Analysis of cardiovascular dynamics: new approach for predicting of pre-eclampsia

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ABSTRACT:

Early prediction of Pre-eclampsia (PE), a serious pregnancy complication, is still insufficient in clinical practice. We applied parameters of heart rate and blood pressure variability to detect cardiovascular alterations in order to predict PE.

INTRODUCTION:

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) [1].

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 [2, 3]. 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. 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 [3, 4]. To analyze heart rate and blood pressure interactions, we calculated BRS by the Dual Sequence Method [4].

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.

Tab. 1: *Statistical summary of intergroup calculations Preeclampsia Risk (PE) vs. no Preeclampsia Risk (NoPE). MeanNN: Mean value of heart rate, MeanSBP: mean systolic blood pressure, MeanDBP: mean diastolic blood pressure, DBP1: (HF-dBP) high frequency in diastolic blood pressure; BRS1 (tachy_4-6) the number of tachycardic BRS in a range of 4-6 ms/mmHg; HRV1 (VLFn): normalized very low frequency.*

Parameter	PE	NoPE	p
MeanNN	743.2±125.7	763.6±120.3	n.s.
MeanSBP	129.2±12.8	122.1±17.0	n.s.
MeanDBP	73.2±9.4	67.4±10.9	n.s.
DBP1	8.3±4.5	5.16±1.8	<0.005
BRS1	2.6±0.8	1.8±0.8	<0.001
HRV1	0.44±0.09	0.36±0.13	<0.016

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 AUP 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 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.

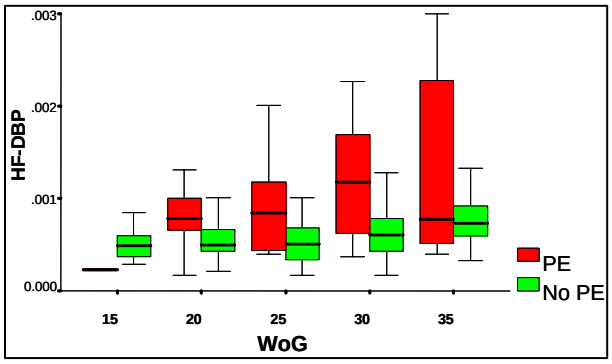

Fig. 1: *Alteration in high frequency range of diastolic blood pressure (HF-DBP) during the course of the gestation (week of gestation, WoG) in pregnant women with PE risk (PE) vs. with no PE Risk (NoPE)*

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. 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 to identify pregnant women who will develop PE. The great negative accuracy allows also excluding women at risk. This is all the more important as our approach of concurrent measurement of uterine perfusion and variability parameters is a feasible, inexpensive, non-invasive one-stop clinical assessment in the second trimester. Follow-up studies must be conducted evaluate prospectively the power of the test.

Our data imply early pathophysiological alterations at a time point (20th WoG) where pregnancies with later PE are clinically healthy. Thus, e.g. the increase in diastolic high frequency, which is modulated by respiratory sinus arrhythmia, may reflect early pathological arterial stiffness. This leads to the undamped respiration-induced pulse wave oscillations detected by our method. This is congruent with the hypothesis that patients later developing PE are characterized by early pathological modifications in vessel behaviour. 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 [5].

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