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Using critical flicker frequency in the evaluation of visual impairment in preeclamptic women

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ABSTRACT

Objective: To assess critical flicker frequency (CFF) in normal uneventful pregnancy and preeclampsia.
Study-design: Case-control observational study at the University Hospital Jena and Outpatient Institute for Prenatal Diagnosis and Preventive Medicine. 25 non-pregnant women, 75 uncomplicated pregnant women in first, second and third trimester, and 15 women with overt preeclampsia. For comparison with preeclamptic patients we matched 15 normal pregnant women (mNP) for age, parity, body mass index, current smoking and family history of cardiovascular disease (CVD). We measured CFF using the portable HEPAtonorm Analyzer (nevoLAB GmbH, Germany). This device generates a flickering red light, starting with a frequency of 60 Hz, giving the subjective an impression of a steady light. The participant signifies once the impression of a flickering light is recognized, and this CFF is recorded. Mean CFF and standard deviation is automatically calculated. Statistical analysis was performed using SPSS Version 22 for Windows. Following assessment of normal distribution with Kolmogorov-Smirnow test, comparisons were made with univariate and multivariate ANOVA and with unpaired and paired *t* test for continuous data and with χ^2 test for categorical data.
Results: Critical flicker frequency in healthy pregnant women does not differ from nonpregnant women. No significant differences in CFF measurements exist in first, second, and third trimester. In preeclampsia, CFF is significantly decreased compared to normal pregnant women (PE 38.80 ± 2.16 vs. mNP 46.23 ± 3.37; $p = 0.000$). This alteration persists even some weeks postpartum (PE 41.17 ± 1.13 vs. mNP 46.45 ± 3.44; $p = 0.003$).
Conclusion: In preeclamptic women, CFF is decreased indicating an altered endothelial situation. The finding that CFF remains reduced postpartum may be explained by either the effect of preeclampsia on maternal endothelium causing longer lasting damage or indicate a preexisting endothelial disorder. Up to this point, precise responsible mechanisms for altered CFF in preeclampsia are currently unclear and further studies are needed.

Introduction

Preeclampsia (PE) afflicts up to 5% of all pregnancies and is a leading cause of maternal and perinatal morbidity and mortality [1,2]. The main symptoms of preeclampsia are hypertension and proteinuria, but this systemic vascular disorder can also include maternal cardiovascular changes, hepatic impairment as well as cerebral manifestations with cognitive and visual changes [3–5]. The most common visual complaints are blurred vision and visual field defects [4,6]. Due to involvement of the occipital cortex, retina or optic nerve, complete blindness may be a rare complication as well [4]. Because of the serious consequences, immediate diagnosis and evaluation is mandatory [4,7]. Recent studies described mechanisms in PE such as retinal thickening [8], retinal oedema or increased intraocular pressure [9] which may lead to the mentioned visual alterations. Nevertheless, not all mechanisms are understood and further examinations are needed to detect visual disturbances and retinal alterations in normal pregnancy and consequently preeclampsia [10–12].

Previously, we could show, that retinal vascular response under the influence of flickering light is altered in women with

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preeclampsia, indicating a commenced retinal microvascular dysfunction [13]. A completely new method arises with the assessment of critical flicker frequency (CFF), a simple and objective method to assess the visual and cognitive function [14,15]. CFF is designed for bed-side use and is reported to be impaired in patients with hypertension, hepatic encephalopathy, and ocular disorders [14,16–19]. So far, measurement of CFF has never been performed in pregnancy nor PE. One advantage of this method is, that CFF is free from educational and cultural bias and thereby can be measured without preconditions [20]. Additionally, it is very simple to perform and easy to interpret [21], can be carried out by clinical personnel, and – as it is a simple device – the running costs are limited.

The aim of this study was to examine CFF for the first time in normal and preeclamptic pregnancies. As it has never been measured before in pregnancy, we investigated CFF in non-pregnant women during menstrual cycle, as well. To explore the development of CFF throughout gestation, we examined CFF in first, second and third trimester and postpartum. We hypothesized that CFF is altered in women suffering from preeclampsia compared to uncomplicated normal pregnant women.

Materials and methods

In this prospective study 120 women were included (Fig. 1). In study part A, 80 pregnant women were recruited, five of these women developed pregnancy complications (IUGR = 3 and HELLP syndrome = 2) and had to be excluded. Finally, 75 women with uncomplicated normal pregnancies (NP) were included (25 women each in 1st, 2nd, and 3rd trimester). 25 non-pregnant women (NC) without hormonal contraceptive use were measured on the 5th day of menstrual cycle, and matched for age, BMI, nulliparity, current smoking and family history of cardiovascular disease (CVD), including family history of hypertension, stroke, and myocardial infarction.

In study part B, 15 women with clinically evident preeclampsia (PE) were recruited, measured and matched with 15 normal pregnant women (mNP) from study group A for age, week of gestation, parity, BMI, current smoking and CVD and 15 non-pregnant women matched for age, parity, BMI, current smoking and CVD. For postpartum analysis (at least 8 weeks postpartum) 8 PE women and 10 mNP women remained (PE: 4 withdrawals and 3 relocations; NP: 2 withdrawals and 3 relocations).

Measurements in PE women had been performed prior to initiation of antihypertensive treatment and none of the subjects had severe preeclampsia.

Measurements were performed between 2013 and 2015 at the Dept. of Obstetrics, University Hospital Jena and at the Prenatal Diagnosis Center Erfurt, Germany. The Ethics Committee of the University of Jena approved the study (Number 3996-01/14).

Women with multiple pregnancy, chronic hypertension, renal disease, previous gestational or gestational hypertension, pregestational or gestational diabetes mellitus, HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome and overt CVD were not included. None of the subjects had any visual symptoms or known ophthalmologic diseases.

According to the guideline of the International Society for the Study of Hypertension in Pregnancy (ISSHP), preeclampsia was defined as new onset of hypertension (≥140/90 mm Hg) with proteinuria ≥300 mg/d or ≥2+ on dipstick or as severe when systolic blood pressure (BP) was ≥160 mmHg and diastolic BP ≥ 110 mmHg and when massive proteinuria occurred (≥5000 mg/24 h) [22,23]. Following 10 min time for accommodation, systolic and diastolic blood pressure were measured on both upper arms with an automatic blood pressure (BP) monitoring device. Hypertensive readings were controlled and hypertension

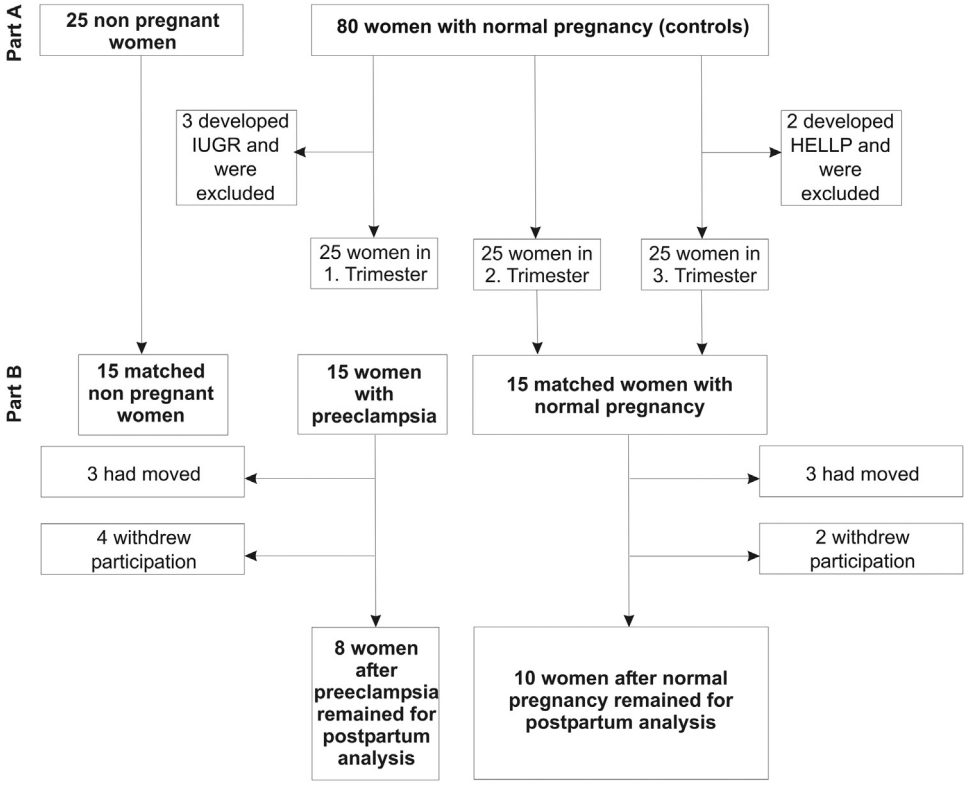

Fig. 1. Flow chart of women enrolled in this study, including 25 non-pregnant controls. Five were excluded from final analysis and 12 were lost of postpartum follow up.