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CLINICAL ARTICLE

Serum adiponectin, leptin and soluble leptin receptor in pre-eclampsia

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Abstract

Objectives: To delineate the changes in serum levels of adiponectin, leptin and soluble leptin receptor, and in the free leptin index in women with pre-eclampsia. *Methods:* Blood samples were collected from 38 pregnant women with pre-eclampsia and 42 normotensive pregnant women as controls. Serum concentrations of adiponectin, leptin and soluble leptin receptor were determined by enzyme-link immunosorbent assay and the free leptin index was calculated as the ratio of serum leptin to soluble leptin receptor for each sample. *Results:* No significant differences were observed between the groups regarding maternal age, gestational age and body mass index. Women with pre-eclampsia had significantly higher levels of serum adiponectin and leptin, and a higher free leptin index than controls ($P<0.01$, $P<0.001$ and $P<0.001$, respectively). There were no significant differences between the two groups in serum levels of soluble leptin receptor ($P>0.05$). *Conclusions:* The study demonstrated elevated serum levels of adiponectin and leptin as well as a higher free leptin index in women with pre-eclampsia, suggesting these as important factors contributing to this complication of pregnancy.

1. Introduction

Pre-eclampsia, a potentially dangerous complication of the second half of pregnancy, labor and the early postpartum, is characterized by hypertension, proteinuria and other systemic disturbances [1—4]. Endothelial dysfunction, placental hypoxia,

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excessive systemic inflammation, coagulopathy and altered metabolism are characteristics of pre-eclampsia [1—4]. The etiology of this disease remains elusive. Although it is likely that the causes of pre-eclampsia are multifactorial and may involve genetic, immune, placental and other factors, insulin resistance may be an important contributor to its development [1—4].

Metabolism is different in pregnant and non-pregnant women [5,6]. An altered metabolism is required to support the rapid fetal and placental growth, and prepare pregnant women for delivery and breastfeeding [5,6]. The second half of pregnancy is a state of physiological insulin resistance and this state is exacerbated in pre-eclampsia [5,6].

Increased risks of pre-eclampsia have been reported, along with several conditions associated with insulin resistance [5—7]. These include gestational diabetes, polycystic ovary syndrome, obesity and excessive weight gain during pregnancy [5—7]. Features of the insulin resistance syndrome have been associated with pre-eclampsia. These include hyperinsulinemia, glucose intolerance, obesity or excessive body weight gain, and lipid abnormality, i.e., high triglyceride levels, low high-density lipoprotein cholesterol levels and high low-density lipoprotein cholesterol levels. Insulin resistance syndrome may also involve other metabolic abnormalities, including an increased concentration of plasminogen activator inhibitor and tumor necrosis factor α (TNF-α) [5—7].

Adiponectin, leptin and resistin are found expressed in human placenta [8—10]. These adipocyte-derived hormones, or adipokines, are thought to be involved in the pathogenesis of pre-eclampsia because of their role in the regulation of energy metabolism and insulin sensitivity [8—10]. The elevation of serum leptin levels in pre-eclampsia has been documented and it has been suggested that it contributed to the disease [9,11,12]. The regulation of circulating leptin levels by the soluble leptin receptor (sLR) has been discussed [13,14], but changes in sLR levels in pre-eclampsia have been less examined [14]. Similarly, until very recently, few publications had documented changes in serum adiponectin levels [15,16]. A previous study by this team of investigators revealed differences in serum resistin levels in women with pre-eclampsia and healthy pregnant women [17]. The aims of the present investigation were to elucidate the changes in serum levels of adiponectin, leptin and sLR as well as the changes in the free leptin index occurring in pre-eclampsia, and to explore their roles in the disease process.

2. Materials and methods

2.1. Patients

A cross-sectional study was conducted at the Women's Hospital of Zhejiang University according to the protocol approved by the hospital's ethics committee, and informed consent was obtained from all participants. In the present investigation, 38 women with pre-eclampsia in the third trimester pregnancy were consecutively recruited and 42 healthy women served as controls. Among the pre-eclamptic women, 23 were diagnosed with severe pre-eclampsia and 15 with mild pre-eclampsia. All participants were nulliparous Chinese women.

Inclusion criteria were normal pregnancy in the third trimester and pre-eclampsia. Study subjects and controls were matched at the time of sampling for age, duration of pregnancy and body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters). Duration of pregnancy was calculated from the last menstrual period and confirmed by ultrasonography in early pregnancy.

Pre-eclampsia was diagnosed according to strict criteria: a systolic blood pressure of 140 mm Hg or higher, or a diastolic blood pressure of 90 mm Hg or higher, on two occasions at least 6 h apart occurring after the 20th week of pregnancy in women with previously normal blood pressure, plus detectable urinary protein ($\geq$1 + by dipstick or $\geq$0.3 g per 24 h). Exclusion criteria were multiple gestation, diabetes mellitus, chronic hypertension, infectious diseases recognized in pregnancy, premature rupture of membranes, active labor, polyhydramnios and signs of other concurrent medical complication.

Severe pre-eclampsia was defined as a blood pressure of 160/110 mm Hg or higher, with either a urine dipstick showing 3+ or 4+ in a random urine sample or a proteinuria of 5.0 g or greater per 24 h. Other evidence of severe disease included elevated levels of serum creatinine, eclampsia, pulmonary edema, oliguria (less than 500 ml per 24 h), fetal growth restriction, oligohydramnios and symptoms suggesting significant end-organ involvement (headaches, visual disturbances, epigastric pain or pain in the right upper quadrant). Women who met the criteria for pre-eclampsia but not for severe pre-eclampsia were diagnosed as having mild pre-eclampsia.

2.2. Sample collection and ELISA analysis

One fasting blood sample was taken from each participant. All samples were left at room temper-