

Abstract

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Vitamins C and E Inhibit Apoptosis of Cultured Human Term Placenta Trophoblast.

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BACKGROUND: Preeclampsia can be lethal to both mother and baby. The prominent symptoms of this syndrome are hypertension, proteinuria and oedema, resulting from an exaggerated aseptic systemic inflammatory response, triggered by placental factors shed into the maternal circulation. Syncytiotrophoblast microparticles (STBM) are one possible factor, shed when the placenta is exposed to stressors such as hypoxia/reperfusion. These can disrupt mitochondria, triggering apoptosis and necrosis, placental pathologies which are increased in preeclampsia.

METHODS: We tested the effects of antioxidant vitamins C (50µM) and E (50µM) on trophoblast in culture, using term villous cytotrophoblast preparations. Following Percoll gradient centrifugation and MHC class I expressing cell depletion of placenta digests, syncytial fragments were removed using anti-placental alkaline phosphatase antibody. This yielded cytotrophoblasts of consistently high purity.

RESULTS: EGF (10ng/ml) stimulated syncytialisation and hCG and progesterone production. However, mitochondrial induced apoptosis (MIA) was evident 96h post-isolation, as mitochondrial membrane potential loss and caspase 9 and caspase 3 activation. ROCK-1 cleavage and syncytiotrophoblast particle shedding increased concurrently with apoptosis induction. Vitamins blocked MIA and syncytiotrophoblast particle shedding and significantly increased hCG ($p<0.005$) and progesterone ($p<0.02$) concentrations in culture supernatants, reflecting the increased survival rates. Although more cells survived in culture, syncytialisation rate (%) was significantly reduced ($p<0.005$).

CONCLUSION: We conclude that vitamins C and E can significantly reduce mitochondrial damage generated following syncytialisation in vitro. However, further work is required to determine whether antioxidant vitamins interfere with normal fusion processes.

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