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Serum Androgens in Preeclamptic Women

S. Taghavi
Department of Obstetrics and Gynecology, Al-Zahra Hospital,
Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: The purpose of the study, was to determine whether maternal serum levels of androgens are higher in patients with preeclampsia than in matched normotensive control subjects. Serum total testosterone, DHEAS, SHBG and estradiol were measured in 100 pregnant womens in third trimester complicated with preeclampsia and the results were compared with 99 healthy pregnant women in the same period. There was no significant relation in serum total testosterone, DHEAS, estradiol and SHBG between two groups. Although the role of androgens as the cause of preeclampsia was not proved in this study, more research is needed to find the definite etiology of this disorder.

Key words: Hormones, preeclampsia, estrogens androgens, serum levels, DHEAS

INTRODUCTION

Preeclampsia is a pregnancy-specific, multisystem disorder that is characterized by the development of hypertension and proteinuria after 20 weeks of gestation in a woman with previously normal blood pressure (Ohkuchi *et al*., 2006; Tan *et al*., 2006; Wagner, 2004). The disorder complicates approximately 3-5% of pregnancies (Skjaerven *et al*., 2005). Although the exact cause of preeclampsia remains unclear (ACOG, 2005; Postovit *et al*., 2001), systemic vasospasm, vascular hemoconcentration, exaggerated inflammatory response, inappropriate endothelial activation, activation of the coagulation cascade and resultant microthrombi formation have all implicated (Roberts and Cooper, 2001).

Previously, it has been reported that circulating estrogens, including estriol, estradiol and estrone, were not reduced in maternal serum from pre-eclamptic compared with uncomplicated pregnancies, with adjustment for gestational age and several other potentially confounding factors. In contrast androgen concentrations were elevated (Troisi *et al*., 2003). Several studies have evaluated the association of serum androgens with Pregnancy-Induced Hypertension (PIH) and preeclampsia. The majority of studies showed that the elevated plasma levels of androgens could contribute to the endothelial dysfunction involved in the pathogenesis of preeclampsia (Serin and Kula, 2001; Laivuori, 1998; Salamalekis *et al*., 2006; Zhorzholadze *et al*., 2006; Atamer *et al*., 2004) although some studies suggest that maternal serum levels of androgens do not exhibit an association with preeclampsia (Miller *et al*., 2003). Previous studies have shown that women with polycystic ovarian disease, a disease associated with hyperandrogenemia, are at increased risk for PIH independent of body mass index (Laivuori, 1998; Michael *et al*., 1999). Jirecek *et al*. (2003) showed that alterations of steroid hormone profiles have been suggested to be involved in the pathophysiology of PIH (Jirecek *et al*., 2003).

We studied primigravid women and compared sex steroid hormone concentrations between those with preeclampsia and normotensive pregnancies after controlling for BMI, maternal age and gestational age, to determine whether elevated androgen concentrations are associated with preeclampsia or not.

MATERIALS AND METHODS

This is a prospective, case-control study conducted on 200 primigravid women with singleton pregnancies at Tabriz Al-Zahra hospital who consented to participate, since Jul 2003-May 2004.

All women included in the study were in third trimester of pregnancy; all of them were taking multivitamin supplement with iron and none were receiving or had received antihypertensive medications or exogenously administered hormones. None of the subjects had a history of hypertension, hyperandrogenism, or polycystic ovarian disease.

The subjects were divided into two groups that were similar with respect to maternal age and gestational age: group A consisted of 100 women in the third trimester of pregnancy with preeclampsia at the time of admission; and group B consisted of 100 healthy, normotensive women in third trimester of pregnancy. One patient of group B was excluded for moving from the city.

Preeclampsia was defined as new-onset hypertension after 20 week's gestation such that Systolic Blood Pressure (SBP) of ≥140 mm Hg, Diastolic Blood Pressure (DBP) of ≥90 mm Hg, or both were seen on two occasions ≥6 h apart, with significant proteinuria (≥300 mg $24h^{-1}$) (Wagner, 2004).

Venous blood was sampled, labeled and sent to laboratory promptly. Serum samples were stored at -20°C until testing. Levels of total testosterone, Dehydroepiandrosterone Sulfate (DHEAS) and estradiol were determined by means of commercially available radioimmunoassays (Orion Diagnostica, Finland, Spectria) and Sex Hormone Binding Globulin (SHBG) levels were determined by means of enzyme-linked immunosorbent assay (DRG Instruments GmbH, Germany). The collected data were recorded on questionnaires including maternal age, gestational age, BMI, SBP and DBP on two occasions ≥6 h apart, 24 h urine protein, newborn sex and levels of measured hormones.

Chi-2(χ^2)-test was used for comparison of qualitative variables and student t-test was used for comparison of quantitative variables between case and control groups. Analysis was performed by SPSS-12 statistical software and P-values less than 0.05 was considered significant.

RESULTS AND DISCUSSION

Mean maternal age, mean gestational age and BMI were not significantly different between two groups (Table 1). There were 49 (49%) male and 51 (51%) female infants born to the preeclamptic group (A) in comparison with 52 (51.48%) male and 47 (46.53%) female infants born to the control group (B). According to the χ^2-test, the sex of offspring was not significantly different between two groups (pV = 0.619).

Table 2 shows the measured serum hormone levels. The mean levels of total testosterone, SHBG, DHEAS and estradiol were not significantly different between two groups (pV>0.05).

According to the studies in North Oakland (Michael *et al*., 1999) New York (Miller *et al*., 2003) and Maryland (Troisi *et al*., 2003), the differences of maternal age, gestational age and BMI in our study were not significant.

Also, as other studies, the infant sex was not significantly different between normal and preeclamptic women (Troisi *et al*., 2003; Miller *et al*., 2003; Michael *et al*., 1999; Jirecek *et al*., 2003; Cunningham *et al*., 1999; Hallak, 1999; Troisi *et al*., 2003).

Salamalekis *et al*. (2006) suggest that the levels of total and free testosterone appear to be higher in patients with preeclampsia compared to normotensive pregnant women during the third trimester of pregnancy. This difference could indicate an involvement of testosterone in the pathophysiology of preeclampsia (Zhorzholadze *et al*., 2006). In our study, the total testosterone level was not significantly higher in preeclamptics than normotensive women. Also, there was not significantly difference of DHEAS and SHBG and estradiol between two groups.

Innes recently restated the estrogen hypothesis and suggested that lower estrogen concentrations in preeclampsia could be due to reduced aromatase activity which in turn could explain higher circulating androgen concentrations observed in some studies of preeclampsia (Troisi *et al*., 2003). In our study, the estradiol level was higher in preeclamptic women, but this difference was not significant.

Zhorzholadze *et al*. (2006) concluded that disorders of hormone homeostasis play an important role in the pathogenesis of endothelial dysfunction during preeclampsia. They suggest that decrease of vasodilatatory hormones (progesterone and estradiol) content and hypoxia-induced deposition of free NO (Nitric Oxide) in hemoglobin promotes increasing of vascular reactivity and development of hypertension Zhorzholadze *et al*. (2006). Other studies also suggest the association of circulatory sex hormone levels and preeclampsia (Serin and Kula, 2001; Michael *et al*., 1999; Jirecek *et al*., 2003).

Troisi *et al*. (2003) showed that serum unconjugated estradiol, estrone and estriol concentrations were not lower in preeclamptic pregnancies in a matched analysis with adjustment for race. Serum unconjugated androstenedione and testosterone concentrations however, were significantly higher in preeclamptic compared with control pregnancies, whereas DHEA and DHEAS did not differ (Troisi *et al*., 2003).

However, Troisi *et al*. (2003) in the other study suggest that estriol, estradiol, estrone, DHEA, DHEAS androstenedione and testosterone concentrations measured in cord sera were not significantly different in preeclamptics compared with uncomplicated pregnancies.

Miller *et al*. (2003) concluded that maternal serum levels of testosterone, sex hormone binding globulin, estradiol and DHEAS do not exhibit an association with preeclampsia in primigravid women (Miller *et al*., 2003).

It seems that the differences between our findings with other researches is due to race difference of our studied patients with European or American populations studied by others, or due to larger sample size in our study in comparison with previous ones. This hypothesis is confirmed by the fact that Troisi *et al*.

Table 1: Mean maternal age, mean gestational age and body mass index of patients in both groups

	Group A (preeclamptic women) (n = 100)	Group B (Normal women) (n = 99)	P-value	df	t
Maternal age (Y)	24.98±5.023	25.76±5.220	0.286	197	1.071
Gestational age (W)	32.29±2.709	32.03±2.555	0.482	197	0.704
Body mass index (kg m^{-2})	25.9070±2.63938	25.8545±2.42345	0.884	197	0.146

Table 2: The levels of serum hormones in both groups

	Group A (preeclamptic women) (n = 100)	Group B (Normal women) (n = 99)	P-value	df	t
Total testosterone (ng dL^{-1})	97.1870±49.501	107.2727±40.448	0.117	190.180	1.575
DHEAS (µg dL^{-1})	158.616±37.4937	156.956±39.244	0.761	197	0.305
SHBG (nmol L^{-1})	83.742±32.93	89.3303±30.7372	0.217	197	1.237
Estradiol ng mL^{-1})	16.036±3.707	15.294±2.468	0.099	172.539	1.661

(2003) in a study with comparable sample size (86 cases and 86 controls) obtained the same results as ours.

CONCLUSION

In summary, we found no difference in concentrations of androgens in the sera of pre-eclamptic and uncomplicated pregnancies. These data are not consistent with the hypothesis that higher blood androgen levels in preeclamptic patients implicate in the pathogenesis of preeclampsia. However, with respect the results of other studies, it is recommended to check the serum androgens before pregnancy to determine the patients with elevated serum androgens preconceptionally (e.g. PCOS, etc) and planning a close antenatal care for them.

In addition, regarding the harmful endocrine or metabolic changes specific for preeclamptic pregnancy, further studies should attempt to address more comprehensively the changes in pregnancy hormones and other mechanisms associated with etiology of preeclampsia.

REFERENCES

ACOG, 2002. Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. No. 33, January 2002. American College of Obstetricians and Gynecologists. Obstet. Gynecol., 99: 159-67.

Atamer, Y., A.C. Erden, B. Demir, Y. Kocyigit and A. Atamer, 2004. The relationship between plasma levels of leptin and androgen in healthy and preeclamptic pregnant women. Acta Obstet. Gynecol. Scand., 83: 425-30.

Cunningham, F., G. Norman, J. Kenneth and L. Gilstrap, 2001. Williams obstetrics, (21st Edn.), Mc Graw - Hill, New York, 1: 567-617.

Hallak, M., 1999. High Risk pregnancy, (2nd Edn.), Harcout Company, London, pp: 639-663.

Jirecek, S., E.A. Joura, C. Tempfer, M. Knofler, P. Husslein and H. Zeisler, 2003. Elevated serum concentrations of androgens in women with pregnancy-induced hypertension. Wien Klin Wochenschr, 31: 162-6.

Laivuori, H., 1998. Evidence of high circulating testosterone in women with prior preeclampsia. J. Clin. Endo. Meta., 83: 344-347.

Michael, T., S. Christos, E. Richard and G. Leonard, 1999. Androgens in preeclampsia. Am. J. Obstet. Gynecol., 180: 60-63.

Miller, N.R., D. Garry, H.W. Cohen and R. Figueroa, 2003 Serum androgen markers in preeclampsia. J. Reprod. Med., 48: 225-259.

Ohkuchi, A., R. Iwasaki, H. Suzuki, C. Hirashima, K Takahashi and R. Usui *et al*., 2006. Normal and high-normal blood pressures, but not body mass index, are risk factors for the subsequent occurrence of both preeclampsia and gestational hypertension: A retrospective cohort study. Hypertens. Res., 29: 161-167.

Postovit, L.M., M.A. Adams and C.H. Graham, 2001. Does nitric oxide play a role in the aetiology of pre-eclampsia? Placenta, 22: 51-55.

Roberts, J.M. and D.W. Cooper, 2001. Pathogenesis and genetics of pre-eclampsia. Lancet, 357: 53-56.

Salamalekis, E., P. Bakas, N. Vitoratos, M. Eleptheriadis and G. Creatsas, 2006. Androgen levels in the third trimester of pregnancy in patients with preeclampsia. Eur. J. Obstet. Gynecol. Reprod Biol., 126: 16-19.

Serin, I. and M. Kula, 2001. Androgen Levels of preeclamptic patients in the third trimester of pregnancy and 6 weeks after delivery. Acta Obstet. Gynecol. Scand., 80: 1009-1013.

Skjaerven, R., L.J. Vatten, A.J. Wilcox, T. Ronning, L.M. Irgens and R.T. Lie, 2005. Recurrence of pre-eclampsia across generations: Exploring fetal and maternal genetic components in a population based cohort. BMJ., 15: 877.

Tan, K.H., K. Kwek and G.S. Yeo, 2006. Epidemiology of pre-eclampsia and eclampsia at the KK Women's and Children's Hospital, Singapore. Singapore Med. J., 47: 48-53.

Troisi, R., N. Potischman, C.N. Johnson, J.M. Roberts and D. Lykins *et al*., 2003. Estrogen and androgen concentrations are not lower in the umbilical cord serum of pre-eclamptic pregnancies. Cancer Epidemiol Biomarkers Prev., 12: 1268-70.

Troisi, R., N. Potischman, R. Ness, D. Lykins, R. Hoover and W. Crombleholme, 2003. Maternal serum estrogen and androgen concentrations in preeclamptic and uncomplicated pregnancies. Int. J. Epid., 32: 455-460.

Wagner, L.K., 2004. Diagnosis and management of preeclampsia. Am. Fam. Physician., 15: 2317-24.

Zhorzholadze, E.D., T.V. Sanikidze and I.V. Dzhikiia, 2006. The role of hormonal homeostasis in pathogenesis of endothelial dysfunction during preeclampsia. Georgian. Med. News, 130: 104-107.