Trakia Journal of Sciences, No 1, pp 55-58, 2014

Available online at:
http://www.uni-sz.bg

ISSN 1313-7050 (print)
ISSN 1313-3551 (online)

Original Contribution

PREHYPERTENSION AND PLASMA LEPTIN IN WOMEN WITH METABOLIC SYNDROME

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ABSTRACT
Contemporary consensus for diagnosis of metabolic syndrome (MS) by International Diabetic Federation is central obesity in combination with 2 of the following parameters: increased triglycerides, decreased HDL-C, arterial blood pressure ≥ 130/80 mmHg, increased fasting plasma glucose ≥ 5.6 mmol.L^{-1} or diagnosed already diabetes mellitus type II/ impaired glucose tolerance. Prehypertension (PH) is introduced by Joint National Committee – 7 in USA at 2003 year. Different population data show that its frequency is over 30% in adults and overweight is a major risk factor. Leptin plays key role as in carbohydrates' and lipids' metabolism as in regulating appetite and energy balance. The *goal* of our study was to establish the PH frequency in 32 clinically healthy women with normal body mass index (BMI) and in 46 women with MS. Plasma leptin level was going to be registered and followed up its correlation to PH within the two groups. The *results* show that PH in MS women is 39%. Plasma leptin level in women with MS is 35.33±9.74 ng.ml. *Conclusions:* PH is 2 times higher in MS women. Plasma leptin's level is significantly higher in MS women. There is a significant positive correlation of plasma leptin to diastolic arterial blood pressure values.

Key words: prehypertension, leptin, metabolic syndrome, women

INTRODUCTION

Contemporary consensus for diagnosis of metabolic syndrome (MS) by IDF - International Diabetic Federation **(**Circulation. 2009; 120:1640-1645**)** is central obesity (waist ≥ 94 cm for men and ≥ 80 cm for women from European race and specific values in other ethnic groups of China, Japan and South Asia in combination with 2 of the following parameters: triglycerides ≥ 1.7 mmol.L^{-1}, decreased HDL-C < 1.04 mmol.L^{-1} for men and < 1.29 mmol.L^{-1} for women, Arterial Blood Pressure (ABP) ≥ 130/80 mmHg or treatment of already diagnosed hypertension and increased fasting plasma glucose over 5.6 mmol.L-1 or diagnosed already diabetes mellitus type II/ impaired glucose tolerance (IGT).

Prehypertension (PH) is introduced by Joint National Committee (JNC) – 7 in USA at 2003 year. According to it, Systolic Arterial Blood Pressure (SABP) ranges are 120 – 139 mmHg and Diastolic Arterial Blood Pressure (DABP) - 80-89 mmHg. European Association of Cardiology, World Health Organization and British League of Hypertension continue to categorize values below 140/90 mmHg as normal and highly normal ABP. Elevated BP is a

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risk factor for total organ damage in both man and women. Patients with PH have higher cardiovascular risk - increased ABP with 20mmHg/10mmHg respectively for systole and diastole doubles it. Different population data show that PH frequency is over 30% in adults and overweight is a major risk factor (1-6). Being one of the major products of mast tissue, leptin and adiponectin play key role as in carbohydrates' and lipids' metabolism as in regulating appetite and energy balance. It has been suggested that the major physiological role of leptin is not as a "satiety signal" to prevent obesity in times of energy excess, but as a "starvation signal" to maintain adequate fat stores for survival during times of energy deficit, and that leptin resistance in overweight individuals possibly confers a survival advantage. (7, 8)

There is an increasing evidence of the direct correlation between the circulating leptin and insulin and fasting plasma glucose, HOMA-index and other components of MS as dyslipidaemia and hypertension independently or partially of obesity (6, 9). The data on the association between hyperinsulinaemia and CV risk in women are scarce and conflicting.

GOAL

To be established the PH frequency in clinically healthy women with normal body mass index (BMI) and in women with MS and its relationship to other risk factors for cardiovascular pathology as MS components. To be registered plasma leptin adiponectin ratio and their correlation to the upper mentioned parameters within the two groups.

MATERIAL AND METHODS

46 women of age 36.68±6.48 with proved MS (MS group) and 32 clinically healthy women (C – control group) of age 35.54±5.39 are followed up.

The registered indexes are : Arterial Blood Pressure (ABP – systolic ABP and diastolic ABP), BMI, clinical chemical: plasma glucose level (RA 1000 Technicon, USA), plasma insulin, HOMA – index (MEIA, ABBOTT, USA, AxSYM), lipids profile (Optima KONE) and human leptin ELISA - BioVendor Laboratory, Medicin, Inc., Czech Republic (Intra-assay CV≤ 7.5%, Inter-assay CV ≤ 9.2%) and human adiponectin ELISA - BioVendor Laboratory, Medicin, Inc., Czech Republic (Intra-assay CV≤ 7.0%, Inter-assay CV ≤ 8.2%) and oral glucose tolerance test - oGTT (Omnitest plus, B. Braun, Germany).

The data are statistically processed by SPSS 16.0 (Windows) and expressed as X ±SD.

RESULTS

MS women are with BMI: 35.43±3.18 $kg.m^2$ and HOMA – index: 4.15±1.10. BMI and HOMA – index in clinically healthy women are respectively 23.43±5.11 $kg.m^2$ and 1.15±0.80.
The percentage of PH in MS women and in clinically healthy women is respectively 39 and 20.

There is insulin resistance in 45% of MS women. The registered plasma leptin level in MS women is 35.33±9.74 $ng.ml^{-1}$, while in C group it is 8.63±1.35 $ng.ml^{-1}$. Leptin: adiponectin ratio in blood plasma is given in **Figure 1**.

Some clinical chemical indexes values are given in **Table 1.**

Table 1. *Some clinical chemical indexes in both groups.*

INDEXES	**GROUPS**	
	C	**MS**
Total CHOL **mmol.L^{-1}**	4,1±0,9	6,3±0,28 p<0,001
TRIGLY **mmol.L^{-1}**	1,5±0,3	2,1±0,73 p<0,05
GLUC **mmol.L^{-1}**	4,46±1,53	6,91±1,04 p<0,05

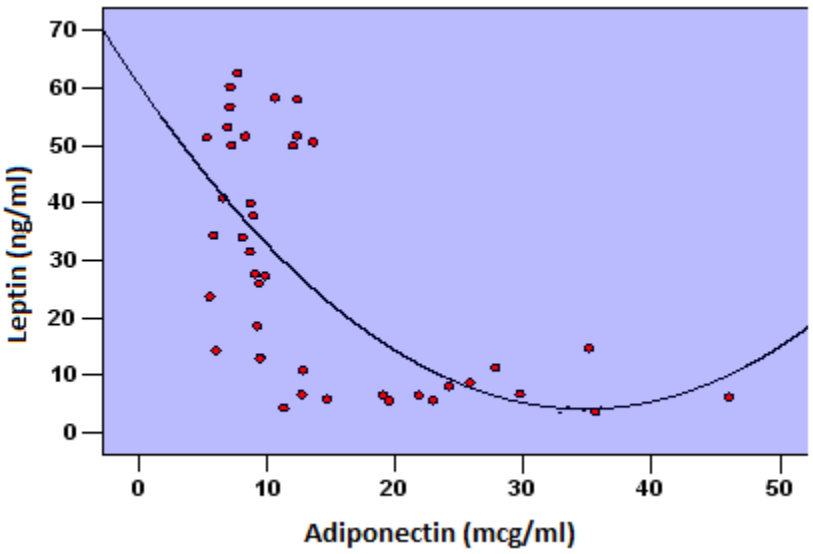

Figure 1. Plasma Leptin: Adiponectin ratio

DISCUSSION AND CONCLUSIONS

In one third of people of age 35 – 64, the registered PH progresses in hypertension within 4 years. Clinical studies TROPHY and PHARAO proved that early treatment of PH prevents or slows the appearance of hypertension I degree. Overweight is one of the major risk factors for PH. Obesity, indicated as "abdominal obesity" gives specific attention to an important sign of MS as a risk factor for PH and hypertension. Results from prospective epidemiological studies have consistently shown that the presence of MS is associated with a significantly increased risk of coronary heart and CV diseases. In the Diabetes Epidemiology - Collaborative analysis of Diagnostic criteria in Europe (DECODE) Study, involving European men and women was found that hyperinsulinaemia was significantly associated with CV mortality in both non - diabetic European women and men independently of other risk factors. Decreased insulin sensibility is usually concerned with impaired lipids profile. High triglycerides and low HDL – C, being part of MS diagnostic constellation, are associated with four fold increased risk of cardiovascular diseases and five fold when combined with hyperinsilinaemia. Chronic hyperinsilinaemia leads to glycolisation and premature colagene aging and vascular wall rigidity. (8, 9, 10) MS is associated with high levels of atherogenic adipocytokines, thus leading to higher cardiovascular risks for incidents.(11) Leptin's role as an inflammatory marker is to respond specifically to adipose-derived inflammatory cytokines. The high sustained concentrations of leptin result in leptin desensitization. Leptin resistance is often described as a metabolic disorder that contributes to obesity, similar to the way insulin resistance is sometimes described as a metabolic disorder that has the potential to progress into the type 2 diabetes. Leptin resistance is extremely common in obese individuals. (12) The role of adipocytokinines and energy homeostasis regulators, concerning the changes in body mass, and leptin insulin resistance interaction is still an object of investigation.

In our study plasma leptin's level and plasma leptin: adiponectin ratio are significantly higher ($p<0.01$ and $p<0.001$respectively) in MS women. There is a significant positive plasma leptin to insuline correlation within oGTT and SABP and DABP. PH is 2 times higher in MS women - clinically measured DABP is significantly higher ($p<0.05$).

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