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Remzi GÖKDENİZ[1]
Erdal ARIGULOĞLU[2]
Nursel BAZOĞLU[1]
Özcan BALAT[1]

Elevated Serum β-hCG Levels in Severe Preeclampsia

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[1]Departments of Obstetrics and Gynecology, Faculty of Medicine, Inönü University, Malatya-Turkey
[2]Kahramanmaraş State Hospital, Section of Obstetrics and Gynecology, Kahramanmaraş-Turkey

Abstract: Most current hypotheses regarding the pathophysiologic mechanisms of pregnancy-induced hypertention point to early placental abnormalities. Therefore, we attempted to determine whether serum human chorionic gonadotropin (hCG) levels reflect a different trophoblastic secretory response of preeclampsia. Thirteen pregnant women with severe preeclampsia were matched with twenty-one normotensive pregnant women with singleton pregnancies in the third trimester. Serum b-hCG levels were found to be significantly higher in severe preeclampsia, compared with controls ($p<0.05$). This indicates that an abnormal secretory function of the placenta exists in patients with severe preeclampsia.

Key Words: Preeclampsia, human chorionic gonadotropin.

Introduction

Pregnancy associated hypertensive disorders and intrauterine growth restriction are common complications responsible for fetal, neonatal, and maternal morbidity (1, 2). Most current hypotheses regarding the pathophysiologic mechanisms of pregnancy-induced hypertention point to early placental abnormalities. Human placenta synthesizes steroid, protein, and glycoprotein hormones throughout gestation (3). The production of hCG by the placenta in early pregnancy is critical for implantation and maintanance of the blastocyst. Since it is postulated that preeclampsia is likely a trophoblastic disorder (4), it may be essential for understanding of this disease, to investigate the pathologic and secretory reaction of the placenta. Twin pregnancies (5) and molar pregnancies (6) produce higher levels of hCG and they are associated with a higher incidence of preeclampsia than uncomplicated singleton pregnacies. An association was reported between preeclampsia and elevated third trimester hCG levels (7), whereas early experience with second trimester levels suggests a link between increased hCG and other adverse pregnancy outcomes (8, 9). Considerable evidence suggests an association between serum hCG levels and preclampsia (9-14). We therefore investigated whether the level of serum b-hCG does correlate with the severity of preeclampsia and might reflect a different trophoblastic secretory response of this disease.

Materials and Methods

Thirteen women with severe preeclampsia and twenty-one normotensive, healthy pregnant women with singleton pregnancies in the third trimester were matched. None of them had a history of chronic hypertention. This investigation was designed as a prospective study. Subjects were mathced for gestational and maternal age. The criteria for severe preeclampsia were (1) systolic blood pressure ≥160 mm Hg or diastolic ≥110 mm Hg and (2) proteinuria >5 gm in 24 hours. In addition, any patient with oliguria (400 ml in 24 hours), cerebral or visual disturbances, epigastric pain, pulmonary edema, or abnormal platelet count and liver function profile was included in severe preeclampsia.

The venous blood samples were obtained from the subjects and centrifugated at 2000g for 10 minutes at 4°C. Sera were collected and stored at - 20°C until analysis. Serum levels of β-hCG (Immulite β-hCG, DPC® Los Angeles, CA) were measured by chemilluminecence. Total blood and urine biochemistries were examined. Student's t test and the Mann Whitney U test were used for statistical analysis. For statistical significance, a p value was set at < 0.05.

Results

Clinical data and serum β-hCG levels are shown in Table 1. and are expressed as mean±SEM. There was no difference between the two groups in terms of mean

Table 1. Subject data and serum β-hCG levels in severe preeclampsia and controls.

	Severe preeclampsia (n=13)	Controls (n=21)
Maternal Age (yr)	20.7±1.1	21.3 ±1.6
Gestational age (wk)	33.9±2.0	35.1±2.2
Serum uric acid (mg/dl)	6.2±2.1*	3.5±0.8
Serum creatinin (mg/dl)	0.82±0.1	0.79±0.1
MAP (mm Hg)	121.8±4.7*	73.4±5.8
Serum β-hCG (mIU/ml)	33960±4048.74*	18634±1618.47

MAP: Mean arterial pressure, * $p < 0.05$.

age, gestational age or serum creatinine levels (20.7±1.1, 33.9± 2.0, 0.82± 0.1 vs 21.3± 1.6, 35.1± 2.2, 0.79± 0.1 respectively) ($p > 0.05$). In the preeclamptic group, mean arterial tensions, serum uric acid and β-hCG levels were significantly higher than in the controls (121.8± 4.7, 6.2± 2.1, 33960± 4.48.74 vs 73.4± 5.8, 3.5± 0.8, 18634± 1618.47 respectively) ($p < 0.05$).

Discussion

In this study, we found that serum β-hCG levels were significantly elevated in severe preeclampsia, compared with the controls. This finding indicates that an abnormal secretory function exists in patients with severe preeclampsia.

In preeclampsia, placental pathologic examination reveals focal cellular necrosis in the syncytiotrophoblast and increased mitotic activity with cellular proliferation in the cytotrophoblast (15). In addition, the proliferating cytotrophoblast in severe preeclampsia is rapidly transformed into syncytiotrophoblast within 72 hours (16). The normal placenta differentiates during pregnancy with the cytotrophoblast dominant in early gestation and the syncytotrophoblast dominant in late pregnancy (17). It is well known that the cytotrophoblast is an undifferentiated stem cell and the syncytotrophoblast is a differentiated trophoblast transformed from the cytotrophoblast (18). Although the mechanism of regulation of gestational hCG remains largely unknown, it is generally accepted that hCG, are only secreted by syncytotrophoblasts (19). Recently Maruo et al. (20) showed that β-hCG could be detected in the cytotrophoblast in very early pregnancy. In a clinical study, hCG levels were assayed in 62 patients with toxemia; 28 of the 62 patients had serum hCG levels above the normal range, indicating that early placental vascular damage leading to decreased oxygen supply might result in increased hCG production by hyperplastic cytotrophoblastic cells (21). Also, hCG production has been shown to increase when normal placental villi in organ cultures were maintained under hypoxic conditions (22). Typically, the placenta is the affected tissue in pregnancies complicated by hypertention (23).

As it is known that total hCG and β-hCG are predominantly produced by syncytiotrophoblast and they can be also detected in the differentiating cytotrophoblast (20), many authors studied serum levels of hCG and β-hCG in preeclampsia to define an abnormal placental secretory function or to predict the development of preeclampsia before this disease is manifest. In 1934, Smith et al. (10), talked about increasing hCG Levels in severe preeclampsia for the first time. Taylor et al. (24) in 1939 and Loraine et al. (25) in 1950, reported similar results. However, contrary results have been reported in 1968 by Teoh and Sivasamboo (26). But recently, an association was found between elevated serum β-hCG levels and preclampsia in the third trimester (7), whereas an elevation in serum β-hCG levels in the second trimester has been linked with the devolopment of preeclamsia (11, 13, 14). A relationship was also reported between adverse pregnancy outcome and elevated second trimester serum β-hCG levels (8, 9, 27).

In conclusion, we found a strict relationship between severe preeclampsia and elevated serum β-hCG levels, indicating that there should be an abnormal placental secretory function in patients with severe preeclampsia. The use of these findings to prevent adverse pregnancy outcome should be further investigated.

Correspondance author:
Remzi GOKDENIZ
Zafer Mah. Korukent Sitesi
A Blok, Daire No: 10
Malatya-TURKEY

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