Editorial

Clinical and biochemical markers for prediction of preeclampsia

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Editorial

Preeclampsia (PE) is a leading cause of maternal and perinatal death worldwide. This multisystem disorder is a common, yet incompletely understood syndrome, unique to humans and delivery is the only "cure". In the same time, PE is a major cause of iatrogenic prematurity.[1,2]

PE affects 2-5% of all pregnancies.[3,4] Over four million women will develop the disorder worldwide every year, 50.000-100.000 women die from the preeclampsia each year, and it's responsible for approximately 300.000 perinatal deaths.[5-7]

Usually, women with PE after the 20th week of gestation develop hypertension, proteinuria, and varying degrees of ischemic end-organ damage, caused by widespread endothelial dysfunction. PE is also associated with abnormalities of coagulation system, disturbed liver function, renal failure and cerebral ischemia. PE is characterized by vasospasm, increased peripheral vascular resistance, and thus reduced organ perfusion.[8]

Pregnancy per se is a state of oxidative stress arising from the increased metabolic activity in placenta mitochondria and the reduced scavenging power of antioxidants.[9] The aetiology of PE is still not completely understood, although many facts of the disease have been illuminated. Endothelial cell dysfunction would seem to be the common denominator in the various stages of PE and appears to be present from the first trimester of pregnancy.[10,11]

Prediction and prevention of PE is a very important contribution for maternal health. The only guaranteed primary prevention of PE is avoidance of pregnancy; there are identified risk factors (maternal age, interval between pregnancies and maternal weight). Prevention of PE demands knowledge of the pathophysiological mechanism. Availability of techniques for early detection and intervention in the pathophysiological process are necessary. Finally, prevention of PE is a proper antenatal care which provides screening for hypertension and proteinuria, making intervention, such as timely delivers possible. With an organised antenatal care, such as found in most high income countries, the maternal mortality and serious morbidity have decreased.

First step in prediction and prevention of PE is detection of women's level of risk for PE, based on factors in her history. Major risk factors for PE are: nuliparity, maternal age >40, prior PE, anti phospholipid antibody syndrome, family history of pe in first-degree relative, renal disease, chronic hypertension, diabetes mellitus, multiple gestations, strong family history of cv disease (heart disease or stroke in ≥2 first-degree relatives), obesity etc.[1,3,12] The maternal demographic characteristics, including medical and obstetric history, are potentially useful in screening for PE, but only when the various factors are incorporated into a combined algorithm derived by multivariate analysis.[3]

Blood pressure measurement is a screening test routinely used in antenatal care to detect or predict a hypertensive disease. Studies investigating the predictive accuracy of blood pressure measurement report conflicting results. In the period within 20 week of gestation the values of MAP over 85-90 mmHg and values of DBP over 75mmHg are an important predictive indicator for determination of the risk of hypertensive disorders in pregnancy, especially PE.[13] Regarding these conflicting reports, it is uncertain whether blood pressure measurement should be used routinely as a predictive test or should only be used to diagnose hypertensive disorders in pregnancy once they are suspected.[14,15]

Normal placentation is a process that starts in the first trimester and is more or less completed at the end of the second trimester. In PE, defective invasion of the spiral arteries by cytotrophoblast cells is associated with inadequate uteroplacental blood flow.[3,12,16] Doppler ultrasonography might be used to assess the velocity of uterine blood flow and indirectly evaluate the trophoblastic invasion of the spiral arteries. The impaired placental perfusion reflects in increaseduterine artery pulsatility index (PI). The ability to achieve a reliable measurement of uterine arteryPI is dependent on appropriate training of sonographers.[3] One of the most widely studied Doppler indices is the pulsatility index (calculated as the peak systolic flow minus specificity the end diastolic flow divided by the mean flow). The increased PI has been associated with an increased risk for PE and intrauterine growth restriction. The presence of an early diastolic notch in the waveform has also been shown in several studies, to be associated with adverse outcomes. Cnossen and colleagues found that uterine artery Doppler ultrasonography is predicted more accurately PE than intrauterine growth restriction and that the most powerful Doppler index for predicting PE was an increased PI with notching in the second trimester. For severe PE, they found that an increased

PI or bilateral notching best predicted the condition.[17] A large number of biochemical markers have been investigated for a prediction of PE. Several biochemical markers (PAPP-A, PlGF, PP13, Sendoglin, Inhibin-A, Activin-A, Pentraxin 3 and P-Selectin) as potential predictors describe the foetal and placental endocrine functions and the maternal endothelial dysfunction.[18] Some studies are concluding that the major phenotype of PE, hypertension and proteinuria, may be due to an excess of circulating anti-antigenic growth factors, most notably soluble fms-like tyrosine kinase 1 (SFLT1) and soluble endoglin (SENG), and reduced levels of placental growth factor (PlGF).[19] Maternal serum PAPP-A and PlGF are two biochemical markers that have been investigated extensively and have shown promising results in the early prediction of PE. They have both been shown to be useful inscreening for aneuploidies at 11-13 weeks' gestation.[3] In chromosomally normal pregnancies, there is evidence that low maternal serum PAPP-A in the first- and second-trimesters is associated with increased risk for subsequent development of PE. Measurement of PAPP-a alone isn't an effective method of screening for PE.

Several studies reported that during the clinical phase of PE, the maternal serum PlGF concentration is reduced. These reduced levels of serum PlGF precede the clinicalonset of the disease and are evident from both the first and second-trimesters of pregnancy. First-trimester maternal serum concentrations of PAPP-A and PlGF have shown to be affected by gestational age at screening, maternal weight, maternal age, racial origin, cigarette smoking, conception by IVF, nulliparity and pre-existing diabetes mellitus. Consequently, the measured concentrations of PAPP-A and PlGF must be adjusted for these variables before comparing results with pathological pregnancies. The MoM values of PAPP-A and PlGF are significantly reduced at 11-13 weeks' gestation in women who subsequently develop PE.[3,18]

Prediction of PE in the first-trimester of pregnancy is of great interest. Early and improved prediction of PE would allow early administration of Aspirin, appropriate antenatal surveillance and better target research into preventive interventions.[3,20] The combination of maternal, biophysical and biochemical markers at 11-13 week of gestation could effectively identify women at high risk for PE.[3,21] These may help improve the predictive accuracy of the tests to clinically important values.

Abbreviations:

PE, Preeclampsia; PI, Pulsatility Index; SFLT1, Soluble Fms-like Tyrosine Kinase 1; SENG, Soluble Endoglin; PIGF, Placental Growth Factor

Acknowledgments

None.

Conflicts of interest

None.

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