STUDIES IN PHYSICAL CULTURE AND TOURISM
Vol. 16, No. 2, 2009

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ASSOCIATION BETWEEN OXIDATIVE STRESS MARKERS AND METABOLIC DISTURBANCES IN OVERWEIGHT AND OBESE WOMEN

Key words: oLAB, TBARS, TAS, AIP, blood pressure.

ABSTRACT

The aim of study was to investigate the association between oxidative stress and anthropometric and metabolic parameters in middle-aged, overweight or obese women. Venous blood samples were taken from each subject after an overnight fast, and the following parameters were assessed: plasma total antioxidant status (TAS), plasma concentrations of thiobarbituric acid reactive substances (TBARS), serum levels of antibodies against oxidized low density lipoproteins (oLAB), serum lipid profiles, and serum glucose and insulin concentrations. Additionally, serum low density lipoprotein (LDL) cholesterol and insulin resistance indices and atherogenic index of plasma (AIP) were calculated. Correlations were noted between plasma thiobarbituric reactive substances (TBARS), antibodies to oxidized LDL (oLAB), and total antioxidant status (TAS); and blood pressure (BP), insulin resistance parameters and lipids profile. The levels of antibodies to oxidatively modified low-density lipoproteins oLAB correlated with systolic and diastolic BP, TAS correlated negatively with the atherogenic index of plasma (AIP). An association was found between oxidative stress and BP, and lipid risk factors in obese and overweight women.

INTRODUCTION

Obesity is associated with several metabolic disorders such as atherogenic dyslipidemia, hyperinsulinemia, hyperglycemia and insulin resistance, imbalance between clot formation and fibrinolysis, excessive activation of the rennin-angiotensin-aldosterone system and chronic inflammation. It has been found that obesity combines with systemic oxidative stress [8]. Available data suggest that metabolic disturbances associated with obesity are interrelated, and oxidative stress may be one of the common causative factors [10]. The aim of the present study was to investigate the association between oxidative stress markers and selected parameters of insulin resistance, lipids profile, body composition and blood pressure values in a group of middle-aged, healthy women with overweight or mild to moderate obesity.

METHODS

The study sample consisted of 45 women with overweight (BMI 25.0 – 29.9 kg/m^2) or mild to moderate obesity (BMI 30 – 39.9 kg/m^2) aged>18 years, who volunteered to participate in

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a slimming program offered by the University School of Physical Education in Poznan (Poland) and declared good health status. In particular, the subjects were asked questions about smoking, diabetes mellitus, hypertension, renal or hepatic impairment, congestive heart failure, pregnancy, active inflammatory disease, history of a myocardial infarction or stroke, and any chronic drug administration. Each of these conditions was an exclusion criterion. Blood pressure, body height and body mass were measured in all women. Additionally, body composition was assessed in each subject using a bioelectric impedance method (Spectrum Lightweight analyzer made by Acern, Italy).

Blood samples were taken from the antecubital vein after an overnight fast. The total antioxidant status (TAS) was measured in the heparinized plasma samples with a commercially available assay (Randox Laboratories Ltd., Crumlin, Co. Antrim, U.K). TAS reflects the residual antioxidant capacity after the neutralization of free radicals in plasma, and is a measure of the current balance between oxidants and antioxidants. Plasma concentration of thiobarbituric acid reactive substances (TBARS), regarded as a measure of lipid peroxidation in plasma, was assessed using a modified spectrophotometric method with chromogen extraction with n-butanol, described by Buege and Aust [4]. This method involves the acidic breakdown of lipid peroxides into malondialdehyde molecules. In the serum samples, levels of antibodies to oxidized LDL were measured with a commercially available enzyme-linked immunoassay (Biomedica GmbH, Austria).

The concentrations of glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides (TG) were measured in the serum samples (Cormay, Poland). LDL-cholesterol concentration was calculated with the formula proposed by Friedewald. To assess the atherogenicity of plasma lipoproteins, we calculated the logarithm of the ratio of plasma concentration of triglycerides to HDL-cholesterol (atherogenic index of plasma, AIP) [6].

The insulin level was assessed using a commercially available radioimmunoassay (INS-IRMA, BioSource S.A., Belgium). Insulin sensitivity index $HOMA_{IR}$ (Homeostasis Model Assessment Insulin Resistance) was calculated according to the formula of Matthews et al. [9].

Informed, written consent was obtained from each subject prior to the enrolment in the study. The study protocol was accepted by the local Ethics Committee for Research in Humans.

The results are shown as mean ± standard deviation (SD). Data were analyzed using Spearman rank correlation; $p<0.05$ was considered statistically significant.

RESULTS

The mean age of our study population was 47±10.2 years. The mean body mass was 86.3±11.94 kg, the mean BMI was 30.7±3.32 kg/m^2. The body fat mass assessed with the bioelectric impedance method was 32.4±7.87 kg. The mean systolic blood pressure was 129.6±17.31 mmHg, and the diastolic blood pressure was 81.5±10.87 mmHg. The mean values of oxidative stress markers and total antioxidant status in plasma, insulin resistance parameters and lipid profile are presented in Table 1.

Table 1. Oxidative stress markers, total antioxidant status in plasma and metabolic parameters in the group of overweight or obese women (mean ± SD)

	Overweight and obese women (n = 45)
Total cholesterol (mmol/L)	5.42 ± 0.76
HDL-cholesterol (mmol/L)	1.57 ± 0.38
LDL-cholesterol (mmol/L)	3.2 ± 0.8
Triglycerides (mmol/L)	1.3 ± 0.54
AIP	–0.12 ± 0.19
Glucose (mmol/L)	5.54 ± 1.09
Insulin (μU/mL)	10.07 ± 5.96
$HOMA_{IR}$	2.63 ± 2.10
TBARS (μmol/L)	2.6 ± 0.49
oLAB (mU/mL)	572.7 ± 410.38
TAS (mmol/L)	1.2 ± 0.33

AIP – Atherogenic Index of Plasma; HDL – high-density lipoproteins; $HOMA_{IR}$ – Homeostasis Model Assessment Insulin Resistance; LDL – low-density lipoproteins; oLAB – antibodies to oxidized low-density lipoproteins; TAS – plasma total antioxidant status; TBARS – thiobarbituric acid reactive substances.

Table 2. Correlations between oxidative stress markers and anthropometrical variables, and selected metabolic parameters in the group of overweight and obese women

	TBARS	TAS	oLAB
BMI	0.183	–0.095	0.099
Body mass	0.099	–0.023	0.173
Body fat mass	0.101	–0.023	0.192
SBP	0.099	0.051	0.532**
DBP	0.072	–0.085	0.510**
TC	0.207	0.030	0.276
HDL	–0.051	0.053	–0.132
LDL	0.160	0.042	0.271
TG	0.047	–0.044	0.288
AIP	0.071	–0.061	0.305*
Glucose	0.087	–0.056	0.083
INS	0.035	–0.089	0.176
$HOMA_{IR}$	0.085	–0.132	0.157
TBARS	–	–0.010	0.239
TAS	–0.010	–	–0.491*
oLAB	0.239	–0.267	–

*p<0.05, **p<0.01, AIP – Atherogenic Index of Plasma; BMI – body mass index; DBP – diastolic blood pressure; HDL – high-density lipoproteins; $HOMA_{IR}$ – Homeostasis Model Assessment Insulin Resistance; INS – insulin; LDL – low-density lipoproteins; oLAB – antibodies to oxidized low-density lipoproteins; SBP – systolic blood pressure; TAS – total antioxidant status; TBARS – thiobarbituric acid reactive substances; TC – total serum cholesterol; TG – triglycerides.

To investigate the relationship between oxidative stress and metabolic disturbances in overweight and obese women, the Spearman rank correlation was used.

A significant positive correlation was found between the oLAB level and systolic and diastolic blood pressure, and between the oLAB titres and atherogenic index of plasma. The serum oLAB level was negatively correlated with TAS (Table 2).

DISCUSSION

There is growing evidence that severe obesity induces systemic oxidative stress [10]. The relationship between overweight and mild obesity is controversial.

To estimate the intensity of oxidative stress in women with overweight or mild to moderate obesity, we assessed plasma levels of thiobarbituric acid-reactive substances (TBARS), levels of antibodies to oxidatively modified low-density lipoproteins (oLAB), and total antioxidant status (TAS) of plasma. The plasma levels of TBARS, TAS and serum levels of oLAB were within the reference range (Table 1), indicating the absence of evident oxidative stress in our study population. It is noteworthy that we found no significant metabolic disturbances in our study population – lipid profile, AIP, glucose and insulin levels, systolic and diastolic blood pressure values were normal or near-normal (Table 1).

Available data from experimental studies suggest that oxidative stress may be involved in the pathogenesis of hypertension, probably *via* decreasing bioavailability of nitric oxide (NO), and down-regulating the expression of eNOS [5]. On the other hand, elevated intraluminal pressure in hypertension, and increased levels of angiotensin II and other RAA hormones were shown to stimulate the formation of reactive oxygen species [7]. The data concerning association between oxidative stress and hypertension in humans are scarce. In a large, community-based study Keaney et al. [8] found no positive association between urinary 8-epi-$PGF_{2\alpha}$ levels and blood pressure. In contrast, we observed a significant, positive correlation between the serum oLAB titres and systolic and diastolic blood pressure values in healthy women with overweight or mild to moderate obesity.

The association between hypercholesterolemia and oxidative stress is controversial. There are some data indicating that elevated serum cholesterol levels correlate with increased oxidative parameters. Similarly to the results of Keaney et al. [8], we found no correlation between serum total cholesterol or LDL-cholesterol and oxidative stress markers.

It is suggested that intracellular triglycerides may evoke oxidative stress on several metabolic pathways. Bakker et al. [2] found that intracellular accumulation of triglycerides inhibited transport of adenyl nucleotides and thus increased the generation of superoxide in the mitochondrial chain. It has been also shown that monocytes and neutrophils in subjects with elevated serum triglycerides generate more peroxides than in patients with hypercholesterolemia [3]. On the contrary, high-density lipoproteins, which are rich in antioxidant enzymes such as paraoxonase (PON) and platelet activating factor acetylhydrolase (PAF

AH) [10], may have antioxidant potential. Although we found no association between triglycerides or HDL-cholesterol and oxidative stress markers, a positive correlation was noted between the oLAB titres and atherogenic index of plasma, which is calculated as the logarithm of the ratio of plasma concentration of triglycerides to HDL-cholesterol. AIP may reflect the balance between the actual concentration of plasma triglycerides and HDL, and this balance determines cholesterol transport and metabolism in the vascular lumen. AIP was found to correlate well with the LDL particle size [1], and small dense LDL particles are known risk factors of coronary artery disease. Our finding may point to an association between oxidative stress and atherogenicity of plasma lipoproteins.

Oxidative modification of low-density lipoproteins is a process mediated predominantly by macrophages in the vascular wall. Interestingly, we found a negative correlation between the TAS and oLAB levels, which indicates that plasma antioxidants can have some potential to prevent oxidation of low-density lipoproteins.

The results of our study suggest an association between oxidative stress and blood pressure, and between oxidative stress and lipid risk factors in women with overweight or mild to moderate obesity.

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