EFFECT OF SMOKING ON LEPTIN CONCENTRATION IN NORMAL SUBJECTS AND DURING ACUTE MYOCARDIAL INFARCTION

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SUMMARY: The purpose of this study was to measure leptin concentrations in the blood of smokers and non smokers during ST elevation acute myocardial infarction, and to compare them with values obtained from normal smoker and non smoker subjects. Leptin serum concentrations were measured in 58 patients (34-75 years of age) with acute myocardial infarction and 38 normal subjects (36-69 years of age). Leptin serum concentrations were measured using two-site immunoradiometric assay (IRMA) principle. In normal smokers (N=20) leptin concentration was 5.8 ± 2.5 ng/ml (mean ± SD), while in non smokers (N=18) this value was 5.9 ± 4.1 ng/ml (mean ± SD). Data showed no significant difference in both groups (p > 0.05). While leptin concentration was 7.8 ± 2.9 ng/ml in smoker patients (N=32) which was significantly higher than in normal smoker subjects (p=0.02). Also leptin value was 9.2 ± 3.7 ng/ml in non smoker patients (N=28) which was also significantly higher than in normal non smoker subjects (p=0.001). Our results demonstrated that smoking has no effect on leptin concentrations in normal subjects and in patients with acute myocardial infarction, but leptin concentration increases significantly during ST elevation acute myocardial infarction in smoker and non smoker patients.

Key Words: Smoking, Leptin, Myocardial infarction.

INTRODUCTION

Leptin is a 16-KDa protein produced by obesity gene, first implicated in the regulation of metabolism and food intake (1). Cardiovascular risk factors such as hypertension and atherosclerosis, which increased with increasing obesity, were associated with increased circulating plasma leptin levels (2-4). Leptin is also produced in addition to the adipose tissue by heart, vascular smooth muscle, placental tissue, digestive epithelia and gastric mucusa (5-8). There is a conflict on vascular function of leptin. Some studies indicated that leptin is a nitric oxide (NO) dependent vasodilator in various non coronary vascular beds (9, 10) whereas others showed that it exerts NO-independent vasodilatation

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(11). Other studies have shown that leptin increases peripheral resistance through increasing sympathetic nervous activity (12,13-15). Leptin is also involved in many atherogenic processes common to pathogenesis of cardiovascular disease, including platelate aggregation and thrombosis (16-18). In addition leptin causes cardiac hypertrophy (19, 20) and vascular smooth muscle hypertrophy (21).

Atherosclerosis is one of known high risk factors in cardiovascular disease and mortality. Peelman *et al.* (22) identified high expression levels of leptin receptors in atherosclerosis lesions. Atherosclerosis causes also abnormalities in endothelial function and leptin induces directly endothelial cell migration (23, 24) which contributes to the peptides proatherogenic effects.

Leptin receptors are present in coronary arteries and hyperleptinemia produces significant coronary endothelial dysfunction (25). In addition hyperleptinemia is an independent risk factor for coronary artery disease (26) and strong predictor of acute myocardial infarction (27). Other studies reported hyperleptinemia in patients with acute myocardial infarction (25, 28, 29).

Smoking is the other risk factor for cardiovascular disease like coronary artery disease and hypertension. The effect of smoking on the plasma leptin concentration level is still controversial, some studies showed an increase leptin concentration in smoker people (30-32), other studies reported a lower leptin level in smoker people (33, 34) while third group studies showed no significant difference of plasma leptin level in smoker and non smoker people (35, 36).

With all these findings regarding the different effects of leptin on cardiovascular system, mainly on development of coronary artery disease. This study is planned to examine the concentration of leptin hormone level during ST segment elevation acute myocardial infarction (STEMI) in smoker and non smoker men. We also examined the effect of smoking on leptin concentrations in normal subjects. In addition we measured the level of total cholesterol (TC) and triglyceride (TG). All these values will be compared to the values obtained from smoker and non smoker control group without coronary artery disease.

MATERIALS AND METHODS

Patients and methods

The subjects participated in this study were grouped into group 1 (normal) and group 2 (patients). The study population of group 2 includes fifty eight male patients with acute ST elevation myocardial infarction (STEMI), 32 smokers aged from 34 to 75 (mean, 50.1; SD ± 9.1) years and 26 non smokers aged from 35 to 75 (mean, 55.4; SD ± 11.8) admitted to the department of cardiology, coronary care unit in Queen Alia Heart Institute and Princess Basma Teaching Hospital. Patients with valvular heart disease, congenital heart disease, diabetes mellitus, hypertension and congestive heart disease were excluded from the study. Also patients with hepatic, renal and thyroid diseases were excluded from the study.

Thirty eight normal male volunteer subjects without history of chest pain, coronary artery disease (CAD), ECG changes, hypertension, or diabetes were included in this study and this group designated group 1 normal control; twenty smoker normal subjects aged from 36 to 68 (mean, 52.8; SD ± 10.4) years and eighteen non smoker normal subjects aged from 39 to 69 (mean 51.2; SD± 9.9) years were also studied.

Informal consents were obtained from all patients and volunteers. The base line characteristics of patients such as age, blood pressure, smoking status and body mass index (BMI) were recorded.

Analysis of blood samples

Blood samples were withdrawn from all patients with STEMI within 24 hours from the time of admission to the coronary care unit after 14 hours fasting. Also blood samples from normal volunteer subjects taken after 14 hours fasting. Serum was obtained from all blood samples and frozen at -70°C for later determination of leptin levels. Leptin concentrations were measured using two-site immunoradiometric assay (IRMA) principle. All kits were purchased from Diagnostic System Laboratories, INC. Webster, Texas 77598.

Statistical analysis

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

RESULTS

The characteristics of the normal volunteer subjects (group 1) are shown in Table 1. Subjects in this group had similar mean age and other anthropometric measures in smoker and non smoker people. No significant difference was seen between smokers and non smokers regarding age, body mass index (BMI), triglyceride and

Table 1: Characteristic of normal volunteers participated in the study.

	Normal non smokers (n=18)	Normal smokers (n=20)	P
Age (year)	51.2 ± 9.9	52.8 ± 10.4	NS
BMI (kg/m^2)	27.9 ± 2.2	28.3 ± 1.9	NS
Total cholesterol (mg/dl)	233.7 ± 15.8	217 ± 21.5	0.01
Triglyceride (mg/dl)	194.1 ± 9.3	195.7 ± 12.3	NS
Leptin (ng/ml)	5.9 ± 4.1	5.8 ± 2.5	NS

Table 2: Comparison between normal smokers and smoker patients.

	Normal smokers (n=20)	Patient smokers (n=32)	P
Age (year)	52.8 ± 10.4	50.1 ± 9.1	NS
BMI (kg/m^2)	28.3 ± 1.9	27.8 ± 8	NS
Total cholesterol (mg/dl)	218.6 ± 13.2	246.6 ± 12.3	0.0001
Triglyceride (mg/dl)	195.7 ± 12.3	220.6 ± 5.8	0.001
Leptin (ng/ml)	5.8 ± 2.5	7.8 ± 2.9	0.02

Table 3: Comparison between normal non smokers and non smoker patients.

	Normal non smokers (n=18)	Patient non Smokers (n=26)	P
Age (year)	51.2 ± 9.9	55.4 ± 11.8	NS
BMI (kg/m^2)	27.9 ± 2.2	27.3 ± 2.5	NS
Total cholesterol (mg/dl)	242.9 ± 8.8	253.3 ± 8.7	0.02
Triglyceride (mg/dl)	194.1 ± 9.3	212.8 ± 8.8	0.001
Leptin (ng/ml)	5.9 ± 4.1	9.2 ± 3.7	0.001

BMI: body mass index All values are mean±SD

leptin but there was significant difference regarding total cholesterol which is higher in non smoker people. Table 2 shows comparison between control smoker and smoker patients with acute MI. There is no significant difference regarding age and BMI, but significant difference in leptin, triglyceride and total cholesterol which are all higher in patients with acute myocardial infarction than control group. Table 3 compares the control non smoker with patient non smoker groups. It shows no significant difference regarding age and BMI, but significant differences in total cholesterol, triglyceride, and leptin again all are higher in patients compared to the normal group.

DISCUSSION

In our study, serum leptin levels were not significantly affected by smoking in normal healthy subjects as it is shown in Table 1 where there are no significant dif-

ferences between values of serum leptin in smoker subjects and non smoker normal subjects. Similar findings were also reported by other investigators (35, 36). Table 1 also shows that there is no significant difference in TG but higher TC in non smoker than smoker subjects. This high level of TC in non smokers could be due to the type of food intake. Comparisons between the serum levels of TC, TG and Leptin in acute myocardial infarction patients smoker and non smoker with their levels in normal subjects are shown in (Tables 2 and 3). In smoker patients there was significant increase in serum levels of leptin than in normal smoker subjects and also significant difference in TC and TG between smoker patients with AMI and normal smoker subjects (Table 2). We also found same observations in non smoker patients compared to non smoker normal subjects for TC, TG and leptin (Table 3). This high level of leptin in patients with AMI was found by many previous studies (25, 28, 29, 37, 38, 39). An evidence suggests that myocardial infarction is associated with local and systemic inflammation (40) and this inflammatory effect could contribute to increase C-reactive protein from the liver which is also reported by Wong *et al.* (41) and C-reactive protein may act directly on fat cells to increase leptin secretion in setting of acute myocardial infarction (42-44). Hyperliptenemia increases stimulation of the sympathetic system to increase catecholamine (45). TC and TG results showed also significant difference between patients and normal subjects as they are well known risk factors for development of atherosclerosis and coronary artery disease. Despite small sample size in our study, serum leptin level appeared higher in acute myocardial infarction in addition to high level of TG and TC and there was no significant change in leptin concentration in smoker and non smoker normal subjects. There are several reasons for increased serum leptin to increase the cardiovascular risk; leptin stimulates vascular smooth cell proliferation (46), accelerates vascular calcification (47), induces oxidative stress in endothelial cells that may contribute to atherogenesis (48), and promotes coagulation by increasing platelet adhesiveness (49).

In conclusion our observations strongly indicate that serum leptin level is elevated in acute ST elevation myocardial infarction in smoker and non smoker patients. Thus serum leptin may be an important metabolic factor during acute myocardial infarction and it could be possibly a risk factor. Also our findings indicate that smoking has no significant effect on leptin concentration in normal subjects and patients with acute myocardial infarction.

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