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**OXIDATIVE STRESS INVOLVEMENT IN THE RETINAL
PATHOLOGY IN PREGNANCY COMPLICATED WITH
PREECLAMPSIA**

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INTRODUCTION

Preeclampsia is a multisystemic disorder that complicates 3% -8% of pregnancies in Western countries and is a major source of morbidity and mortality worldwide. Overall, 10% -15% of maternal deaths are directly associated with preeclampsia and eclampsia.

Although the exact mechanism leading to the installation of preeclampsia remains poorly defined due to the intense scientific research in this field, promising new insights are discovered with each study.

Preeclampsia and eclampsia were associated with severe retinopathy similar with hypertensive retinopathy, retinal detachment, retinal pigment opaque lesions and cortical blindness. While most patients will recover normal vision a few weeks after birth, some will remain with series of injuries. Permanent blindness due to retinal vascular changes is rare and is usually reversible.

Oxidative stress exacerbation can damage the vascular endothelium and can affect relaxation dependent of the endothelium and increase vascular contractile activity. All these effects on the vascular system may explain how oxidative stress can cause hypertension.

A prompt treatment of the preeclampsia -eclampsia syndrome and fetal birth, can reduce ocular manifestations associated with this condition

GENERAL PART

The overall incidence of pre-eclampsia is between 10 and 15% of all pregnancies. Multiple criteria for the diagnosis of severe preeclampsia illustrates the multifocal nature of the disease. Identifying women at increased risk of developing preeclampsia has proven difficult and is the subject of numerous research studies in the last decade.

Pregnancy is associated with increased oxidative stress and oxidative damage exaggeration can become an important component of pregnancy complications such as preeclampsia. The role of oxidative stress in human placentation and the complications of pregnancy are a relatively recent area of research, but is expanding rapidly.

Ischemic retinopathy develops when blood flow is insufficient to retinal metabolic demand, which is the tissue with the highest oxygen demand. Hypertensive retinopathy

represents the ophthalmological manifestation of the organ damage that may occur as a complication of systemic hypertension.

A major product of lipid peroxidation is the group of compounds usually called isoprostanes.

In the first quarter, creating sanguine flow in the intervillus space is associated with a real burst of oxidative stress. Inability to achieve an effective defense against antioxidants leads to miscarriage. In late gestation increase oxidative stress is encountered in pregnancies complicated by diabetes, preeclampsia, IUGR associated with increased trophoblastic apoptosis and modified placental vascular reactivity.

Since there is a positive correlation between placental and systemic oxidative stress, it is reasonable to assume that these processes are related and that the placenta could release lipid peroxides in the maternal circulation, which could in return contribute to maternal endothelial cell dysfunction.

PERSONAL CONTRIBUTIONS

PURPOSE AND OBJECTIVES

The purpose of this study was to determine the prevalence of hypertensive retinopathy, hypertensive retinopathy features and visual outcome in hypertensive disorders of pregnancy complicated by preeclampsia, in the present context of oxidative stress.

The study presented is structured around the following major objectives:

1. Evaluation of risk factors involved in preeclampsia etiology.
2. Evaluation of retinal changes according to quantified parameters and their correlation with oxidative stress markers.
3. Assessment of the relationship between hypertensive retinopathy and the severity of preeclampsia in the context with plasma levels of 8-iso -PG F₂ α .
4. Laboratory evaluation of the evolution of normal pregnancy and preeclampsia.
5. Histologic evaluation of placental changes consistent with the presence of oxidative stress, preeclampsia, retinal changes evolution, since it has been suggested that retinal changes in preeclampsia may indicate indirectly the placental vascular status and therefore placental insufficiency and fetal weight at birth.

6. Evaluation and comparison of serum 8-iso -PG F2 α in women with normotensive pregnancies and pregnancies with preeclampsia.

MATERIAL AND METHOD

It was performed a prospective study including 158 pregnant women studied between October 2010- March 2013. The study was held in the Clinic of Obstetrics and Gynecology Hospital Municipal Philanthropy and Emergency County Hospital Craiova, Department of Ophthalmology County Hospital emergency Craiova.

Preeclampsia was defined according to the criteria ISSHP -International Society for the Study of Hypertension in Pregnancy.

In our study we addressed only the two forms of preeclampsia, GHT and preeclampsia (mild and severe) to have a better representation of the cases studied.

Based on ophthalmoscopy examination of the fundus, women with preeclampsia and hypertensive retinopathy were divided into four groups according to the Keith-Wagener-Barker classification system.

8-isoprostane (8-iso-PGF α F2) has been proposed as a marker of oxidative stress and antioxidant deficiency.

RESULTS

The results of the clinical trial and statistical analysis

Compared to the literature that shows that mild preeclampsia is found in nearly 75% of all cases of preeclampsia, in our study the percentage was 40.51%.

We noted in our study, that preeclampsia was encountered, in most cases, in age groups between 20 and 30 years.

Obesity is also incriminated in increased risk of preeclampsia. In our study, we found a highly significant statistical difference between severe PE and a high BMI.

We found that the presence of a cardiological history may influence the appearance and also the type of preeclampsia.

Statistically correlating the number of normal births in history, we found that parity, especially nulliparity, does not significantly influence the occurrence of preeclampsia in the groups we studied.

Following statistical analysis we found the presence of a statistically significant link between: the presence of IUGR in a previous pregnancy and the presence of preeclampsia and IUGR in the current pregnancy; the presence of thrombophilia and PE installation; normal pregnancy and severe PE involving average values of Hb and Ht; the amount of uric acid level between severe PE and the rest of PE types and also between GHT and mild PE; between the occurrence of IUGR and the type of PE and between an early onset of preeclampsia and the evolution of the pregnancy.

The results of oxidative stress characterization in preeclampsia pregnancy:

In this study, we speculated that pregnant women plasma levels of 8-iso-prostaglandin F2 α could be increased during the course of pregnancy with preeclampsia and we investigated its potential role in hypertensive retinopathy and the maternal and fetal complications of preeclampsia.

Our research supports the hypothesis that high isoprostane excretion with low antioxidant production, causes an imbalance of oxidative stress and may precede recognition of preeclampsia installation.

The results of hypertensive retinopathy assessment in the context of oxidative stress in preeclampsia

Hypertensive retinopathy is found in 60% of patients and is the most common ocular complication related to preeclampsia and eclampsia.

In our study, hypertensive retinopathy was detected in 36.70% of patients with preeclampsia.

After the statistical analysis we can say that the degree of retinopathy is positively correlated with the PE severity. Our results suggest that the degree of hypertensive retinopathy in women with preeclampsia is a valid and reliable prognostic factor, which provides prognostic information available on the assessment of the severity of preeclampsia and the neonatal outcome.

Histological evaluation of the placental results in patients with preeclampsia in the context of oxidative stress

To see what may be the placental induced lesions in women with PE in the context of oxidative stress and to determine the prevalence of histological results suggestive for poor maternal perfusion of the placenta; we performed a histological study of the placenta, which was collected immediately after birth.

We considered that the characteristic histopathology appearance for oxidative stress in preeclampsia, is the appearance of the hypoplastic villous with a pseudoangiomatos layout.

By analyzing the concordance between the placental lesions and the degree of the Keith-Wagener-Barker retinopathy, we can say that hypoplastic villous with a pseudoangiomatos layout changes, limestone impregnation, funicular vascular thrombosis show a highly significant correlation ($p < 0.0001$) with the degree of retinopathy.

DISCUSSION

Risk factors for preeclampsia include: socio-demographic factors (extremes of reproductive age, socio-economic status), genetic factors, factors specific to pregnancy (multiparous, primiparous, previous preeclampsia), medical history (obesity, renal disease, diabetes, chronic hypertension, thrombophilia).

Following statistical analysis we found the presence of a statistically significant link between: the presence of IUGR in a previous pregnancy and the presence of preeclampsia and IUGR in the current pregnancy; the presence of thrombophilia and PE installation; normal pregnancy and severe PE involving average values of Hb and Ht; the amount of uric acid level between severe PE and the rest of PE types and also between GHT and mild PE; between the occurrence of IUGR and the type of PE and between an early onset of preeclampsia and the evolution of the pregnancy.

Tsukimori (Tsukimori 2007) demonstrated a significant increase of the superoxide anions production rate by the neutrophils in preeclampsia pregnant women.

A novel mechanism of action of 8 isoprostane F₂- α has been described on the vasculature including the neural retina, in which 8-isoprostane F₂- α causes vasoconstriction by releasing

TXA2 from the endothelium and lamina by a mechanism dependent upon the activation of calcium channels on cell surface (Hou 2000).

CONCLUSIONS

The highest rate of early PE was severe PE (78.95%), with 15 pregnant women out of a total of 19 pregnant women.

We recommend using cut-off value of 780 pg / ml as the threshold for severe PE and use the value of 435 pg / ml as the threshold for mild PE.

After the statistical analysis we can say that the degree of retinopathy is positively correlated with the PE severity. Our results suggest that the degree of hypertensive retinopathy in women with preeclampsia, is a valid and reliable prognostic factor, which provides prognostic information available on the assessment of the severity of preeclampsia and the neonatal outcome.

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