SERUM ALANİNE AMİNOTRANSFERASE AND GAMMA-GLUTAMYLTRANSPEPTİDASE ACTİVİTİES: NEW MARKERS FOR POLYCYSTIC OVARY SYDROME

Halime Kılıç[1], Fatma Aydın[2], Burak Uz[3], Feridun Karakurt[4], Mustafa Köroğlu[5], Ayşe Kargılı Çarlioğlu[6]

[1]Nenehatun Hospital of Gynecology and Obstetrics, Erzurum, TURKEY; [2] Department of Gynecology and Obstetrics, Şifa Hospital, Erzurum, TURKEY; [3]Department of Hematology, Fırat University Medical School, Elazığ, TURKEY; [4]Department of Endocrinology, Selçuk University Medical School, Konya, TURKEY; [5] Department of Hematology, Karaelmas University Medical School, Zonguldak, TURKEY; [6] Department of Endocrinology, Erzurum Regional Training and Research Hospital, Erzurum, TURKEY

OBJECTIVES

Polycystic ovary syndrome (PCOS) is associated with insulin resistance, central obesity and dyslipidemia.

Furthermore, abnormal aminotransferase activity is common in women with polycystic ovary syndrome. The aim of this study is to assess the gamma-glutamyltranspeptidase (GGT) and alanine aminotransferase (ALT) levels in women with PCOS in whom non-alcoholic fatty liver disease was excluded by history, serum testing and abdominal ultrasonography.

METHODS

Present work is included 135 consecutive outpatient between January to July 2006. Ninety patients for the diagnosis of PCOS and 45 age-matched healthy subjects in the control group. Women with PCOS were separated into two groups. Group A were treated with 0.035 mg of Ethinyl Estradiol and 2 mg of cyproterone acetate for six months. Group B did not take any drug. Serum levels of ALT, AST, GGT, ALP, lipid and glucose metabolism parameters were measured on the sixth month of treatment. All blood samples were taken in the morning, after a 12-h fasting on the second to third day of a spontaneous or progesterone-induced menstrual cycle. Fasting blood glucose, ALT, AST, GGT, ALP, total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglycerides were measured by standard methods. Serum levels of ALT, AST, GGT, ALP, lipid and glucose metabolism parameters were measured on the sixth month of EE/CA treatment. Low-density lipoprotein cholesterol (LDL-C) was calculated with the Friedewald equation. The homeostatic model assessment for insulin resistance was also used because of it's strong relationship with the euglycemic-hyperinsulinemic clamp. It was calculated from insulin and glucose values using the formula of Matthews and associates: HOMA IR = Fasting insulin (mU/L) x Fasting glucose (mmol/L) / 22.5. CRP was measured using with image Beckmann coulter bnnephelometric method.

Table 1. Descriptive characteristics of the PCOS (total) and control group.

Variable	PCOS (total)	Controls	p
n	90	45	
Age (yr)	25.97 ± 5.5	26.63 ± 4.4	0.50
Waist circumference (cm)	81.33 ± 3.4	82.15 ± 3.6	0.82
BMI (kg/m^2)	25.74 ± 4.4	23.91 ± 2.2	0.06
ALT (units/l)	21.87 ± 11.1	18.20 ± 5.2	0.031
AST (units/l)	18.80 ± 8.2	18.12 ± 5.5	0.60
GGT (units/l)	25.81 ± 14.9	16.46 ± 6.7	<0.001
ALP (units/l)	110.78 ± 47.3	96.90 ± 42.0	0.09
Tryglyceride (mg/dL)	108.23 ± 58.8	96.79 ± 18.1	0.24
Total cholesterol (mg/dL)	149.39 ± 32.3	126.71 ± 19.9	<0.001
HDL-C(mg/dL)	55.63 ± 12.4	52.92 ± 8.5	0.23
LDL-C (mg/dL)	78.51 ± 23.6	65.61 ± 16.0	0.003
Fasting plasma glucose (mg/dL)	85.84 ± 10.2	83.11 ± 6.6	0.11
Insulin (mU/L)	8.38 ± 5.4	6.58 ± 1.4	0.032
HOMA IR	1.8 ± 0.6	1.34 ± 0.3	0.054
CRP (mg/dl)	4.09 ± 2.7	4.65 ± 2.05	0.22

Abbreviations: PCOS, polycyctic ovary syndrome; BMI, body mass index; ALT, alanine aminotransferase; GGT, γ-Glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HOMA IR, homeostasis model assessment; CRP, C-reactive protein.

'a': $p < 0.05$ for PCOS women using Diane 35 compared to the controls,: 'b': $p < 0.05$ for PCOS women with no treatment compared to the controls.

Table 2. Descriptive characteristics of the PCOS A, PCOS B and control groups.

Variable	Group A (EE/CA)	Group B (ilaçsız pkos)	Controls
n	45	45	45
Age (yr)	25.86 ± 5.1	26.16 ± 6.3	26.63 ± 4.4
Waist circumference (cm)	82.16 ± 3.3	79.66 ± 3.5	82.15 ± 3.6
BMI (kg/m^2)	24.49 ± 3.3	28.10^b ± 5.4	23.91 ± 2.2
ALT (units/l)	20.42 ± 1.4	24.13^b ± 2.3	18.20 ± 5.2
AST (units/l)	18.80 ± 8.1	18.82 ± 8.6	18.12 ± 5.5
GGT (units/l)	28.26^a ± 2.3	22.00^b ± 2.2	16.46 ± 6.7
ALP (units/l)	109.57 ± 51.8	112.65 ± 40.06	96.90 ± 42.0
Tryglyceride (mg/dL)	105.60 ± 9.8	111.50 ± 11.4	96.79 ± 18.1
Total cholesterol (mg/dL)	150.4^a ± 5.8	148.14 ± 5.6^b	126.71 ± 19.9
HDL-C(mg/dL)	55.84 ± 1.7	55.37 ± 2.8	52.92 ± 8.5
LDL-C (mg/dL)	81.4^a ± 4.2	75.11^b ± 4.2	65.61 ± 16.0
Fasting plasma glucose (mg/dL)	84.43 ± 1.3	87.65^b ± 2.2	83.11 ± 6.6
Insulin (mU/L)	8.51^a ± 4.8	8.24 ± 6.01	6.58 ± 1.4
HOMA IR	1,6 ± ,69	1,84 ± 1,68	1,34 ± ,3
CRP (mg/dl)	3.90 ± 0.3	4.38 ± 0.6	4.65 ± 2.05
LH	12,37^a ± 11,3	9,75^b ± 5,53	4,9946 ± ,3
FSH	10,41 ± 15,34	8,02 ± 11,16	6,1 ± 1,78
LH/FSH	1,63^a ± 1,11	1,67^b ± 1,84	,89 ± ,23
DHEAS	158,76 ± 63,78	178,4 ± 77,28	152,81 ± 70,44
T.Testosterone	37,7 ± 22,12	43,39^b ± 24,98	29,72 ± 5,93

RESULTS

The plasma levels of both ALT and GGT were significantly higher in the subjects with PCOS (total) compared to the controls. Serum GGT levels were significantly higher in the group A and B than in controls, whereas no difference was found between group A and B. On the other hand group B had significantly higher ALT levels than in controls. However, no differences in ALT levels were found between group A and controls. Total cholesterol and LDL-C levels were significantly higher in the subjects with group A and B than the control group. In addition, BMI and fasting plasma glucose levels were significantly higher in the group B compared to the controls, whereas HOMA-IR and serum insulin levels were significantly higher in the subjects with group A than in controls. Serum GGT level was found to be positively correlated with PCOS, T. testosterone, DHEAS, LH and LH/FSH.

CONCLUSIONS

Our study has several limitations. First, serum concentrations of hepatic enzymes during follow-up were not included in the analysis. Second, NAFLD was excluded by biochemistry and abdominal ultrasonography because of ethical concerns. However, liver biopsy, an invasive procedure with certain risks, is the gold standard for NAFLD diagnosis. Ultrasonography was reported to have up to 89% sensitivity and 93% specificity for detection of NAFLD.

The presence of raised hepatic enzymes may help identify an individual who is likely to have PCOS who is at particularly high risk. Our study supports the suggestion that GGT and ALT are important in the pathogenesis of PCOS and that hepatic enzymes may be useful in identifying women at high risk of metabolic syndrome. To better clarify that issue, additional prospective studies of greater number patients are needed.

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Fatma AYDIN

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