Testosterone level in angiographically detected coronary artery disease and myocardial infarction

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Abstract

Background: Coronary artery disease a dominant cause for morbidity and mortality. Risk factors in the form of clinical data or biomarkers for atherosclerosis are useful for risk stratification, treatment and prevention.

Objective: This study aims to assess the level of testosterone in stable atherosclerotic heart disease and myocardial infarction compared to normal and effect of DM on testosterone in ischemic heart disease in both stable ischemia and myocardial infarction.

Patients and Methods: In this cross sectional study a total number of 65 male patients were taken. 35 patients with angiographically detected atherosclerosis and 30 patients admitted with acute myocardial infarction that compared to 30 normal controls in Hawler cardiac center during the period from 8th September 2014 till 2nd February 2015.

Results: The level of testosterone was 0.470 ± 0.655ng/ml in atherosclerotic coronary arteries, 0.043 ± 0.008ng/ml in patients with history of acute myocardial infarction and 1.12 ± 0.29 ng/ml in healthy control male, which was statistically significant (P-value 0.002), diabetic patient had further lower testosterone level in all group.

Conclusion: Testosterone assessment may be beneficial in patients with recognized coronary artery disease with no significant conventional risk factors and it could be a novel risk factor .if larger studies performed assessing testosterone level in atherosclerosis.

Key words: Testosterone, Coronary atherosclerosis, Myocardial infarction**.**

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Introduction

Coronary artery disease (CAD) is the leading cause of mortality and morbidity. It is a chronic progressive condition that requires an indefinite treatment. The death risk of coronary disease is twofold higher in male than female which persists even after the cardiovascular risk factors are controlled [2].

Atherosclerosis affects arteries everywhere; complication of this pathology may be fatal in the form of acute stroke, Myocardial infarction and sudden death.

Risk factors in the form of clinical data or biomarkers for atherosclerosis are useful for risk stratification, treatment and prevention [2].

Testosterone has well-recognized roles in men. Inducing secondary sexual characteristics, it is important for preserving sexual function, muscle strength, bone mineral density and mood in adult male [3]. This hormone has a circadian and circannual rhythm; in view of the fact that it has a peak blood levels during morning and in the spring season respectively. Testosterone is a strong coronary vasodilator, an effect mediated by the action of a calcium channel antagonist which consequently has benefits on the angina threshold, particularly in men suffering from a low baseline testosterone [4, 5].

Testosterone therapy reduces total cholesterol, waist circumference, and fat mass as well as pro-inflammatory cytokines that are associated with atherosclerosis, diabetes and metabolic syndrome [6, 7]. Testosterone also, in men with heart failure, improves functional capacity and insulin resistance [8, 9].

In elderly people whose prevalence of CAD is highest, the testosterone level is relatively lower than other groups. Furthermore, males with CAD have lower testosterone levels when compared with men at matched age with normal coronary angiograms [3]. There is a bulk of evidence that testosterone therapy delays the onset of cardiac ischemia which is likely to be as a result of a coronary vasodilator mechanism, and improving the symptom of Angina [10].

Deficiency in testosterone, can lead to undesirable effects including loss of bone and lean body mass, low energy, and impaired physical and sexual function, increased adiposity. Up until recent years, such effects have been considered as the natural ageing physiology; nonetheless, latest studies have recognized that low testosterone can be associated with increased mortality after controlling for baseline morbidity and age[6]. The impact of testosterone on mortality is independent after baseline covariates being adjusted. The majority of the hormone (68%) is present bound tightly to the sex-hormone- binding globulin, with about 30% being loosely bound to albumin and only 2–3% in the free form. The biologically active moiety is the albumin bound that frees testosterone; this is called the 'bio-available' portion [11].

This study aims to assess the level of testosterone in stable atherosclerotic heart disease and myocardial infarction compared to normal and effect of DM on testosterone in ischemic heart disease in both stable ischemia and myocardial infarction.

Patients and Methods

A cross sectional study carried out on total number 65 male patients; 35 patients with angiographically detected atherosclerosis and 30 patients admitted with acute myocardial infarction compared to 30 normal controls in Hawler cardiac center during the period from 8th September 2014 till 2nd February 2015.. At the start of the study, permission of local health authorities to access patients obtained, in addition informed consent of patients obtained too. Patients interviewed and filled out a designed questionnaire for the purpose of this study.

Data collected from each patient using special designed questionnaire. Demographic data include information about the name, age, residence, BMI, history of DM, HT, Smoking, with the level of lipid profile HbA1c and testosterone.

The Assay biotek-Human testosterone ELISA kit (Bioscience, WA, USA) was used to detect anti-testosterone anti-body in the serum.

Statistical analysis

Entered into a computer using the statistical package for social science (SPSS) version [21]. Quantitative variables summarized by finding mean ±SD. P-value

of < 0.05 consider as statistically significant by using Chi Square test.

Hawler cardiac center catheterization lab used to visualize coronary arteries using both GE and Philips machine that are available there, lesion more than 50 % recruited as atherosclerosis and completely normal coronary for healthy control to decrease the bias of observer variability.

Results

Table (1): Demographic characteristics of patients.

Measurements	Value
CA, MI, HC	35, 30, 30
Measurements (MI): Mean± SE	
(Urea (ng/ml	28.32±1.474
(Creatinin(ng/ml	0.817±0.0436
(Troponin(ng/ml	4.413±1.901
(CK-MB(ng/ml	108.27±17.386
(%) Type of MI: No	
Non STEMI	3(10%)
STEMI	23(76.66%)
(%) Location of MI in STEMI: No	
Anterior	18(60%)
Inferior	10(33%)
Lateral	2(6.66%)
(%) .Smoking history: No	
(/Smoker/ (CA/MI	18(51.42)/ 22(73.33)
Non- smoker/ (CA/MI/)	17(48.57)/8(26.66)

Table (1) lists the demographic characteristics of patients, including the relationship between different variables. The age of patients in this study ranged from 30-75 years in which 35 were coronary atherosclerotic patients, 30 patients were having myocardial infarction and 30 of them were healthy A range of measurements were performed for each patient including urea, creatinin, troponin and CK-MB with their respective mean calculated as 28.32, 0.817, 4.413and 108.2Eighteen CA and twenty two MI patients were smoker 18(51.42)/ 22(73.33). There were (3) non- STEMI and (23) STEMI of MI patients.

Mean serum concentration of testosterone among coronary atherosclerotic, myocardial infarction patients and healthy control.

Table (2): Mean serum concentration of testosterone among coronary atherosclerotic, myocardial infarction patients and healthy control.

Parameters	CA No.35	MI patients No.30	HC No.30	P value (F-test)
	Mean ±SE	Mean ±SE	Mean ±SE	
Testosterone (ng/ml)	0.47 ± 0.6	0.043 ± 0.008	1.12 ± 0.29	P=0.002
CA VS MI patients	Testosterone	P value (t-test)	P=0.001	
CA VS HC patients			P=0.001	
MI VS HC patients			P=0.002	
HC: Healthy control; MI: Patient co; P≤0.01: Highly significant; P>0.05:Non significant				

The mean serum concentration of testosterone in CA, MI patients and healthy control were detailed in table (2). There was highly significant difference between three groups in terms of the mean of testosterone.

Parameters	Body mass index	No.	CA Patients	No.	MI patients	P value T-test
			Mean ± SE		Mean ± SE	
Testosterone (ng/ml)	Obese	13	0.518±0.1	14	0.048±0.01	0.001
	Non obese	22	0.439±0.07	16	0.045±0.01	0.001

Table (3): Mean serum concentration of testosterone among CAPs, MI patients and healthy control.

Table (3) shows the probability of testosterone between CA and MI patients regarding their obesity. Serum concentrations of testosterone in obese patients were 0.518±0.1 and 0.048±0.01 respectively with statistically high significant difference. Regarding non-obese serum concentrations were 0.439±0.07 and 0.048±0.01 respectively with highly significant difference.

Table (4): Mean serum concentration of testosterone among (DM and non DM, HTN and non HTN, smoker and non-smoker) CA and MI patients.

Parameter	Patients	No.	CA Patients	No.	MI patients	P value T-test
			Mean ± SE		Mean ± SE	
Testosterone(ng/ml)	DM	10	0.29±0.1	11	0.031±0.01	0.028
	Non DM	15	0.51±0.07	19	0.047±0.01	0.001
	HTN	24	0.52±0.09	15	0.039±0.01	0.001
	Non HTN	11	0.36±0.1	15	0.046±0.01	0.006
	Smoker	18	0.52±0.1	22	0.012±0.8	0.002
	Non smoker	17	0.385±0.8	8	0.0376±0.01	0.013

The mean of testosterone concentration in diabetic and non-diabetic, hypertensive and non-hypertensive, smoker and non-smoker patients were detailed in table (4). There was significant difference between the groups in terms of the mean of diabetic and non-smoker patients. There was highly significant difference between the groups in terms of non-diabetic, hypertensive, non-hypertensive and smoker patients.

Table (5): Baseline characteristics among CAPs and healthy control.

Parameters	CA patients No (35)	MI patients No (30)	P value T-test	Probability
	Mean ± SE	Mean ± SE		
Age (years)	53.89± 2.4	58.093 ± 1.6	0.001	HS**
HDL(mg/dl)	32.625±1.3	30.07.87 ±1.13	0.290	NS
LDL (mg/dl)	106.87± 5.1	102± 7.9	0.362	NS
Body mass index	27.135± 2.8	28.035 ± 2.9	0.380	NS
Hemoglobin A1c%	7.34 ± 0.4	9.763± 0.4	0.005	HS*

LDL: Low density lipoprotein; **HDL**: High density lipoprotein* P >0.05: **Non significant**; **P<0.01: **Highly significant**

The mean serum concentration of total age, HDL, LDL, body mass index and hemoglobin were detailed in table (5). There were highly significant differences between CA and MI patients regarding age and hemoglobin (P<0.01). There were non-significant differences between CA and MI patients regarding HDL, LDL and body mass index (P<0.05).

Discussion

The most effective independent risk factors for CAD are that of advanced age and the male gender. Despite a wide discrepancy in CAD mortality between countries, a constant male: female ratio of about 2:1 can be seen [12]. Such data paved the way to conclude that male hormones particularly testosterone, exert a detrimental influence on cardiovascular system.

In this study, males with established coronary artery disease by coronary angiography or presenting as acute myocardial infarction had a statistically significant lower level of androgens in their serum compared to control males whose coronary angiogram found to be normal. Men with proven normal coronary arteries were chosen as control in order to exclude individuals with subclinical coronary artery disease as controls.

Review of the published cross-sectional studies which have reported the serum levels of testosterone in men with CAD, demonstrates that in the majority of cases serum levels of testosterone are reduced in men with CAD [13]. Recent studies which have specifically investigated the association between endogenous sex hormones and CAD, also report a negative correlation between serum levels of testosterone and atherosclerotic burden. Similarly, Keating et al. [16] report that androgen deprivation therapy via gonadotropin-releasing hormone agonism, in men with prostate carcinoma, is associated with an increased risk of diabetes, coronary heart disease, myocardial infarction and sudden cardiac death. Furthermore, a study by Phillips et al. [17] of 55 men aged 39-89 years, also reported an inverse relationship between serum testosterone and the degree of CAD which was similar to what we detected that myocardial infarction presenting with total coronary occlusion had significantly lower testosterone level than stable coronary lesion.

Studies consistently show significant relationships between serum testosterone and body fats in obese individuals and to a great extend in healthy population [18]. Free levels of testosterone have been found to be inversely related to obesity in a number of studies with the link dominantly seen with central obesity. Most of these studies report correlations with waist-to-hip ratios but one study of 23 men confirmed that visceral fat level assessed by CT scan, was negatively correlated with free and total testosterone [19]. Our study similarly concluded that obese patients based on BMI, have a lower level of testosterone than non- obese. Obesity can be considered as one of the causes of hypotestosteronaemia in view of two separate mechanisms. In men with high BMI, may be expected to have low levels of testosterone as a result of augmented conversion in body fat as well as muscle of androstenedione to oestrone via aromatase [24]. Obesity can also inhibit the hypothalamic-pituitary-gonadal network most probably in the presence of substances like leptin [18].

Furthermore results of this study confirmed that diabetic patients found to have significantly lower level of testosterone than non-diabetic patients in all the three groups. Studies dating back nearly 30 years have described low total testosterone in men with type 2 diabetes. A meta-analysis of 21 studies including data from 3,825 men confirmed this and suggested that levels were on average 2.66nmol/l lower in men with diabetes compared with controls [19]. We postulate that androgen deficiency plays a central role in the pathology of metabolic syndrome, type 2 Diabetes, and Insulin resistance, and contributes significantly to processes of adipogenesis and increased accumulation of visceral fat, resulting in obesity. Visceral fat serves as an endocrine organ, which produces proinflammatory

cytokines affecting multiple tissues and organs and further increasing the risk for insulin resistance, type 2 DM, metabolic syndrome and endothelial dysfunction leading to vascular complications [20]. However, to date no studies have specifically investigated whether testosterone therapy reduces cardiovascular events, although a number of studies have investigated the effect of testosterone therapy on measures of myocardial ischaemia in men with angina.

Recent evidence suggests that this may be a population as large as 1 in 4 of all men afflicted with the condition [21]. Constituting a considerable population worldwide. Androgen replacement as a therapy seems to be valuable for certain patents at their advanced ages. Hence, this study implies on the fact that such therapeutic approaches not only would confer lower cardiovascular risk but rather it would be of cardiovascular benefit. The findings in this work therefore, provide a great support for a further extensive evaluation. It also provides a large and long-term clinical trial for the role of androgens in the development of cardiovascular disease in men. Moreover, its role as being an overlooked therapeutic opportunity for this patient population need to be revised [22].

In conclusion, testosterone assessment may be beneficial in patients documented to have coronary heart disease with no significant conventional risk factors.

A study to perform for the possible beneficial effects regarding symptomatic, angiographical coronary changes or prognostic improvement on patients with documented low testosterone when no other significant risk factor detected.

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