Leptin Values in Maternal and Umbilical Cord Blood in Pregnant Women with Preeclampsia

Neşe Yücel, Fikret Gökhan Göynümer, Ergün Bilgiç, Cengiz Omurcan, Tonguç Arslan

Göztepe Training and Research Hospital, Obstetrics and Gynecology, Istanbul

Abstract

Objective: To compare the maternal plasma and umbilical cord blood leptin values in the prenatal and postnatal periods of women with normal pregnancies and pregnant women with preeclampsia.

Methods: The prenatal and postnatal maternal plasma and umbilical cord blood leptin values in the preeclampsia group (n=40) with the patients selected to have similar body mass indexes and to be at the similar gestational weeks were compared with those of the normal pregnancy group (n=32).

Results: We found a significant difference in the maternal plasma leptin concentrations between the groups. The leptin concentration in the preeclampsia group was significantly high (p=0.048) . No difference in the umbilical cord blood leptin concentrations was detected (p>0.05).

Conclusion: We detected an increase in maternal plasma leptin concentrations in preeclamptic women independent from the pregnancy body-mass index. We found remarkable but non statistical difference of leptin values in the postnatal maternal plasma and the umbilical cord blood between the preeclampsia group and the matched control group. However, our knowledge about leptin is limited, and more studies are needed to explain the reason for the increase in leptin in such patients.

Keywords: Preeclampsia, leptin, obesity.

Preeklamptik gebelerde maternal plazma ve kordon kanı leptin konsantrasyonları

Amaç: Preeklamptik ve normal gebelerde, gebelikte ve gebelik sonrasında maternal plazma leptin değerleri ile her yenidoğan kordon kanı leptin değerlerini karşılaştırmaktır.

Yöntem: Gebelikte maternal plazma, doğumda kordon kanı, postpartum dönemde maternal plazma kanı leptin değerleri, örnekleme zamanındaki gestasyonel yaşa ve gebelik vücut indeksine göre denkleştirilmiş preeklampsi grubu (n=40) ile normal gebelik grubu ile (n=32) karşılaştırıldı. İstatistiklerde student t ve Mann Whitney U testleri kullanıldı.

Bulgular: Maternal plazma leptin konsantrasyonu gruplar arasında istatistiksel anlamlı bir farklılık göstermektedir. Preeklamptik grupta leptin konsantrasyonu anlamlı olarak yüksek bulunmuştur (p=0.048). Kordon kanı ve doğum sonrası leptin değerlerinde, gruplar arasında istatistiksel fark saptanmamıştır (p>0.05).

Sonuç: Preeklampside maternal plazma leptin konsantrasyonu artarken, kordon kanı ve doğum sonrası leptin değerleri farklı bulunmamıştır. Ölçümlerdeki dağılım farklılığı daha geniş serilerde çalışmayı gerekli kılmaktadır.

Anahtar Sözcükler: Preeklampsi, leptin, obezite.

Correspondence: Dr. Fikret Gökhan Göynümer, Göztepe Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul
e-mail: goynumergo@ttmail.com

Introduction

Leptin is a proteohormone coded by the obesity gene and produced by adipocytes. Although leptin mRNA has been detected in the human placenta, it is mainly found in adipose tissue.[1] During the pregnancy period a considerable amount of leptin is secreted from the placental trophoblastic cells into the maternal circulation.[2] Leptin concentrations are 3 to 4 times higher in pregnant women than non pregnant women.[3] Leptin increases significantly in women with preeclampsia, and especially in those with severe preeclampsia. This increase correlates with placental mRNA expression, and following the delivery of the placenta, decreases immediately to expected values. An increase in leptin secretion has been shown in hypoxia in laboratory conditions. The increase in placental leptin production in preeclampsia is thought to happen in response to hypoxia.[4] Leptin levels have been shown to increase in preeclamptic women.[5-7] Increased levels of leptin is thought to be an indication of maternal steatosis and placental insufficiency. Leptin may also cause to endothelial dysfunction by increasing free fatty acid oxidation.[8]

Our aim in this study is to compare the prenatal and postnatal maternal plasma and umbilical cord blood leptin values of women with normal pregnancies and women with preeclampsia.

Methods

This study was designed as a randomized prospective case-control study. Forty women in their third trimester of singleton pregnancies internalized in our obstetrics and gynecology clinic with the diagnosis of preeclampsia between April 2004 and October 2004 and 32 normotensive women with singleton pregnancies determined to be healthy and free of chronic diseases (diabetes, heart disease, thyroid disease) by medical examination and tests were included in the study. The inclusion criteria for the preeclampsia group were a blood pressure of 140/90mmHg or more, measured on at least two times 6 hours apart; 500 mg or more protein in a 24 hour urine sample, or a 2(++) proteinuria dipstick finding in a random urine sample.[9] Preeclamptic patients with these criteria who had not received any medication were included in the study. No medication was given to these patients before blood was taken for leptin levels and other routine tests. Because of the possibility of smoking affecting plasma leptin levels, all patients were selected to be nonsmokers. Fasting venous blood samples were drawn from the antecubital veins from all pregnant women in the study and control groups at a state of rest between 08.00 and 10.00 a.m. Following vaginal or cesaerean delivery a second clamp was placed on the umbilical cord at the placental end and blood samples were taken from either the vein or arteries of the umbilical cord. Within the first 24 hours following delivery, blood samples were taken at 8.00-10. a.m. The weight and height of all pregnant women in both the study and the control group were recorded during the initial examination and their body mass indexes (BMI) were calculated with the [kg / m2] Formula.[10]

The groups were stratified according to the maternal age, gestational age and body mass index doing randomization. The cases of the groups were selected by the way of simple randomization. The maternal plasma, umbilical cord blood, and postpartum maternal plasma leptin concentrations of the preeclampsia group (n=40) with the patients selected to have similar body mass indexes and to be at the similar gestational weeks were compared with those of the normal pregnancy group (n=32). During the evaluation of the study data, besides descriptive statistical methods (mean, standard deviation), Student t test and Mann-Whitney U tests were used when comparing quantifiable data. The results were evaluated at the 95% confidence interval, and $p<0.05$ significance level.

Results

The gestational ages at the time of sampling were found to be 38.40±1.90 weeks in the preeclampsia group, and 39.00±1.75 weeks in the normal pregnancy group. No significant difference was found to exist in the gestational ages at the time of sampling and the time that passed from the date of sampling for maternal plasma leptin concentrations (MPLC) until delivery amongst the two groups (p>0.05). The mean of BMI in the preeclamptic pregnancy group was 28.11±3.88 kg/m2, and 26.76±3.38 kg/m2 in the normal pregnancy group. There were no significant differences in the mean of BMI's and serum creatinin levels between two groups (p>0.05). The maternal plasma leptin concentrations (MPLC) were significantly different between the two groups. The mean leptin concentration in the preeclamptic pregnancy group (196.8 ng/ml) was found to be significantly higher than that in the normal pregnancy group (60.3 ng/ml) (P<0.05) .

Although we found 2 or 2.5 times differences in the postnatal maternal plasma (77.5±109.2 ng/ml and 31.3±23.5 ng/ml, P>0.05) and umbilical cord blood (16.7±17.2 ng/ml and 8.2±5.2 ng/ml, P>0.05) leptin values between the groups, no significant difference in the umbilical cord blood leptin levels between the two groups has been found. The difference leptin value inthe prenatal and postnatal period were found significantly different between the groups (p<0.05) (Table:1).

Discussion

In the non-pregnant, leptin is mainly produced in adipose tissue.[1] Metabolic changes such as glucose intolerance and insulin resistance encountered in obesity can also be seen in preeclampsia. The increase in leptin levels in both obesity and preeclampsia is an important finding. During their study in 1998, Mise et. al detected for the first time a significant increase in serum leptin levels of preeclamptic, especially severely preeclamptic pregnant women.[4] They have shown an increase in placental leptin mRNA expression proportional to an increase in serum leptin levels in these patients, and a decrease in serum leptin levels following delivery of the placenta. This situation points to the fact that an increase serum leptin levels in preeclamptic women is related with placental production. The increase in placental leptin is an indication of placental hypoperfusion and/or hypoxia. Hypoxia increases placental leptin production by induction of a group of placental genes in the trophoblastic cells. Therefore, it can be concluded that increasing leptin levels is a general reaction of the cells to hypoxia.

In severe preeclampsia leptin is an indicator of placental hypoxia.[11] Similar to Mise et al,[4] Mc Carty et al,[5] Ouyang et al[12] and Sharma et al[13] have detected a significant increase in plasma leptin levels in preeclamptic cases. In our study, the mean leptin level of the preeclamptic group was 3.26 times the mean leptin level of the normal pregnancy group.

Table 1. Comparison of the leptin levels between the groups.

	Preeclampsia (n:40)		Control (n:32)		
	Mean ± SD	Median	Mean ± SD	Median	p
Maternal plasma leptin(ng/ml)	196.8±190.8	124	60.3±45.2	40.5	Z=-1.751; 0.048*
Cord plasma leptin (ng/ml)	16.7±17.2	12	8.2±5.2	8.5	Z=-1.146; 0.252
Postpartum plasma leptin	77.55±109.2	35	31.3±23.5	22.2	Z=-0.478; 0.633
Difference of leptin between before and after delivery (ng/ml)	119.2±126.7	83	29.0±40.6	16.1	Z=-2.308; 0.021*

**p<0.05 statistical importance*
Z Mann-Whitney U test

Even though quite a number of studies questioning the relation between the ethiopathogenesis of hypertension and increasing plasma leptin levels have been reported, an increase in blood pressure only is not enough to explain the increase in leptin levels.[14-17] In our study, in the early postpartum period, when the blood pressure is going at the high level, the fact that maternal plasma leptin levels of preeclamptic women are similar to those of normotensive cases, supports the idea presented above.

Renal dysfunction, one of the pathologic findings in pregnant women with preeclampsia; and therefore decreased renal clearances, may be responsible for the high leptin levels in preeclamptic pregnant women. In our study, creatine clearances were not calculated in the control and study group however no statistically significant difference in creatine levels was detected between the two groups. This leads to the conclusion that the difference in leptin levels between the two groups can not be explained by differences in renal function. Decreased plasma volumes sometimes seen in preeclampsia may have a role in the increase in serum leptin level by causing hemoconcentration.

Leptin levels in non-pregnant women correlate with the body mass index. However, in the pregnant state, the body mass index may not accurately show the amount of body fat because the fetus, placenta, amniotic fluid, increased plasma volume and accumulation of various amounts of extracellular fluid increase the maternal weight.[5] In the preeclamptic women extracellular fluid distribution is quite prominent. In our study, no statistically significant difference in the body mass indexes between the preeclamptic and normal pregnancy groups was detected. The relation between the BMI and plasma leptin levels seen in the first and second trimesters is not present in the third trimester.[18] In our study the patients have been been examined in the third trimester of their pregnancy only once and their BMI's have been calculated. For this reason, we have not been able to detect the changes in the body mass indexes. In a normal pregnancy, taking into account the lack of a correlation between the maternal and umbilical cord blood leptin levels, the fetoplacental leptin regulation can be said to be a non communicating, double compartment model.[5] However in preeclampsia, the strong correlation between the maternal and fetal leptin concentrations is indicative of a change, resulting in communication between the two compartments.[5]

Mc Carthy et al have found a strong correlation between the maternal plasma leptin concentrations and umbilical cord blood leptin concentrations in the pregnant women with preeclampsia.[5] However no statistical difference in the the postnatal maternal plasma and the umbilical cord blood leptin levels was detected between the groups in our study.We thought that the most important cause of no statistical difference of leptin levels in the postnatal maternal plasma and the umbilical cord blood between the groups was the wide distributions of the leptin value.

Conclusion

In conclusion, independent of the maternal body mass index, comparing the preeclampsia group with the matched control group; we have found the increases of leptin value in the maternal plasma concentrations in preeclampsia. We found remarkable but non statistical difference of leptin values in the postnatal maternal plasma and the umbilical cord blood between the groups We thought that the most important cause of no statistical difference of leptin levels in the postnatal maternal plasma and the umbilical cord blood between the groups, was the wide distributions of the leptin value.

Nevertheless, more studies are needed to find the main reason for the increase in leptin concentrations with preeclampsia

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