Blood pressure peaks correlated with plasma fibronectin levels and microalbuminurin in hypertensive pregnancies

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Summary

A group of 32 selected hypertensive pregnant women under antihypertensive therapy, with biochemical parameters, functional parameters, plasma fibronectin levels (PLF), microalbuminuria (MA) levels and continuous 24 h blood pressure monitoring, were followed monthly until delivery and during puerperium. Also possible biochemical and clinical markers and the predictive value in the complications during PIH were attempted to be identified.

There was a statistical correlation between systolic pressure peaks associated with high levels of PLF and MA in hypertensive pregnant women who may have a higher risk of pregnancy or cardiovascular complications. Continuous 24 h blood pressure monitoring in hypertensive pregnancies was found to be helpful in identifying the highest risk patients especially by reading the night peak percentages.

Key words: Pregnancy; Hypertension; Blood pressure peaks; Continuous 24 h blood pressure monitoring; Plasma fibronectin levels; Microalbuminuria.

Introduction

Sometimes hypertensive disorders in pregnancy are associated with cardiovascular complications possibly meaning a materno-fetal well-being compromise and leading, in many cases, to emergency resolutions. It should be noted that during pregnancy every blood pressure rise, even the slightest one, may develop into these complications [1]. For this reason many studies have been carried out to find early clinical-functional signs useful in predicting a complication in hypertensive pregnancies.

In recent years scientific attention has been directed towards testing the physiopathologic function of plasma fibronectin levels (PLF) and microalbuminuria (MA) [2-13], the modifications during pregnancy with or without complications, and if the changes have a “predictive value” for the complications [6, 8, 14, 15, 16]. On the other hand, the prognostic-evolutional role of the blood pressure peaks, noticed with continuous 24 h monitoring, is important for the increased risk of cardio-vascular disease during some hypertensive complications or in association with other vascular diseases (i.e. diabetes, etc.) [17-25].

In our study we tried to identify with serial controls: 1) possible biochemical and clinical markers; 2) a possible correlation between plasma fibronectin levels, microalbuminuria and blood pressure peaks; 3) the predictive value in the complications during PIH and the modifications of antihypertensive therapy.

Materials and Methods

Thirty-two pregnant women with hypertensive disease, maternal age range 16-48 years (mean age 27 + 11), gestational age range 12-35 weeks (average week’s gestation 28 + 2) vs sfx pregnant women without hypertensive disease with an age range of 19-32 (28 + 3), with gestational range 20-24 weeks (22 + 3) and with a negative pathological pregnancy history were followed. All selected patients had no diabetes, vascular nephropathy or other diseases able to modify PLF and MA levels.

All patients were controlled with biochemical parameters (BUN, glycaemia, Na+, K+, etc.), functional parameters (electrocardiogram, blood pressure, Doppler velocimetry, etc.), PLF, MA levels and in hypertensive pregnancies, continuous 24 h blood pressure monitoring with a monthly follow-up until delivery and during puerperium. In all hypertensive pregnancies other “clinical risk factors” than hypertension were considered, such as gestational age, parity, edema, and previous gestosis. The hypertensive pregnancies were grouped following the American College of Obstetricians and Gynecologist classification [26]: 1) pregnant women hypertensive gestosis (17 patients); 2) pregnant women with pre-existing chronic hypertension (7 patients); 3) pregnant women with late-transient gestosis (relapsing, 8 patients).

Hypertensive patients, already treated elsewhere, discontinued antihypertensive treatment for at least ten days before check-up. Every hypertensive patient was treated with alpha-methyldopa (max. 500 mg x 2/die) or nifedipine (max. 80 mg/die).

The fibronectin level was dosed in platelet-free plasma (centrifuged with Antagosan 5 ml) by immunoturbidimetry (Fibronectin Opsonic-Protein, Boehringer-Mannheim).

The microalbuminuria level was dosed at 24h urinary output and tested with colorimetry (Mical Test Zestfare Care), the RIA method (Pharmacia Albumin RIA) and radioactivity (Gammacounter).

Continuous 24 h blood pressure monitoring (every 15 min. during the day and night) was executed with Takeda TM 2420.

Blood pressure readings were calculated as peak percentages (systolic, diastolic 24h, nocturnal and diurnal), as reported in the literature [23, 25] and in our study [24, 27]. “No risk” limits were set up <= 10% of peaks [23, 24, 27]. For statistics we used...
the linear regression test (Pearson’s “r”). For every test the statistical significance was calculated.

**Results**

The results of our study are grouped in figs. 1-2-3. If only PLF is analyzed in the three groups of hypertensive patients, we notice that before treatment more elevated values were present in the relapsing gestosis group and in the chronic hypertension patients than in the normal pregnancies. In the three groups the anti-hypertensive treatment reduced puerperal (post-partum) PLF independently of the kind of therapy.

MA levels were slightly higher in the chronic hypertensive pregnancies, but the variations in the three groups of patients resulted in no statistical significance in basal conditions as well as during gestation and without hypertensive treatment. A significant increase (p<0.01) occurred in the same group only immediately before delivery. In the figures the three groups blood pressure systo-diastolic values (media + DS) and the variations until delivery and after one month are reported. During the observation the median 24h blood pressure peak percentages were: a) in pregnancies with hypertensive gestosis = systolic 10% and diastolic 19%; b) in pregnant women

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**Figure 1.** — Pregnancies with pre-existing chronic hypertension.

**Figure 2.** — Pregnancies with late-transient gestosis (relapsing).

**Figure 3.** — Pregnancies with hypertensive gestosis.
with relapsing gestosis = systolic 12% and diastolic 20%; c) in pregnant patients with pre-existing chronic hypertension = systolic 28% and diastolic 22%.

In the groups of hypertensive gestosis and relapsing gestosis patients antihypertensive treatment presented a significant reduction of 24h blood pressure systo-diastolic peaks after delivery. In chronic hypertensive patients there was no statistical significance.

In our study among the 20 pregnant women who underwent cesarean section (CS) (64% of 32 hypertensive patients) because of their clinical and cardiovascular risks who did not respond to antihypertensive therapy, 12 patients (6 with chronic hypertension, 6 with hypertensive gestosis) had preterm cesarean sections and as a result they had an Apgar index <7 at 1 min. in six babies, and at 5 min. in three cases; one of these died due to prematurity after intrauterine growth retardation (IUGR).

These 12 patients presented the median 24h blood pressure systolic peaks of about 50% + 25; in particular on the same day they had: diurnal systolic peaks = 39% + 27, nocturnal = 40% + 36; diurnal diastolic peaks = 53% + 25, and nocturnal = 41% + 26. In these patients significant correlations, were observed between: 1) MA and the 24h systolic median (r = 0.77; p <= 0.05); 2) MA and the diurnal systolic median (r = 0.52; p <= 0.07); 3) MA and the nocturnal systolic median (r = 0.67; p <= 0.03); 4) PLF and 24h systolic median (r = 0.66; p <= 0.02); 5) PLF and 24h diastolic median (r = 0.51; p <= 0.1); 6) PLF and the nocturnal systolic median (r = 0.61; p <= 0.06); 7) PLF and the nocturnal diastolic median (r = 0.61; p <= 0.06).

The best statistical significance is correlated with: MA and the 24h systolic median (r = 0.7; p <= 0.01); MA and nocturnal systolic peaks (r = 0.81; p <= 0.01); PLF and the 24h systolic median (r = 0.64; p <= 0.03); MA and nocturnal systolic peaks (r = 0.86; p <= 0.006).

Among the correlations of clinical risk factors it was observed that in all hypertensive pregnancies, parity was a reduction factor for blood pressure peaks: nocturnal diastolic peaks 0.77, nocturnal systolic peaks 0.56 and 24h diastolic peaks 0.50, respectively.

Analysing the type of delivery we noticed that some cases had emergency problems. Indeed, of 32 patients only 40% had vaginal deliveries, and frequently induced labor. Prematurity was not very influential on the outcome of the babies as in the control group: only four babies born from hypertensive mothers had an Apgar index at 5<7, and only two babies were admitted to the Department of Neonatology. IUGR was present in ten cases, one of these died afterwards.

**Comments**

Even if in all hypertensive pregnancies higher PLF levels may be observed, mostly in pregnant women with chronic hypertension (because of vascular damage due to long lasting high blood pressure), the difference between this group and normotensive pregnancies was not remarkable.

Higher MA levels were also of no statistical significance, except in pregnant women with pre-existing chronic hypertension and in patients with clinical conditions needing preterm delivery. The evaluation of continuous 24h blood pressure monitoring peaks is more interesting. These peaks, which do not appear to be correlated with blood pressure systo-diastolic absolute values, occurred most frequently in cases of chronic hypertension or when there was no response to antihypertensive therapy.

The correlations among continuous 24h blood pressure monitoring peaks (especially nocturnal), PLF and MA were much more evident in patients in whom, due to clinical conditions and no response to antihypertensive therapy, a preterm delivery was necessary.

Numerous studies [2, 6, 7, 8, 28] have been published on preeclamptic pregnancies demonstrating the correlation between the increase of PLF and vasospasms during hypertensive peaks; however, vasoconstriction was a cause or effect of vascular endothelium damage related to MA increase [11, 29, 30, 31, 32]. The “endothelial stressor” is more evident in cases of elevated blood pressure peaks during hypertension [18, 20, 21, 23, 24, 27]. Indeed, during hypertension the arterial wall may be damaged much more from frequent blood pressure changes than from absolute blood pressure values. These frequent changes might damage the placental circulation as well as has been demonstrated in the cerebral and coronary vascular districts [18, 22, 23, 25, 32, 33].

The relation between the reduction of blood pressure peaks and pregnant parity is difficult to interpret; this is probably related to a cardiovascular adaptation to the utero-placental haemodynamic variations during previous pregnancies.

In conclusion, we observed that higher PLF and MA levels alone do not mean higher risk for hypertensive pregnant women. A significant percentage of blood pressure peaks, associated with high levels of PLF and MA, may be a better index of higher risk in hypertensive pregnancies. Thus, continuous 24h blood pressure monitoring in hypertensive pregnant women can help to identify the highest risk patients especially by reading the night peak percentages.

**References**


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