Järvenpää, Jouko, Placental angiogenesis and angiogenesis related risk factors in severe pre-eclampsia
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Abstract

The incidence of pre-eclampsia (PE) is 2-7% in different populations and in the worst cases PE may threaten the survival of both mother and newborn; its pathogenesis is not resolved. Field literature today considers PE an angiogenic disorder. Coordinated vascularization is essential for placental development.

We wanted to find novel factors in the etiology of PE, and focused our attention on angiogenesis, inherited thrombophilia and folate-homocysteine metabolism. Homocysteine inhibits endothelial cell proliferation, which is closely related to angiogenesis. We performed gene expression profiling of placental tissue using microarray chips, studied the prevalence of factor V Leiden (FVL), prothrombin (F5) G20210A and methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism in patients with severe pregnancy complications and normal controls, compared the expression of the placental adiponectin, leptin and their receptor genes and the relationship of each to trophoblast apoptosis and further, studied the effect of folic acid fortified mineral water on plasma homocysteine concentration during pregnancy.

Gene expression profiling revealed downregulation of nine and upregulation of four genes**.** Interestingly, in one PE patient with cord compression during delivery the profile resembled that observed in normals. The expression level of the leptin and the adiponectin receptor 1 (ADIPOR1) genes was significantly higher in PE. No other significant expression changes were observed. The rate of apoptosis was higher in patients with PE. The FVL prevalence was 9.5 %, in PE cases and 1.8 % in the controls; a difference of 7.7 %, (95 % CI 2.0 – 13.4 %). No statistical difference was found in other polymorphisms.. Maternal serum folate concentration increased in our intervention group, but decreased in the control group ($p<0.05$). The plasma homocysteine concentrations decreased more in the intervention group ($p<0.001$).

The expression of angiogenesis-related placental genes can be altered in PE and cord compression cases. The activity of adipocytokine genes in PE may mean

that they have a role in placental angiogenesis and apoptosis. Women with FVL may have an increased risk of PE. Fortified mineral water will help us to ensure that especially pregnant women achieve adequate folate intake.

Key words**:** adipocytokines, angiogenesis, apoptosis, food fortification, genes, homocysteine, placenta, pre-eclampsia, thrombophilia,

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