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Original Article

Evaluation of Androgen and Progesterone Levels in Women with Preeclampsia

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Abstract

Background: Preeclampsia along with its complications seems to be one of the major causes of maternal morbidity and mortality. Despite numerous studies, the pathology of preeclampsia has not yet been fully elucidated. This study, therefore, determines whether maternal serum levels of androgen and progesterone are higher in patients with preeclampsia than in matched control subjects.

Methods: Serum progesterone, free and total testosterone, and dehydroepiandrosterone levels were measured in 19 women in their third trimester of pregnancy having preeclampsia, as patient group, and in 17 healthy normotensive pregnant women, as control group, with similar maternal and gestational ages. All women were primigravida with singleton pregnancy.

Results: There were no significant differences between the two groups in body mass index, maternal and gestational ages. Progesterone and free testosterone levels were significantly lower ($P<0.01$) in patients (75.1±8.6 ng/dl and 2.27±1.74 pg/dl) than of control group (111.6±9.71 ng/dl and 3.73±1.31 pg/dl). Whereas, the levels of total testosterone (1.02±0.10 ng/dl vs. 1.37±.019ng/dl) and dehydroepiandrosterone (0.99±0.13 µg/dl vs. 0.98±5.15 µg/dl) of patients and control groups were not significantly different.

Conclusion: Levels of progesterone were pathologically and statistically lower in preeclampsia than of control women with similar age, gestational age and body mass index. It seems that accentuate increase sex hormone binding globulin is the cause of deceased free testosterone in preeclampsia.
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Keywords ● Preeclampsia ● androgen ● progesterone ● pregnancy

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Introduction

Preeclampsia is defined as new onset of hypertension after 20 weeks of gestation with high systolic (≥ 140 mmHg) and diastolic blood pressures (≥90 mmHg) and proteinuria (300mg/24 h).[1] Preeclampsia is a transient but potentially dangerous complication of pregnancy that affecting 3 to 5% of pregnancies.[2,3] In spite of numerous studies, the pathology of preeclampsia has not been fully elucidated. Many studies have concluded that high levels of blood androgens observed in preeclamptic patients may implicate the pathogenesis of

preeclampsia.[4,5] Whereas, other studies have failed to show an association between the concentrations of unconjugated estrogen and androgen of the cord sera of preeclampsia patients and uncomplicated pregnancies.[6] Subcutaneous injection of progesterone to pregnant mouse with preeclampsia has reduced blood pressure.[7] Some studies have highlighted that changes in plasma progesterone in pregnant animals are the cause of preeclampsia, therefore, attentions have focused on the impact of alterations of plasma progesterone on preeclampsia in humans.

On the basis of some studies showing that progesterone has a relaxant effect on the omental vessels of pregnant women,[6-8] we, therefore, tried to find out whether there is a correlation between preeclampsia and the level of serum progesterone of pregnant women. This was done by measuring the concentrations of total and free testosterone, dehydroepiandrosterone along with progesterone in primigravida preeclamptic women.

Patients and methods

The study was approved by Ethical Committee of Uromia University of Medical Sciences and a written consent was obtained from subjects participated in the study. Thirty six primigravida women, in their third trimester with singleton pregnancies, admitted to Kosar Obstetrics Hospital of Uromia Medical Sciences University, Uromia, Iran. Nineteen pregnant women with preeclampsia and 17 healthy pregnant normotensive women were enrolled in the study. Inclusion criteria based on the maternal chronological age, body mass index, gestational age, having no history of hypertension as well as other diseases associated with hormone disorders. During their pregnancy they did not receive antihypertensive medications or hormone replacement therapies. At the time of enrolment venous blood samples were collected and their sera were obtained by centrifugation and stored at –70˚C until analysis. Standard radioimmunoassay techniques were used to obtain the levels of progesterone, dehydroepiandrosterone, total and free testosterone.

Statistical analyses

Data are presented as mean±SD. Comparison of hormonal levels between the two groups was performed by Student's t test and $p<0.05$ was considered as statistically significant.

Results

The mean values of body mass index, mean maternal and gestational age of the two groups were not statistically different (Table 1). There were no significant differences in serum concentrations of total testosterone (1.02±0.10 ng/dl vs. 1.37±0.02 ng/dl) and dehydroepiandrosterone of preeclapmsia and of healthy control groups (0.99±0.13 µg/dl vs. 0.98±5.15 µg/dl), whereas, free testosterone and progesterone levels of preeclapmsia groups (2.8±1.7 pg /dl and 75.1±8.6 pg /dl) were significantly lower (Table 2) than of healthy control group (3.7±1.3 pg/dl and 111.6±9.7 pg /dl).

Table1: Mean age, Body mass index (BMI) and estimated gestational age (EGA) of preeclampsia (case) and control groups on admission

	Case (n=19)	Control (n=19)
Age (Yrs)	25.7±1.2	22.7±1.5
BMI (kg/m^2)	12.58±5.22	12.385.13
EGA (weeks)	35.2±0.8	36.7±1.1

Table 2: Serum concentration of progesterone (PR), total and free testosterone (TT and FT) and Dihydroepiandrosterone (DHA) in preeclampsia (case) and control groups

	Case (n=19)	Control (n=19)
PR (ng/dl)	75.1±8.6	111.6±9.71*
TT (ng/dl)	1.02±0.10	1.37±.019
FT (pg/dl)	2.27±1.74	3.73±1.31*
DHA (µg/dl)	0.99±0.13	0.98±0.15

Discussion

In many studies, an increase in androgen levels has been considered as the cause of preeclampsia pathogenesis.[9,10] Miller et al. did not find a relationship between the levels of androgens, therefore, proposed that these hormones may not clinically participate in the pathogenesis of the preeclampsia.[11] The results showed a significant reduction in the levels of free testosterone in preeclapmsia group as of healthy pregnant individuals, which is incompatible with the results of Miller et al.[11] Sex hormone binding globulin was found to be significantly higher in the preeclampsia than in normal pregnancy. This increase may lead to the reduction of free testosterone without affecting total serum testosterone levels.[12]

Progesterone was considered as a main steroid hormone that reducing vascular tones during pregnancy.[13] It has been shown that injection of progesterone to rats with induced preeclampsia leads to the reduction of blood pressure.[7] Administration of progesterone in pregnancy induced hypertension has shown to lower both systolic and diastolytic blood pres-

sures and also increasing urinary output significantly, ameliorates edema and slightly reduces weight gain without changing proteinuria.[14] In a study conducted by Belfort on isolated human arteries obtained from premenopausal non pregnant, normotensive, and preeclampsic women, demonstrated that progesterone had a direct relaxant effect on human omental artery from normal and hypertensive women.[8] From these observations, we are forced to conclude that preeclampsia seen in some pregnant women might be due to the reduced levels of progesterone and free testosterone. This is so, because our preeclampsic patients had a significantly lower serum progesterone and free testosterone than of healthy pregnant women with similar body mass index, gestational and chronologic ages (Table 2).

Alterations of vascular sensitivity to androgen hormones concomitantly with the reduced or absence of nitric oxide may have an important role in the elevation of blood pressure observed in preeclampsia.[15] Vascular relaxant effects of progesterone, on the other hand, seem to ameliorate hypertension by releasing prostacycline or nitric oxide.[16] Progesterone is an essential hormone for the achievement of full term pregnancy in human.[18] By terms the daily production of progesterone reaches to 250 mg/day, 10 fold greater than its peak during the luteal phase of normal menstrual cycle.[19] It is possible that hypoperfusion of placenta in preeclampsia might be associated with the reduced production of progesterone. Therefore, we believe that preeclampsia seen in pregnant women might be caused by the reduction of progesterone associated with the reduced level of plasma progesterone. This conclusion is also in accordance with other investigators reports.[13-19]

Conclusion

The results of this study are indicating that the low levels of plasma progesterone seen in pregnant women might be the cause of preeclampsia. Additional studies, however, are needed to explore the effect of progesterone on preeclampsia.

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