Abstract: P549

Is ANGPTL4 marker the epigenetical program predisposition to CAD in offspring?

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Background: Endothelial dysfunction (ED) is one of the key risk factors for almost all of cardiovascular diseases. There is a convincing evidence that gestational diabetes mellitus (GDM) is associated with structural and functional changes in various tissues, including the ED as well as future development of chronic disease in offspring. Angiopoietin-like protein 4 (ANGPTL4) is a multifunctional signal protein, expressed in many tissues and involved in different physiological processes regulation, such as: plasma glucose level and tolerance regulation, angiogenesis, vascular permeability in acute myocardial infarction experimental models and so on. Today there is no sufficient data on the role of ANGPTL4 human umbilical vein endothelial cells (HUVECs) in GDM patients.

Purpose: The aim of this study was to investigate the maternal hyperglycemia influence on the manifestation of fetal endothelial dysfunction through the ANGPTL4 expression in HUVEC.

Materials and methods: the study included 41 women with GDM that were treated for GDM started before the 30-th week of gestation (GDM1), 9 women treated for GDM after the 34-th week of gestation (GDM2) and 25 women without any GDM (the control group). The diagnosis of GDM was based on International Association of Diabetes and Pregnancy Study Groups criteria. Age and pregestational body mass index did not differ between the groups.

HUVECs were isolated and expanded in vitro up to passage 2 and tested for viability and replicative senescence. Immunophenotype was determined by the Flow Cytometry analysis. The level of genes expression was determined by the RT-PCR. ANGPTL4 concentration in conditional medium was measured using the ELISA kit. Statistical significance was assessed by the Mann Whitney test, using the Graph Pad software; results were considered significant for a p-value<0.05.

Results: the ANGPTL4 expression differed significantly between the control and GDM groups: 98,33±20,92 vs 22,27±3,97 (control vs GDM1; p<0,001), and 98,33±20,92 vs 13,55±4,32 (control vs GDM2; p<0,01) while no substantial difference between the GDM1 and GDM2 groups was observed.

Sperman’s correlation showed association between the levels of ANGPTL4 mRNA expression and angptl4 protein in conditional medium in the control (r=0,788, p<0,0001) and GDM1 (r=0,376, p=0,031) groups. In the GDM2 group the correlation between ANGPTL4 expression and secretion was disrupted (r=-0,714, p=0,088).
Conclusion: ANGPTL4 expression in HUVECs from GDM patients was found out to be lower compared to the control groups. In the GDM-derived samples the correlation between the ANGPTL4 expression and secretion was disrupted, which could indicate the alterations in post-transcription regulation of ANGPTL4 in endothelial cells. That may explain a potential mechanism of the intrauterine hyperglycemia influence on the development of epigenetic program predisposition to CAD in offspring.