ORIGINAL ARTICLE

Serum levels of sex hormones in men with acute myocardial infarction

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Abstract

OBJECTIVE: To compare the serum levels of total testosterone(TT), free testosterone (FT), estradiol, sex hormone binding globulin (SHBG), and androstenedione (AS) in patients with acute myocardial infarction (AMI) at the time of hospitalization, patients with old myocardial infarction (OMI), and patients with normal coronary arteries (NC) admitted for diagnostic coronary angiography.

METHODS: Serum sex hormones and lipid profile were measured in 79 male patients; 30 patients with AMI, 21 patient with OMI and 28 patients with NC. Ages ranged from 33-68 years. Androstenedione, estrogen, both total and free testosterone levels were quantified using coat-a-count radioimmunoassay kits. Sex hormone binding globulin was analyzed using immunoradiometric assay (IRMA)-count kits.

RESULTS: The levels of serum estradiol in the AMI were significantly higher and serum levels of TT, FT, and SHBG were significantly lower in AMI than in OMI and NC but there was no difference found for the levels of AS in all groups. Estradiol level was also higher in OMI than in control group but no significant changes found for other sex hormones in OMI and control group. Also triglyceride, high density and low density lipoprotein in AMI were significantly different from that in OMI and control groups.

CONCLUSIONS: Serum estradiol and low density lipoprotein levels are increased but TT, FT and SHBG levels are decreased in men with AMI compared with patients with NC.

INTRODUCTION

The ischemic heart disease is expected to become the leading disease burden by year 2020 [1]. The relationship between serum levels of endogenous sex hormones in male and myocardial infarction was the subject of many studies with no clear cut results. For example an increase in serum estradiol hormone levels during acute myocardial infraction was reported by many studies [2-5] while other showed a decrease in estradiol level in CHD [6]. Other studies showed a decrease [7,8,9], no change [10] in serum testosterone level. Cauley *et al.* [11] reported no significant difference in sex hormones concentration including TT, FT, estradiol, SHBG and AS, between patients with CAD and controls with normal coronaries.

The question whether sex hormones serum levels could be a risk factor for coronary artery disease (CAD) or not had been explored by many investigators. High androgen levels [12], low testosterone [6,13], high estradiol levels [14,15] were considered as a risk factors for CAD.

Exogenous testosterone in supraphysiological doses was reported to improve myocardial ischemia and induces beneficial effects on exercise- induced myocardial ischemia in men with CAD [16,17], but increasing testosterone concentration 2-6 times had neither beneficial nor deleterious effects on the onset or magnitude of stress induced myocardial ischemia in patients with stable CAD [18] Testosterone was also reported to induce direct relaxation of preconstricted rabbit coronary artery [19] and estradiol was reported to exert rapid and long term vasodilatory effect on blood vessels of human and animals [20,21].

With all these findings regarding different effects of sex hormones on the cardiovascular system particularly on the development of CAD and different levels of sex hormones during acute myocardial infarction, this study is planned to examine the concentration of endogenous sex hormones during acute myocardial infarction in men. Also we looked at the levels of serum total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG). All those values will be compared to the values obtained from control group with normal coronaries and patients with old myocardial infarction.

PATIENTS AND METHODS

The study population includes 79 male patients. Patients with valvular heart disease, congenital heart disease or congestive heart failure were excluded from the study. Also patients with hepatic, renal, and thyroid diseases were excluded from all groups. Informal consents were obtained from all participants in this study. The research was approved by ethics and human research committee at Jordan University of Science and Technology.

The 79 patients are grouped into three groups:

Group 1.

Patients with acute myocardial infarction (AMI): These 30 men aged 37-66 years, mean 52.3±5.2 (SD) had electrocardiography (ECG) and serum creatine kinase (CK) evidence of acute myocardial infarction and were admitted to a coronary intensive care unit and coronary angiography was done for all patients within one month after discharge from the hospital.

Group 2.

Patients with old myocardial infarction (OMI): These 21 men aged 39-66 years, mean 54.8±7.6 (SD) had myocardial infarction before 4-6 months and admitted to cardiology department for coronary angiography for evaluation and diagnosis of their coronaries.

Group 3.

28 Patients aged 33-68 years, mean 51.1± 6.5 (SD) admitted to cardiology department for diagnostic coronary angiography because of frequent attack of chest pain without electrocardiography evidence of CAD, and found to have normal coronaries. These patients included in the study as control subjects but exposed to physical and emotional stress of severe medical illness.

Left heart catheterization and coronary angiography were performed to all patients from femoral approach.

Analysis of blood samples

Blood samples were withdrawn from patients with OMI and NC between 8 and 9 am after 14 hours fasting and just before coronary angiographic procedure. Blood samples from patients with AMI, blood samples were obtained during acute illness as proved by ECG and cardiac enzyme (creatine kinase). Serum was separated from the formed element by centrifugation and kept frozen at –70 °C until analyzed. Androstenedione, estrogen, both total and free testosterone levels were quantified using coat-a-count radio immunoassay kits. Sex hormone binding globulin was analyzed using IRMA-count kits. All kits were purchased from diagnostic products corporation, Los Angeles, CA. Blood samples were collected in 0.1% EDTA tubes, centrifuged for 20 minutes at 1 000×g at 4 °C to obtain plasma for assessment lipid profile.

Statistical analysis

Data are expressed as mean ± standard deviation (SD). Significant test were carried out using one-way ANOVA and unpaired student t-test for intergroups analyses. p-values less than 0.05 were taken as being significant.

RESULTS

Table 1 shows the characteristics of the participants in the three groups enrolled in this study. There was no significant difference between the three groups in regard to age and other anthropometric measures.

Table 1. Characteristics of men participated in the study.

	Patients with AMI (n=30)	Patients with NC (n=28)	Patient with OMI (n=21)	p-value
Age (yr)	52.3±5.2	51.1±6.5	54.8±7.6	0.2
Height (cm)	170.4±4.1	171.7±3.7	171.9± 3.5	0.3
Weight (kg)	75.2±6.8	75.5±.3.8	75.1±5.5	0.6
Body Mass Index (BMI) (kg/m^2)	25.9±2.7	25.6±2.9	25.1±1.8	0.3

All values are mean ± SD

Table 2 compares the mean concentrations of sex hormones and lipoprotein in patients with AMI and OMI. Data showed there were significant different of TT, FT, estradiol, SHBG, TG, HDL (p=0.002, 0.0001, 0.002, 0.0001, 0.002, 0.03) respectively. While there were no significant difference of mean concentration of AS, TC, and LDL between the two groups.

Table 3 compares the mean concentrations of sex hormones and lipoprotein in patients with AMI and men with NC .Data showed there were significant different of TT, FT, estradiol, SHBG, TG, HDL, LDL (p=0.0001, 0.0001, 0.0001, 0.04, 0.007, 0.03, 0.005) respectively. But there were no significant difference of mean concentration of AS and TC between the two groups.

Table 4 compares the mean concentrations of sex hormones and lipoprotein in patients with OMI and men with NC. Data showed there were significant elevations of estradiol and LDL in patients with OMI (p=0.006, 0.05), but no significant different for other hormones and lipid profile between the two groups.

DISCUSSION

We study the relationship between serum levels of estrogen, TT, FT, SHBG, and AS in acute myocardial infarction patients and compare them with their levels in patients with OMI and NC. During AMI, estradiol plasma levels were significantly higher than that in OMI and NC (Table 2 and 3). This finding was reported by other investigators [2,6,8]. The increased level of estradiol could be protective mechanism since it increases the vasodilatation and inhibits the response of blood vessels to injury [22]. The high estradiol level in AMI patient could be due the stress factor associated with severe medical illness like myocardial infarction. However no similar rise in estradiol level in NC patients was observed even these men experienced chest pain and emotional stress similar to that of myocardial infarction but to a lesser extent. Also he levels of AS did not differ significantly in all three groups and this rules out the possibility that stressful conditions were behind the high level of estradiol in AMI patients.

TT, FT and SHBG serum levels were significantly lower in AMI patients than in patients with OMI and

Table 2. Plasma sex-hormones and lipoprotein in men with AMI and men with OMI.

	Patients with AMI (n=30)	Patients with OMI (n=21)	p-value
Total testosterone (ng/ml) (TT)	12.4±3.1	15.5±3.7	0.002
Free testosterone (pg/ml) (FT)	49.2±10.9	64.9±12.6	0.0001
Estradiol (pg/ml)	52.9±10	45.2±8.5	0.002
Sex hormone-binding globulin (nmol/L)	23.6±4.8	31.7±4.6	0.0001
Androstenedione (ng/ml)	8.5±2.4	8.4±2	NS
Total cholesterol (TC) mg/dl	215±42	226±40	NS
High density lipoprotein (HDL) mg/dl	39±7	44±10	0.03
Low density lipoprotein (LDL) mg/dl	133±20	144±35	NS
Triglyceride (TG) mg/dl	226±54	187±42	0.002

Values are mean ± standard deviation. p>0.05; Not significant (NS)

Table 3. Plasma sex-hormones and lipoprotein in men with AMI and men with NC.

	Patients with AMI (n=30)	Patients with NC (n=28)	p-value
Total testosterone (ng/ml) (TT)	12.4±3.1	16.9±4.5	0.0001
Free testosterone (pg/ml) (FT)	49.2±10.9	61.9±12.7	0.0001
Estradiol (pg/ml)	52.9±10	39.2±6.7	0.0001
Sex hormone-binding globulin (nmol/L)	23.6±4.8	28.3±10.5	0.04
Androstenedione (ng/ml)	8.5±2.4	7.8±2.2	NS
Total cholesterol (TC) mg/dl	215±42	208±35	NS
High density lipoprotein (HDL) mg/dl	39±7	44±9.6	0.03
Low density lipoprotein (LDL) mg/dl	133±20	121±15.7	0.005
Triglyceride (TG) mg/dl	226±54	196±33	0.007

Values are mean ± standard deviation. p>0.05; Not significant (NS)

Table 4. Plasma sex-hormones, concentrations in men with OMI and NC.

	Patients with NC (n=28)	Patients with OMI (n=21)	p-value
Total testosterone (ng/ml) (TT)	16.9±4.5	15.5±3.7	NS
Free testosterone (pg/ml) (FT)	61.9±12.7	64.9±12.6	NS
Estradiol (pg/ml)	39.2±6.7	45.2±8.5	0.006
Sex hormone-binding globulin (nmol/L)	28.3±10.5	31.7±4.6	NS
Androstenedione (ng/ml)	7.8±2.2	8.4±2	NS
Total cholesterol (TC) mg/dl	208±35	226±40	NS
High density lipoprotein (HDL) mg/dl	44±9.6	44±10	NS
Low density lipoprotein (LDL) mg/dl	121±15.7	144±35	0.05
Triglyceride (TG) mg/dl	196±33	187±42	NS

Values are mean ± standard deviation. p>0.05; Not significant (NS)

NC (Table 2 and 3). This low level of testosterone in patients with either myocardial infarction or CAD was found by 16 studies (see the excellent review by Wu and von Eckardstein ref. 23). Is this low level of testosterone a precipitating factor for development of myocardial infarction? Many studies supported this hypothesis as it has been found that testosterone increases fibrinolytic activity [24], has antiartherogenic effect [25] and it shows a positive correlation with HDL and inverse correlation with LDL [26]. However these protective actions of testosterone is in supra-physiological concentration; Rosana *et al.* [17] found that testosterone in concentrations of 100 times normal level delayed ST depression during exercise in men with CAD, while Thompson *et al.* [18] had showed that increased testosterone in plasma had neither a beneficial nor deleterious effect on the onset and magnitude of stress-induced myocardial ischemia in men.

Comparing the sex hormones level in AMI patient with those of OMI, it appears that during AMI stage, estrogen level was significantly higher while TT, FT and SHBG were significantly lower than at four to six months afterwards. These findings indicate that during the stress of AMI illness, sex hormones levels were significantly changes and these changes were gradually disappeared except estradiol concentration (Table 4). These changes could be due to elevated serum norepinephrine levels which have been reported in patients with AMI [27]. A major source of estradiol production in normal men is conversion of testosterone to estradiol via aromatization in muscle and adipose tissues [28]. The high levels of norepinephrine, during high stress of acute illness as myocardial infarction, stimulates aromatization of testosterone to estradiol resulting in elevation of estradiol and low testosterone levels in these categories of patients which demonstrated by this study and others [2,3,8]. On the other hand, comparing the concentrations of these sex hormones in patients with OMI and control group of NC, we found that there was no significant changes (Table 4) in the level of TT, FT, SHBG, and AS which was also reported by other studies [5,11], while estradiol was still significantly higher in OMI than in control group with NC as also demonstrated by other studies [2,3,5,13].

Our Study examined also serum levels of lipoproteins in AMI, OMI, and NC patients. During AMI, TG serum levels were significantly higher and HDL was significantly lower than in OMI but there was no significant changes in LDL. These changes in lipid profile during AMI could be secondary to the changes in testosterone serum level [29] or due to changes in estradiol serum levels [30].

CONCLUSION

During AMI, serum estradiol level was significantly higher while TT, FT and SHBG were significantly lower than in OMI and NC patients. Also during AMI, TG were significantly higher than in OMI and NC patients and significant low HDL during acute attack than OMI and NC patients. These changes could be developed because of high stress during AMI. Level of LDL were significantly higher during AMI compared with NC patients, but no significant changes showed with OMI.

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