Original Article

Plasma levels of uric acid and leptin in preeclampsia and normal pregnancies

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Abstract. The aim of this study is to compare the uric acid and leptin levels in preeclamtic and normal pregnants and to investigate the relationship between these levels and the severity of the disease. This study was performed on 40 (20 severe, 20 mild) patients who had received a diagnosis of preecclampsia and on 30 normal healthy pregnant women, a total of 70 singleton pregnancies, at 34-42nd gestational weeks who had recourse to obstetric and gynecology clinic from February to September. Plasma leptin levels were determined by using ELISA method. Levels of those parameters were compared in preeclamptic and normal pregnant woman. Leptin levels were found as 9.6±7.2ng/mL in severely preeclamptic group, 5.4±3.0ng/mL in mildly preeclamptic group and 3.1±3.1ng/mL in control group. In severe preeclampsia group, leptin levels were statistically significantly higher (p=0.001). Uric acid levels were found as 6.3±1.8mg/mL in severe preeclamptic group, 5.0±1.4mg/mL in mildly preeclamptic group and 4.02±0.73mg/mL in control group. When uric acid levels of preeclamptic groups were compared with the control, statistically significant difference was determined among the groups (p=0.001). The highest uric acid level was found in severely preeclamptic group. A weak, positive correlation was determined between serum uric acid and leptin levels (r=0.039). Increased uric acid values were found with increasing serum leptin levels. In preeclamptic patients it was found that uric acid levels were increased with increasing serum leptin levels. We consider that leptin hormone which has various functions may have some role in etiopathogenesis of preeclampsia and may be a useful marker of preeclampsia.

Key words: Leptin, preeclampsia, uric acid

1. Introduction

Leptin is a protein hormone consisting of 167 aminoacids and is similar to cytokines. Molecular weight is 16 kDa and it is known to have functions in many different parts of the body (1,2). It is coded by ob/ob gene present in the long arm of chromosome 7 (7q31), (3,4).

Leptin is majorly synthesized by adipose tissue, and also to a less extent by the placenta, gastric epithelium, striated muscle, pituitary gland and mammary gland (5-10). Preeclampsia is not just an ordinary hypertension; but it is a systemic disease with the characteristics of increased vascular resistance, endothelial dysfunction, proteinuria and coagulopathy and the exact etiology of it has not been clarified, yet. A relation between plasma uric acid concentrations and preeclampsia has been known and serum uric acid levels have been also known to increase with increasing severity of the disease (11-15). In many studies, higher serum leptin levels in preeclamptic patients compared to normotensive pregnants were demonstrated (16-19). In their study Schubring et al demonstrated a correlation between serum leptin levels and pregnancy complications diagnosed during antenatal follow-up (20). In accordance with the outcomes of this study, we hypothesize that increased serum leptin concentrations may be a metabolic-hormonal parameter that can affect the prognosis of pregnancy, thus in the practice of antenatal follow-up it can be a marker especially in the second trimester providing early diagnosis of preeclampsia, diabetes mellitus and intrauterine growth retardation (IUGR). Since there are many conflicts on this issue in the literature, we planned this study to test our hypothesis.

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Received: 15.01.2015
Accepted: 25.02.2015

Table 1. General characteristics of groups

	Control (n=30)	Mild (n=20)	Severe (n=20)	p
Age (year)*	26.5±3.2[#b]	30.2±7.6[#a]	29.5±5.1[#a]	0.043
Gravidity*	2.6±1.5[#c]	5.4±3.7[#a]	3.9±3.0[#b]	0.004
Parity*	1.3±1.4[#c]	3.4±3.2[#a]	2.7±2.6[#b]	0.012
Gestational age at delivery (week)*	38.4±1.31	38.6±1.16	38.7±1.04	0.637
Educational status (n, %)				
Illiterate*	5 (16.6)	9 (45.0)	10 (50.0)	0.073
Literate*	2 (6.6)	0	3 (15.0)	
Primary school*	12 (40.0)	7 (35.0)	4 (20.0)	
Secondary school or higher*	11 (36.6)	4 (20.0)	3 (15.0)	

*Mean± standard deviation [#]Different lower cases represent different means

Table 2. Biochemical and hematological parameters of groups.

	Control (n=30)	Mild (n=20)	Severe (n=20)	p
Uric acid (mg/dL)*	4.2±0.73[#c]	5.0±1.4[#b]	6.3±1.8[#a]	0.001
Creatinin (mg/dL)*	0.51±0.09[#b]	0.61±0.18[#a]	0.65±0.16[#a]	0.004
Hemoglobin (g/dL)*	11.8±1.12	11.4±1.25	12.1±1.23	0.185
Hematocrit (%)*	35.3±3.3	34.7±3.3	35.8±3.3	0.551
Thrombocyte*	222.753±55.433	239.450±77.657	204.675±80.768	0.297
Leptin (ng/mL)*	3.1±3.1[#c]	5.4±3.0[#b]	9.6±7.2[#a]	0.001

*Mean± standard deviation [#]Different lower cases represent different means

2. Materials and methods

A prospective, controlled study was carried out at Department of Gynecology and Obstetrics, Yuzuncu Yil University, Van. From February through September, 70 singleton pregnancies at 34-42nd gestational weeks were enrolled to the study all providing informed written consent. Forty preeclamptic patients were grouped in two as 20 severe and 20 mild. Control group consisted of 30 normal healthy pregnant women. Diagnosis and classification of severe and mild preeclampsia was done according to the 2002 criteria of American College of Obstetrics and Gynecology (ACOG) (21).

Maternal serum uric acid and leptin levels were measured. For measurement of maternal serum leptin, 5 mL venous blood sample was taken from antecubital vein. Serum was separated by centrifuging the samples for 15 minutes at 2000 rpm in NF415 type centrifugation device. The serum was transferred into small plastic godets and kept at -80 °C in deepfreeze.

For leptin levels, all serum samples were thawed and then serums were studied in autoanalyzer ELx808 IU Ultra Microplate Reader (BIO-TEC INSTRUMENTS, INC) by using ELISA method with the commercial kits of BIOSOURCE LEPTIN EASIA (BioSource Eurupe S.A. Rue de I'Industrie 8, B-1400 Nivelles, Belgium). Normal limits of the kit for healthy people were 2.4±1.1ng/mL for thin women and 6.6±3.0ng/mL for thin men.

Statistical analyses of the data obtained were performed with Chi-square and One-Way-Annova tests. Post-hoc Tukey's HSD test was used to determine the group from which the statistical significance had originated with One-Way-Anova test. For the association between leptin and uric acid, Pearson Correlation Analysis was used. All the statistical analyses were performed with SPSS 11.5 package programs.

3. Results

Forty patients who were diagnosed as severe or mild preeclampsia and hospitalized and 30 control subjects who did not have any systemic diseases were included in this prospective study. General characteristics of the subjects are presented in Table 1.

There were no statistically significant differences among groups for maternal age or educational status (Table 1). When groups were compared for gravidity and parity, statistically significant differences were found (relatively; p=0.004, p=0.012). In mildly preeclamptic group, gravidity and parity were higher.

Dispersion of biochemical and hematological parameters of all subjects and comparison of these parameters were presented in Table 2. Hemoglobin and hematocrit values of groups were similar. Leptin levels were 3.1±3.1ng/mL in

control group, 5.4±3.0ng/mL in mild preeclamptic group and 9.6±7.2ng/mL in severely preeclamptic group. Leptin level of severely preeclamptic group was statistically significantly higher (p=0.001).

When groups were evaluated for leptin, the highest serum leptin level was 9.6±7.2ng/mL and it was found in severely preeclamptic group.

Leptin levels were 9.6±7.2ng/mL in severely preeclamptic group, 5.4±3.0ng/mL in mildly preeclamptic group and 3.1±3.1ng/mL in control group. In severe preeclampsia group, leptin level was statistically significantly higher (p=0.001). Uric acid levels were 6.3±1.8mg/mL in severe preeclampsia group and 4.02±0.73mg/mL in control group. When uric acid levels of preeclamptic groups were compared with the control, statistically significant difference was determined among the groups (p=0.001). The highest uric acid level was found in severely preeclamptic group. A weak, positive correlation was determined between serum uric acid and leptin levels (r=0.039).

4. Discussion

Results of this study demonstrated serum leptin levels to be higher in both mild and severe preeclampsia than in healthy gestations. Additionally, depending on the severity of preeclampsia, higher serum leptin levels were determined in severely preeclamptic patients than in mildly preeclamptic cases. In previous studies on preeclampsia, various hematological and biochemical markers have been investigated in order to be able to predict the disease and to determine the prognosis of it. However, a reliable parameter has not been found yet (22). Serum uric acid levels have been shown to be high in preeclampsia by many previous studies (23-25). Results of our study correspond with them. Serum uric acid levels were statistically significantly higher in severe and mild preeclampsia than in control group (p=0.001).

Although the answer to the question of why serum uric acid levels increase in preeclampsia is still not clear. A few theories have been proposed. The most accepted explanation is the decrease in uric acid clearance. Possible causes for this are increased reabsorbtion of uric acid by kidneys, decreased excretion of it or both of these (26-28). All of uric acid is filtrated by glomeruli, almost total of it is reabsorbed by the proximal and just a small part of it is by distal tubular. With this complicated system, 90% of uric acid filtrated is reabsorbed. Glomerular filtration rate that is already decreased in preeclampsia also has a role in decreased clearance of uric acid (29). Increase in serum uric acid levels due to decreased clearance is usually seen earlier than the other parameters of renal dysfunction (30). At the same time, it is reported that increased oxidative stress and formation of reactive oxygen metabolites occurring in preeclampsia have some effects on increased serum levels of uric acid. This effect is proposed to occur via xanthine dehydrogenase/oxidative enzyme system and to cause increase in the formation of serum uric acid (31-34).

In recent times, leptin hormone has been investigated with the aim of decreasing the perinatal mortality and morbidity by determining pregnancy complications (preeclampsia, DM, IUGR) as at an early gestational age as possible.

In a study by Mise et al in 1998, serum leptin levels were demonstrated to be high in preeclamptic patients, especially in severely preeclamptic ones for the first time (35). It was showed that in these patients, placental leptin mRNA expression increased together with the increasing serum leptin levels and serum leptin levels declined just after placental expulsion. So, this point out the possibility that increased leptin levels in preeclamptic women may be related with placental production. Increased placental production of leptin reflects placental hypoperfusion and/or hypoxia. Hypoxia increases placental production of leptin by inducing a group of placental gene in trophoblastic cells. Thus, it was concluded that increased leptin levels were a general reaction of trophoblastic cells to hypoxia (36).

In our study, serum leptin levels were found to be statistically significantly high in accordance with the literature (p=0.001). There are possible mechanisms in preeclampsia that can explain the increased serum leptin levels. Disordered renal function and as a result of this decreased renal clearance that causes uric acid levels to increase in preeclampsia probably increases serum leptin levels by the same mechanisms, too. Apart from this, decreased plasma volume in preeclampsia may increase the serum levels of these substances by causing hemoconcentration.

It is reported that leptin together with uric acid has a role in oxidative stress characterized by increased reactive oxygen compounds which are thought to have role in etiopathogenesis of preeclampsia. Leptin activates the formation of reactive oxygen compounds via its functional receptors which are present on many cells (37,38). Leptin was proposed to be a risk factor for many complications such as hypertension and

atherosclerosis through vascular inflammation that results from accumulation of reactive oxygen compounds in endothelial cells (39).

Uric acid and leptin levels which have been thought to have role in etiopathogenesis of preeclampsia were found statistically significantly high in severely preeclamptic group in our study. We determined that leptin levels increased together with increased serum uric acid levels.

Eventually, we think that it may have some role in etiopathogenesis of preeclampsia and may be a useful marker of preeclampsia. But, since the study population in our study is small, further prospective multicentre studies are required to clarify the issue.

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