Anti-Phospholipid and Anti-DNA Antibodies Are Not Associated with the Elevated Release of Circulatory Fetal DNA in Pregnancies Affected by Preeclampsia

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ABSTRACT

Objectives: We have previously shown that the levels of circulatory fetal DNA are elevated in preeclampsia and that these increases correspond to disease severity. Several reports have indicated that increased levels of antiphospholipid (anti-PL) and anti-DNA antibodies may be associated with preeclampsia, in particular with the severe forms of the disorder. Since the release of cell-free DNA by the placenta is attributed to some form of cell death or damage and as anti-PL and anti-double-stranded DNA (dsDNA) antibodies have been proposed to lead to placental damage, we have studied the relationship between these parameters in preeclampsia. *Methods:* Circulating fetal DNA levels in samples taken from pregnant women with mild (n = 12) or severe (n = 12) preeclampsia and from normal pregnant controls (n = 35) were quantified using a Taqman real-time Polymerase Chain Reaction (PCR) assay. The Anti-PL antibodies (IgG and IgM) were assayed by anticardiolipin ELISA and by commercial anti-β_2-Glycoprotien I (GPI) ELISA kits. Anti-dsDNA antibodies (IgG and IgM) were analyzed by a commercially available anti-dsDNA ELISA kit. *Results:* No correlation could be drawn with the quantity of circulatory fetal DNA in the samples analyzed and corresponding anti-PL or anti-dsDNA antibody levels. Furthermore, no significant difference existed between the levels of these antibodies in the two study groups and the control cohort. *Conclusion:* Our data suggest that the mechanism leading to the increased release of cell-free circulatory DNA from the placenta does not involve trophoblast damage mediated by these agents. Our analysis also questions the reported involvement of anti-PL and anti-DNA antibodies in preeclampsia.

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A Comparative Study of the Effect of Three Different Syncytiotrophoblast Micro-particles Preparations on Endothelial Cells

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Pre-eclampsia is a pregnancy-associated multi-system disorder of unknown etiology, characterized by damage to the maternal endothelium. The latter facet has been suggested to be mediated in part by elevated shedding of inflammatory placental syncytiotrophoblast micro-particles (STBM) into the maternal circulation. In this study, we have examined STBM prepared by three different methods: mechanical dissection, in vitro placental explant culture and perfusion of placental cotyledons. All three preparations yielded morphologically similar STBM, as confirmed by scanning electron microscopy, and all contained syncytiotrophoblast-specific proteins as determined by the presence of placental alkaline phosphatase. The functional properties of the three STBM preparations were examined on human umbilical vein endothelial cells (HUVEC), where the mechanically prepared particles were found to inhibit proliferation to the greatest extent. Furthermore, only mechanically prepared STBM lead to the detachment and apoptosis of HUVEC cells. Our study, therefore, suggests that STBM prepared from placental perfusion or in vitro explant culture are biologically different from mechanically prepared ones, and may provide a better approximation of physiologically produced placental micro-particles.

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Soluble factors released by placental villous tissue: Interleukin-1 is a potential mediator of endothelial dysfunction

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Objective: The purpose of this study was to analyze the potential of placental-conditioned medium to activate endothelial cells in vitro and to identify the placental factors that mediate this effect.

Study design: Placental-conditioned medium was generated by the culturing of normal term placental villous explants for up to 48 hours. Human umbilical vein endothelial cells were exposed to the conditioned media, and cellular proliferation, viability, and activation were investigated.

Results: The proliferation of endothelial cells that were exposed to 20% placental-conditioned medium was reduced by 25%, but their survival was not compromised. Conditioned medium also up-regulated the expression of E-selectin and stimulated the release of soluble intercellular adhesion molecule-1 and the secretion of interleukin-6. Treatment with interleukin-1 receptor antagonist, but not with an anti-tumor necrosis factor-α neutralizing antibody, blocked the release of soluble intercellular adhesion molecule-1 and interleukin-6.

Conclusion: Placentally derived interleukin-1 may be 1 of the potential mediators of the maternal inflammatory response that is observed in late pregnancy.

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