Cell-free Nucleic Acids as Potential Markers for Preeclampsia

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Preeclampsia is one of the leading causes of maternal and fetal/neonatal mortality and morbidity worldwide. Therefore, widely applicable and affordable tests are needed to make an early diagnosis before the occurrence of the clinical symptoms. Circulating cell-free nucleic acids in plasma and serum are novel biomarkers with promising clinical applications in different medical fields, including prenatal diagnosis. Quantitative changes of cell-free fetal (cff)DNA in maternal plasma as an indicator for impending preeclampsia have been reported in different studies, using real-time quantitative PCR for the male-specific SRY or DYS 14 loci. In case of early onset preeclampsia, elevated levels may be already seen in the first trimester. The increased levels of cffDNA before the onset of symptoms may be due to hypoxia/reoxygenation within the intervillous space leading to tissue oxidative stress and increased placental apoptosis and necrosis. In addition to the evidence for increased shedding of cffDNA into the maternal circulation, there is also evidence for reduced renal clearance of cffDNA in preeclampsia. As the amount of fetal DNA is currently determined by quantifying Y-chromosome specific sequences, alternative approaches such as the measurement of total cell-free DNA or the use of gender-independent fetal epigenetic markers, such as DNA methylation, offer a promising alternative. Cell-free RNA of placental origin might be another potentially useful biomarker for screening and diagnosis of preeclampsia in clinical practice. Fetal RNA is associated with subcellular placental particles that protect it from degradation. Its levels are ten-fold higher in pregnant women with preeclampsia compared to controls. In conclusion, through the use of gender-independent sequences, the universal incorporation of fetal nucleic acids into routine obstetric care and into screening or diagnostic settings using combined markers may soon become a reality. Effort has now to be put into the establishment of standardized and simplified protocols for the analysis of these biomarkers in a clinical setting.

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