Correlation between Hormonal Statuses and Metabolic Syndrome in Postmenopausal Women

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Received February 2013; Revised and accepted March 2013

Abstract

Objective: To compare the hormonal status in postmenopausal women with and without metabolic syndrome.

Materials and methods: In this cross sectional study 110 postmenopausal women were enrolled. Participants completed a questionnaire and underwent a medical exam and serum evaluation for serum lipids including cholesterol (Chol), high density lipoprotein cholesterol (HDL), low density lipoprotein (LDL), triglyceride (TG), fasting blood sugar (FBS), sex hormone binding globulin (SHBG), estradiol and testosterone. Metabolic syndrome was defined according to the definition of the National Cholesterol Education Program-Adult Treatment Panel III. In this study P value less than 0.05 was accepted as significant.

Results: There were significant differences between the two groups of participants with and without metabolic syndrome in age, years after menopause, BMI, weight, SHBG and testosterone ($p< 0.01$).

Conclusion: SHBG and testosterone are the most significant correlated factors to metabolic syndrome in postmenopausal women.

Keywords: hormonal status, metabolic syndrome, postmenopausal women

Introduction

The Metabolic syndrome (Mets) identifies a cluster of metabolic disorders that place affected individuals at increased risk for developing cardiovascular disease, as well as increased mortality from all causes (1-4). The third report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholestrol in Adults (ATP III) provides a clinically useful working definition of the metabolic syndrome that includes the presence of at least 3 of the following characteristics: abdominal obesity, increased triglycerides, reduced levels of high–density lipoprotein (HDL) cholesterol, high blood pressure, and increased fasting glucose (5).

The relationships of both androgens and estrogens with individual characteristics of the Mets such as hypertention, insulin resistance and dyslipidemia have been reported in pre and post-menopausal women; however few studies (6- 12) have evaluated the relationship between endogenous sex hormone levels and Mets. Prevalence of Mets increases with age especially while transition occurs from pre to post menopausal state (13- 17). The mechanism through which menopause exerts its effect on the Mets is still unknown.

The present study has therefore been undertaken to examine the relationship between hormonal status (testosterone, estrogen and sex hormone binding globulin serum levels) in postmenopausal women with Mets.

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Materials and methods

This cross-sectional study was conducted on the basis of consecutive recruitment, 110 non-surgical postmenopausal women (more than year since the last menstrual period, plasma 17 β-estradiol level < 35 pg/m) aged 45-75 years were enrolled to the study. The initial screening included medical history, physical and gynaecological examinations. Each participant completed a questionnaire about her characteristics including her lifestyle, occupational sector, smoking history, age at menopause and previous diagnosis for diseases such as diabetes, vascular diseases and so on. Participants, who were currently using antihypertensive medications, were considered to have high blood pressure. Similarly, participants who were currently taking anti- diabetic medications were counted as having diabetes. Participants underwent a medical exam, including measurements of Body Mass Index (BMI), weight and WC(waist circumference). BMI was calculated as body weight (kg) divided by squared body height (m^2).

The serum lipids including cholesterol (CHOL), high density lipoprotein cholesterol (HDL), low density lipoprotein (LDL), triglyceride (TG) and fasting blood sugar (FBS) were determined. Blood samples were taken 12 hours after an overnight fast. Laboratory determination was carried out on the day of blood sampling. CHOL and TG were determined by enzymatic methods (CHOL –PAP and TGO-PAP methods; Thechnicon Instr, NY, USA). The HDL fraction was separated by the Mg^{+2}_phosphotungtic acid precipitation technique followed by enzymatic determination of cholesterol. Glucose was measured using on enzymatic colorimetric method (glucose oxidas) by commercial kit (Pars Azmoon Inc Tehran, Iran).

For the evaluation of the reasons for Mets risk changes, blood chemistry tests were performed for sex hormone binding globulin (SHBG), estradiol and testosterone. The measurement of SHBG, estradiol and testosterone were carried through ELISA (IBL, DRG, DRG Kits respectively). Samples were analyzed in triplicate.

Mets was defined according to the Third Report of the National Cholesterol Education Program expert panel on the detection, evaluation and treatment of high blood cholesterol in adults (NCEP ATP III), as the presence of 3 or more of the following risk determinations: (1) increased waist circumference (WC>88 cm for women), (2) elevated triglycerides (≥ 150 mg/dl), (3) low levels of high-density lipoprotein cholesterol (<50 mg/dl), (4) hypertension (≥ 130 / ≥ 85 mmHg), and (5) impaired fasting blood glucose (≥ 110 mg/dl).

This study was approved by the Ethical Committee of Tarbiat Modares University. An institutionally approved informed consent was obtained for all subjects.

Statistical analysis

Inter group comparisons were made using student t-test. Pearson correlation coefficients were calculated between variables using a two-tailed significance test. A 95% confidence interval (CI) was used to describe the strength of association. The value of $p<0.05$ was considered significant.

Results

The prevalence of metabolic syndrome in our participants was 39.09%. The age, years after menopause, weight, BMI, SHBG, testosterone and estradiol were compared between the participants with and without Mets (table 1) .There were significant differences between the two groups of participants with and without Mets in age, years after menopause, BMI, weight, SHBG and testosterone. For better evaluation of correlation between Mets and mentioned factors, Pearson correlation were calculated and revealed significant correlations between testosterone and SHBG with some risk determinations of Mets ($p<0.05$) (table2).

Table 1: Hormonal data in the two groups*

Parameters	Metabolic Syndrome present (n= 60)	No Metabolic Syndrome (n= 80)	P
Age (years)	57.97±6.56	55.63±6.18	0.035
Years after menopause	7.84 ±2.20	6.61 ±2.53	<0.05
BMI	27.67±2.03	25.86±2.63	<0.001
Weight(kg)	68.42±7.40	63.42±7.18	<0.001
SHBG(nmol/l)	41.63±19.22	53.59±28.74	0.007
Testosterone(ng/ml)	0.58±1.22	0.36±0.30	0.001
Estradiol(pg/dl)	20.73±16.24	21.27±15.31	0.1

* Data are given as mean ± SD Student t- Test ,p value <0.05 was considered significant

Table 2: Correlation between testosterone, SHBG and Metabolic syndrome markers

	Testestrone		SHBG	
	r	P	r	P
WC	0.03	0.76	-0.097	0.31
Blood Pressure	0.29	0.002	-0.164	0.08
FBS	0.28	0.003	-0.080	0.40
TG	0.31	0.001	-0.199	0.037
HDL	0.07	0.46	0.018	0.854

WC: waist circumference,r:pearson correlation,p value <0.05 was considered significant

Discussion

In this cross-sectional study of postmenopausal women mean of age, BMI, weight and the mean levels of testosterone were higher and SHBG was lower among women with Mets. The correlation between SHBG and testosterone among women were particularly strong.

Dramatic alterations in the hormonal milieu and body morphology during menopausal period may have detrimental effects on the body and It may promotes increases in cardiovascular risk factors associated with the Mets in later life.

According to the results of the present study, menopause predisposed individuals to Mets. This finding supports the effect of menopause on Mets independently of aging. These findings are in agreement with those wherein investigators reported that natural menopause is associated with an acceleration of risk of Mets (13-17).

In the present study, women with Mets had higher mean levels of testosterone and lower SHBG levels. In some studies the association between Mets and lower SHBG has been suggested in postmenopausal women (6- 12). The increased prevalence of Mets after menopause may be due to a direct result of ovarian failure or an indirect result of the metabolic consequences of central fat distribution due to estrogen deficiency. There is also a higher androgen to oestrogen ratio in postmenopausal women than premenopausal ones, which may influence the tendency to develop Mets (18). SHBG is a 42-kd circulating glycoprotein involved in the transport of sex steroids, its concentration being a major determinant of their distribution between the protein-bound and free states. SHBG levels have been reported to be significant predictors of diabetes development and cardiovascular disease events in some, but not all prospective studies. Several reports have demonstrated significant associations between SHBG levels and variables of Mets. Our results are concordant with these findings. However, whether SHBG is a causal agent of the metabolic syndrome or only represents a marker for primary endocrine abnormalities leading to these metabolic abnormalities remain unclear until now. Although the cross sectional nature of the present study prevents from concluding on cause and effect relationship, available data suggest that SHBG levels are modulated in response to metabolic signals, rather than the opposite (11).

In conclusion, the results of this study confirmthat age, SHBG and weight are critical correlates of metabolic syndrome in postmenopausal women. However, the study does have some limitations including the use of cross-sectional study. Longitudinal study is necessary and recommended to compare the parameters before and after menopausal state to confirm the conclusions.

Acknowledgments

This study was done with kind cooperation of participating patients. It was funded by Tarbiat Modares University, Tehran, Iran. There is no conflict of interest among the authors.

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