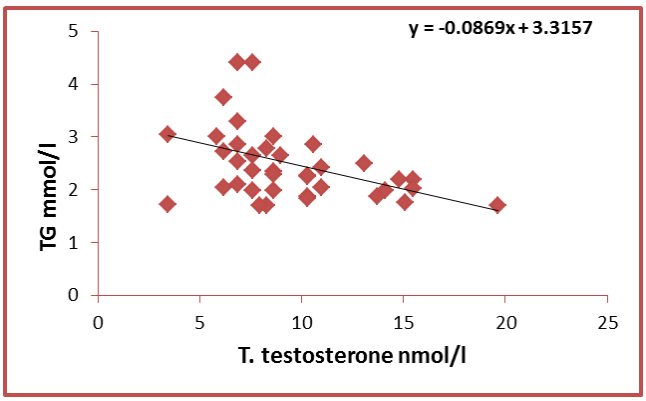

Fig. 3. Correlation between serum total testosterone and postprandial Triglyceride

Discussion

The present results show clearly low serum testosterone in the CVD patients relative to the normal controls, and this reduction in serum testosterone was associated with higher rise in the serum postprandial triglycerides. On the other hand the low serum testosterone negatively correlated with the BMI. Previous report had suggested a role for testosterone in visceral obesity [24]. Visceral fat contains a good number of androgen receptors, and these appear to inhibit the action of lipoprotein lipase and fatty acid/triglyceride uptake; the androgen receptors thus limit fat accumulation [25].

Natural decline of testosterone in the middle aged men and hypogonadism have been reported to associate visceral obesity [26]. Few prospective studies have demonstrated a protective link between endogenous testosterone and CV events [27]. Earlier cohort studies have documented the association of high serum TG with the risk and mortality from ischemic heart disease and stroke [10,28,29].

Increased levels of postprandial TG indicate the presence of increased levels of remnants from chylomicrons and VLDL [28]. These cholesterol-containing, triglyceride-rich lipoproteins penetrate the arterial endothelium, and may get trapped within the subendothelial space potentially leading to the development of atherosclerosis [30,31]. The majority of cross-sectional studies have found a positive correlation of endogenous testosterone with HDL and a negative correlation with total cholesterol, LDLc and triglycerides. Thus normal men with low testosterone appear to have adverse lipid profiles, and hypogonadal men have a potentially atherogenic dyslipidaemia prior to treatment [32,33]. These findings, together with previous reports on the importance of post prandial serum lipids in the prediction of atherosclerosis risk and consequent CVD [34,35], may lead to the speculation that serum testosterone and postprandial TG levels (or either of them) are better predictors than fasting serum lipids for assessment of the CVD risk in normal men or those with classical dyslipidemia. This would, also, necessitate an early testing and early start of preventive measures.

References

1. Antonio M, Gotto Jr. Cholesterol, Inflammation and Atherosclerotic Cardiovascular Disease: Is It All LDL? Trans Am Clin Climatol Assoc. 2011; 122: 256-89.
2. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries. Lancet. 2004; 364(9438): 937-52.
3. Fuster V, Kelly BB, Vedanthan R. Promoting global cardiovascular health: moving forward. Circulation 2011; 123: 1671-78.
4. WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of Diabetes mellitus. Geneva: World Health Organisation, 1999.
5. Bowman TS, Sesso HD, Ma J, et al. Cholesterol and the risk of ischemic stroke. Stroke. 2003; 34: 2930-34.
6. Shahar E, Chambless LE, Rosamond WD, et al. Plasma lipid profile and incident ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. Stroke. 2003; 34: 623-6.
7. Patel A, Barzi F, Jamrozik K, et al. Serum triglycerides as a risk factor for cardiovascular diseases in the Asia-Pacific region. Circulation. 2004; 110: 2678-86.
8. Moreton JR. Chylomicronemia, fat tolerance and atherosclerosis. J Lab Clin Med. 1950; 35: 373-84.
9. Zilversmit DB. Atherogenesis: a post-prandial phenomenon. Circulation 1979; 60:473-85.
10. Freiberg JJ, Hansen AT, Jensen JS, et al. Non fasting Triglycerides and Risk of Ischemic Stroke in the General Population. JAMA. 2008; 300: 2142-52.
11. Yeap BB. Testosterone and ill-health in aging men. Endocrinol Metab. 2009; 5: 113-21.
12. Yeap BB. Are declining testosterone levels a major risk factor for ill-health in aging men? Int J Impot Res. 2009; 21: 24-36.
13. Eckardstein A, Wu FC. Testosterone and atherosclerosis. Growth Horm IGF Res. 2003; 13: S72-S84.
14. Khaw KT, Dowsett M, Folkerd E, et al. Endogenous testosterone and mortality due to all-causes, cardiovascular disease and cancer in men: European prospective investigation into cancer in Norfolk (EPIC-Norfolk) Prospective Population Study. Circulation. 2007; 116: 2694-701.
15. Hayward CS, Webb CM, Collins P. Effect of sex hormones on cardiac mass. Lancet. 2001; 357: 1354-56.
16. Rosano GM, Leonardo F, Pagnotta P, et al. Acute anti-ischemic effect of testosterone in men with coronary artery disease. Circulation. 1999; 99: 1666-70.
17. Jankowska EA, Biel B, Majda J, et al. Anabolic deficiency in men with chronic heart failure: prevalence and detrimental impact on survival. Circulation. 2006; 114: 1829-37.
18. Jackson G. Testosterone deficiency syndrome (TDS) and the heart. Eur Heart J. 2010; 31: 1436-7.
19. Danzer H , Braunstein GD, Rasor J, et al. Maternal serum chorionic gonadotropic concentration and fetal sex predictions. Fertil Steril. 1980; 34: 336-40.
20. Batzer F. Hormonal Evaluation of Early Pregnancy. Fertil Steril. 1980; 34: 1-12.
21. Odell WD, Parlow AF. Cargille CM. Radioimmunoassay for human follicle-stimulating hormone: physiological studies. J Clin Invest. 1968; 47: 2551-62.
22. Moltz L, Schwartz U, Sorensen R, et al. Ovarian and adrenal vein steroids in patients with non-neoplastic hyperandrogenism: selective catheterization findings. Fertil Steril. 1984; 42: 69-75.

23. Selby C. Sex hormone binding globulin: origin, function and clinical significance. Ann Clin Biochem. 1990; 27: 532-41.

24. Vermeulen A, Goemaere S, Kaufman JM. Testosterone, body composition and aging. J Endocrinol Invest. 1999; 22: 110-16.

25. Saad F, Gooren LJ. The role of testosterone in the etiology and treatment of obesity, the metabolic Syndrome, and diabetes mellitus type 2. J Obes. 2011; pii:471584:10 pages.

26. Isidori AM, Giannetta E, Greco EA, et al. Effects of testosterone on body composition, bone metabolism and serum lipid profile in middle-aged men: a meta-analysis. Clin Endocrinol. 2005; 63: 280-93.

27. Ohlsson C, Connor EB, Orwoll E, et al. High Serum Testosterone Is Associated With Reduced Risk of Cardiovascular Events in Elderly Men. J Am Coll Cardiol. 2011; 58: 1674-81.

28. Nordestgaard BG, Benn M, Schnohr P, et al. Non fasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. JAMA. 2007; 298: 299-308.

29. Bansal S, Buring JE, Rifai N, et al. Fasting compared with non-fasting triglycerides and risk of cardiovascular events in women. JAMA. 2007; 298: 309-16.

30. Proctor SD, Vine DF, Mamo JC. Arterial retention of apolipoprotein B (48)- and B(100)-containing lipoproteins in atherogenesis. Curr Opin Lipidol. 2002; 13: 461-70.

31. Kolovou GD, Anagnostopoulou KK, Daskalopoulou SS, et al. Clinical relevance of postprandial lipaemia. Curr Med Chem. 2005; 12: 1931-45.

32. Langer C, Gansz B, Goepfert C, et al. Testosterone up-regulates scavenger receptor BI and stimulates cholesterol efflux from macrophages. Biochem Biophys Res Commun. 2002; 296: 1051-7.

33. Malkin CJ, Pugh PJ, Jones TH, et al. Testosterone for secondary prevention in men with ischaemic heart disease? QJM. 2003; 96: 521-9.

34. Bahir BH, Al-Hadi AHM, Al-Shamma G. Why Not Post Prandial Serum Lipid? Znco J Med Sci. 2008; 22: 165- 8.

35. Ridker PM. Fasting versus Non fasting Triglycerides and the Prediction of Cardiovascular Risk: Do We Need to Revisit the Oral Triglyceride Tolerance Test? Clin Chem. 2008; 54: 111-3.

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Received 19th Nov. 2012: Accepted 13th Feb. 2013.