„New Method for the Prediction of Preeclampsia: Analysis of Heart Rate and Blood Pressure Variability“

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INTRODUCTION

Preeclampsia (PE), a serious pregnancy-specific disorder characterized by proteinuria and hypertension after the 20th week of gestation, is still the main cause of maternal and neonatal morbidity and mortality. It occurs in 3-5% of all pregnancies. As the etiology and pathogenetic factors underlying this complication of pregnancy are still unknown, early risk assessment by Doppler sonography is to improve clinical management and outcome. However, the positive predictive value of Doppler sonography is limited to approximately 30%, as only part of women with disturbed uterine perfusion develop one of the complications of pregnancy, such as PE, pregnancy-induced hypertension (PIH), or intrauterine growth retardation (IUGR) [Chien2000].

Analyses of heart rate (HRV) and blood pressure variability (BPV), and baroreflex sensitivity (BRS), have become powerful techniques for assessing autonomic control in cardiovascular diseases [LaRovere2001]. We considered the possibility of a combination of this technique with Doppler sonography being able to improve the prediction of PE.

PATIENTS AND METHODS

The study includes 58 patients with abnormal uterine perfusion (AUP) examined consecutively and 44 normal pregnancies recruited in parallel who underwent Doppler sonography in the second trimester of pregnancy (median 21 weeks, range 18-22 weeks). All pregnancies were singleton. At the time of examination, the women were healthy, normotensive, without clinical signs of cervical incompetence, and on no medication. Uterine perfusion was defined as pathological when there was bilateral notching or the mean pulsatility index (PI) of both arteries was above 1.45. After Doppler examination, all women underwent non-invasive continuous blood pressure monitoring via finger cuff (100 Hz, Portapres device Mod. 2, BMI-TNO, NL) for analysis of HRV, BPV, and BRS. The parameters of time domain and frequency domain were calculated to HRV task force standards and adapted to BPV [Wessel 2000, TF1996]. To analyze heart rate and blood pressure interactions, we calculated BRS by the Dual Sequence Method [Malberg2002].

Outcome measures of the study were PE, pregnancy-induced hypertension (PIH) and/or intrauterine growth retardation (IUGR).

The Mann-Whitney U test was performed to group differences in variability parameters. Forward stepwise discriminant analysis with a maximum of 3 parameters was used to estimate the group classification rates.

RESULTS

Fifty-eight out of 102 pregnancies were characterized by abnormal uterine perfusion around the 20th week of pregnancy. While age, systolic and diastolic blood pressures, as well as heart rate were not altered, this group delivered significantly earlier, and the neonates were characterized by lower birth weight. Sixteen of the 58 pregnancies developed PE, while none of the 44 women with normal uterine perfusion developed any kind of hypertensive disorder. We combined the analysis of uterine perfusion and the variability and baroreflex parameters (see Table 1).

In the group of abnormal uterine perfusion, three parameters achieved a sensitivity of 93.7%, a specificity of 85.7%, and improved PPA to 71.4% with a negative

Tab. 1: Statistical summary of inter-group calculations

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PE</th>
<th>NoPE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeanNN</td>
<td>743.2±125.7</td>
<td>763.6±120.3</td>
<td>n.s.</td>
</tr>
<tr>
<td>MeanSBP</td>
<td>129.2±12.8</td>
<td>122.1±17.0</td>
<td>n.s.</td>
</tr>
<tr>
<td>MeanDBP</td>
<td>73.2±9.4</td>
<td>67.4±10.9</td>
<td>n.s.</td>
</tr>
<tr>
<td>DBP1</td>
<td>8.3±4.5</td>
<td>5.16±1.8</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>BRS1</td>
<td>2.6±0.8</td>
<td>1.8±0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HRV1</td>
<td>0.44±0.09</td>
<td>0.36±0.13</td>
<td>&lt;0.016</td>
</tr>
</tbody>
</table>

Tab. 1: Statistical summary of inter-group calculations
predictive accuracy (NPA) of 97.3%. It is important to note that the combination of other parameters did not reach a higher PPA.

In Fig. 1 an example of cardiovascular alterations during the course of pregnancy is demonstrated.

![Graph](image)

Fig. 1: Alteration in high frequency range of diastolic blood pressure (HF-DBP) during the course of the gestation (week of gestation, WoG) in pregnant women with PE risk (PE) vs. with no PE Risk (NoPE)

**DISCUSSION**

Many attempts have been made to develop a simple clinically feasible test for early prediction of PE. However, previous studies using one-stage or two-stage Doppler sonography alone or combined with humoral or endothelial parameters achieved neither sufficient sensitivity nor positive predictive value or were costly or invasive. Although HRV and BPV as well as BRS parameters were initially developed for risk stratification in cardiology, the field of clinical applications has broadened in recent years, and these parameters of autonomic cardiovascular control are also influenced in hypertensive pregnancy disorders.

Therefore, we tried the hypothesis whether this method would be applicable in predicting PE, as PE-associated endothelial dysfunction was recognized by these parameters early on. While the incidence of PE in the Western population is 3-5% of all pregnancies, and pathological uterine perfusion in the second trimester is known to be an indirect sign of an inadequate trophoblast while raising positive predictive accuracy only to 30%, we demonstrate in this study that three variability and BRS parameters enabled us to predict PE several weeks before clinical manifestation with a PPA of 50.0%. As no other singular method reached higher predictability, our method has a higher PPA than all independent humoral factors described or single clinical parameters measured. In combination with Doppler sonography of uterine arteries, our method achieves the highest predictive level of all non-invasive trials published. Especially the high positive predictive accuracy of 71.4% attests to the clinical relevance of combining Doppler analysis and beat-to-beat dynamics. In clinical practise our main approach is therefore aimed combining Doppler analysis and beat-to-beat dynamics.

In summary, currently the most precise prediction of PE by concurrent measurement of uterine perfusion and calculation of cardiovascular beat-to-beat parameters in the second trimester may further an early therapeutic strategy to reduce upcoming pathophysiological characteristics of the disease and, consequently, prevent complications which would result in high morbidity and mortality rates [Walther2006].

**REFERENCES**


cardiomyopathy” Clinical Science Vol 102, p 465, 2002