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SERUM LEPTIN LEVELS IN DIFFERENT TYPES OF HYPERTENSION DURING PREGNANCY

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Abstract

We determined the serum levels of leptin in 96 pregnant women with body mass index between 20 to 30, 30 normal (NP), 26 with mild preeclampsia (MPE), 27 with severe preeclampsia (SPE), 6 with chronic hypertension plus preeclampsia (CHT+PE) and 7 with chronic hypertension (CHT). A significant ($p < 0.01$) decrease in leptin levels was observed in the SPE group when compared with the NP group. On the contrary, significant ($p < 0.05$) increases were observed in the CHT and CHT+PE groups when compared with the NP group. Leptin levels were significantly higher in the MPE ($p < 0.001$), CHT ($p < 0.01$) and CHT+PE ($p < 0.5$) groups when compared with the SPE. No significant differences were observed in the CHT group when compared with CHT+PE. Moreover, a positive correlation was encountered ($r = 0.6$, $p < 0.001$) between platelet number and leptin levels for all the patients with preeclampsia. These results suggest that leptin levels may be useful metabolic parameter in different types of hypertension during pregnancy.

Introduction

Pregnancy induced hypertension (PIH) is a clinical event which occurs during gestation and reverts after giving birth; is one of the main causes of death during pregnancy (Sibai, 1990; Cunningham and Lindheimer, 1992; Lockwood, 1991; Lim and Friedman, 1993). Several patients with PIH may develop HELLP (Hemolysis, increased Liver enzymes and Low Platelet count) which is a syndrome characterized by hemolysis, an increase of hepatic enzymes and thrombocytopenia (Sibai, 1990; Cunningham and Lindheimer, 1992; Lockwood, 1991; Lim and Friedman 1993). Patients with chronic hypertension may be complicated with preeclampsia (PE) during pregnancy

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(Sibai, 1990; Cunningham and Lindheimer, 1992; Lockwood. 1991; Lim and Friedman, 1993).

Leptin is a hormone encoded by the *ob* gene. Its major source is adipose tissue (Zhang, Proenca *et al.*, (1994) and its levels increase at night, circulating concentrations reflect body fat stores (Mantague, Farooqi *et al.*, (1997). Several physiological and pathological conditions may affect leptin levels. For example: 1) Butte, Hopkinson and Nicolson (1997) have shown that leptin levels are increased in pregnant women and that its levels decrease at term, and 2) Agata, Masuda *et al.* (1997) have shown that leptin levels are increased in essential hypertension.

However, no reports have assessed the levels of leptin in different types of hypertension. In the present study, we assessed the levels of leptin in pregnant women with different types of hypertension.

Materials and Methods

The patients studied were among those admitted to the Maternity Hospital (Maternidad Concepción Palacios) of Caracas. The study was accepted by the Ethical Committee of the hospital.

We studied 96 pregnant women, 30 normal (NP), 26 with mild preeclampsia (MPE), 27 with severe preeclampsia (SPE), 6 with chronic hypertension plus preeclampsia (CHT+PE) and 7 with chronic hypertension (CHT). After written consent, a sample of blood was taken during pregnancy in the afternoon (4-5 pm).

We used the classification of the hypertensive disorders of pregnancy adopted by the American College of Obstetricians and Gynecologists in 1986 (National High Blood Pressure Education Program Working Group Report on High Blood Pressure During Pregnancy (1990), and Technical Bulletin (1986).

Blood pressure was measured by the first and fifth Kortkoff sounds with patients in the left lateral decubitus position. The blood pressure recordings were ascertained during the admission, before starting anti-hypertensive treatment (patients with preeclampsia) and immediately before blood collection.

All patients were pregnant for more than 20 weeks. Mild preeclampsia was defined for the following: recent hypertension, persistently ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic, mild proteinuria or edema. Patients with severe preeclampsia had one or more of the following: recent systolic blood pressure persistently ≥ 160 mmHg; diastolic blood pressure persistently ≥ 110 mmHg; proteinuria > 2000 mg/24 hr (or > 3+ in semiquantitative tests), increased serum creatinine levels (> 177 μmol/L-2 mg/dl) or oliguria (< 500 cc/24 hr), platelet count < 1 x 10^9/L or evidence of microangiopathic hemolytic anemia (schistocytes, an increase in indirect bilirubin levels, or increase in serum free hemoglobin levels), upper abdominal pain, headache, visual disturbances or other cerebral signs. Women with chronic hypertension were diagnosed as having essential hypertension before pregnancy. Patients with a previous history of chronic hypertension that developed proteinuria, abnormal edema or any signs of severe preeclampsia were classified as chronic hypertension with superimposed pregnancy induced hypertension.

We excluded patients with fever, infection, other chronic diseases (such as diabetes, renal disorders, cardiopathies, etc.); or patients in whom the syndromes were not clearly defined with the aforementioned criteria. A complete medical record of each patient was retained from the admission to the hospital discharge.

Hypertensive patients were treated with α methyldopa hydralazine or nifedipine, alone or in combination, during pregnancy. The doses varied depending on the response.

Leptin levels were assessed in serum samples using a commercial sandwich ELISA assay (R and D systems, UK).

The results obtained are expressed as mean ± SD and were compared using ANOVA analysis and unpaired Student's t test.

Results

In Table I, the general characteristics of the population studied are represented. Patients with chronic hypertension (CHT and CHT+PE) were older ($p < 0.05$) when compared with other groups. Significantly higher values of blood pressure and uric acid were observed in the different groups (MPE, SPE, CHT and CHT+PE) when compared with NP. An increase in creatinine levels, increase in serum transaminase, or a decrease

in platelet count was observed generally in the patients with SPE and SPE and CHT+PE. HELLP syndrome was not observed in these patients (considered as non severe forms of preeclampsia).

Figure 1 illustrates the levels of leptin during pregnancy for the different groups. A significant decrease ($P < 0.01$), when compared with controls, was observed in the SPE group. In contrast, mild but significant increases ($P < 0.05$) were observed in the CHT and CHT+PE groups when compared with NP. Leptin levels were significantly higher in the MPE ($p < 0.001$), CHT ($p < 0.01$) and CHT+PE ($p < 0.05$) groups when compared with the SPE. No significant differences were observed in the CHT group when compared with CHT+PE.

TABLE I

General characteristics of the population studied including clinical and laboratory parameters.

	NP	MPE	SPE	CHT	CHT+PE
n	30	26	27	7	6
Body mass index[a]	25 ± 3	24 ± 4	25 ± 4	26 ± 3	24 ± 3
Age (years)	26 ± 6	24 ± 7	24 ± 6	31 ± 8	34 ± 3
Systolic Pressure	118 ± 5	140 ± 9 **	162 ± 11 ***	157 ± 15 ***	176 ± 28 ***
Diastolic pressure	70 ± 7	91 ± 6 ***	105 ± 5 ***	101 ± 12 ***	118 ± 20 ***
Uric acid mg/dL	3.2 ± 0.6	5.1 ± 1.5 **	5.8 ± 2.5 ****	5.2 ± 1.2 *	6.0 ± 2.4 ***
Total bilirubin mg/dL	0.4 ± 0.2	0.41 ± 0.2	0.47 ± 0.28	0.6 ± 0.19	0.5 ± 0.23
ALT U/L	18.3 ± 6	19.5 ± 3.6	23 ± 11	21.2 ± 12	26.1 ± 23
AST U/L	26.3 ± 5	21 ± 3.4	35 ± 21	27.3 ± 3	86.8 ± 119***
Creatinine mg/%	0.59 ± 0.15	0.62 ± 0.18	0.82 ± 0.14***	0.73 ± 0.1	0.83 ± 0.12 **
Platelet/ mm^3	262000 ± 40000	236000 ± 59140	222000 ± 68640	290000 ± 67509	200000 ± 53398
Weeks of gestation	38 ± 3	37 ± 2	37 ± 3	33 ± 2	31 ± 5

The characteristics of the groups are represented. These characteristics include laboratory parameters as well as the weeks of gestation in which the samples were taken. Statistical differences were observed as compared the different groups with NP by ANOVA (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$, **** $p < 0.0001$). [a] Body mass index was calculated by the method of Velazco-Orellana., Alvarez-Aguilar *et al.*, 1981 and Mejia Rodriguez.

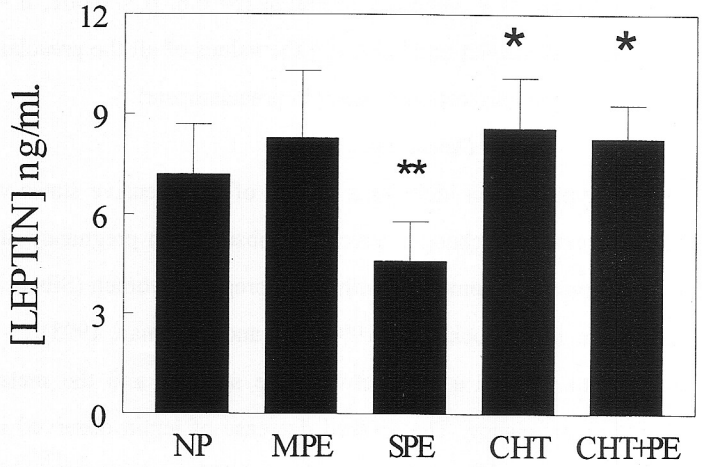

Figure 1. Serum leptin levels during pregnancy. This figure represents leptin levels during pregnancy of the different groups studied: normal pregnancy (NP), mild preeclampsia (MPE), severe preeclampsia (SPE). ** As compared to NP, $p < 0.01$ (ANOVA test).

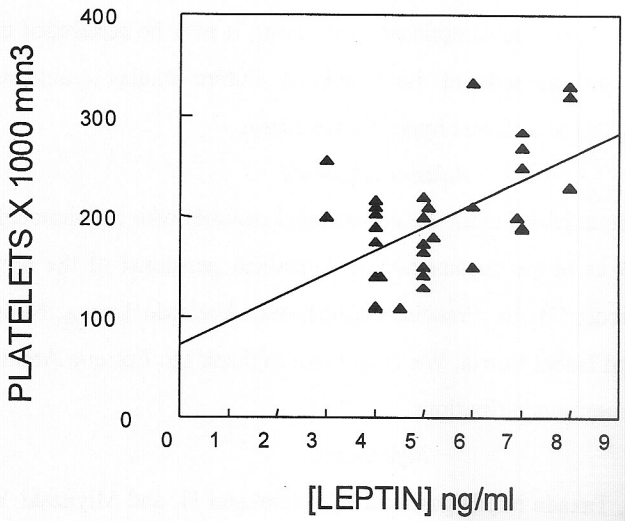

Figure 2. Correlation between platelet number and leptin levels in preeclamptic patients. A positive correlation was found ($r = 0.6$, $P < 0.001$) for all the patients with preeclampsia.

In addition, Figure 2 depicts a positive correlation ($r= 0.6$, $p < 0.001$, $n = 59$) between serum leptin values and platelet number using the values of all the preeclamptic women (one of the most useful paraclinical parameters in preeclampsia).

Discussion

Pregnancy-induced hypertension includes a variety of hypertensive states which reverts at puberty. Marked metabolic changes have been observed in pregnancy and its different types of hypertension when compared with non-pregnant women (Sibai, 1990; Cunningham and Lindheimer, 1992; Lockwood, 1991; Lim and Friedman, 1993).

Leptin levels seem to provide a link between the severity and the metabolic changes which occur during pregnancy. The marked decrease of leptin observed in the SPE patients suggests that SPE is a different hypertensive condition when compared with MPE, CHT and CHT+PE. Leptin levels in the CHT and CHT+PE groups were higher when compared with NP indicating that the metabolic changes produced in hypertension may not be modulated during pregnancy despite its effect in normal pregnant women. These conclusions are supported by the high correlation observed between platelet number and leptin levels in preeclamptic patients. Thus, it may be concluded that leptin levels may be a useful parameter in these patients. Future studies should assess the importance of leptin in these different hypertensive states.

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