INVESTIGATION OF THE EFFECT OF PREIMPLANTATION FACTOR IN A DOXORUBICIN-INDUCED *IN VITRO* CARDIOCITOTOXICITY MODEL

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Introduction: Nowadays, increasing incidence of cancer is a major problem worldwide. Doxorubicin (DOXO) is an effective chemotherapeutic agent used in order to kill the malignant tumor cells. However, application of DOXO has limits because of the severe consequences that mainly affect the cardiovascular system. Therefore, the investigation of the detailed underlying mechanisms and discovery or development of potential drugs that can help to avoid or decrease the DOXO-induced cardiovascular side effects has a huge clinical potential. Our group focus on the examination of endogenous molecules which can act as potential cytoprotective agents on DOXO-induced cytotoxicity. Preimplantation factor (PIF) is a 15-aminoacid peptide which is in correlation with the viability of pregnancies. PIF has been reported to exert antioxidant and antiapoptotic qualities, so it could be used as a potentially protective molecule againts DOXO-induced cardiocitotoxicity.
Aim of the study: To investigate the possible cytoprotective effects of PIF in a doxorubicin-induced *in vitro* model of heart damage.
Materials and methods: We used H9c2 rat cardiomyoblast cell line to test 0.5 and 24 hours pretreatment with a broad range of PIF (0.3-5000 ng/mL) followed by 24 hours of parallel DOXO and PIF treatment. To detect the viability at the end of the protocol, MTT viability assay and measurement of superoxide level with dihydroetidium assay were performed. DAPI staining was applied in order to visualize the apoptotic morphological changes and γ-H2AX immuncytochemistry was used for examining the DNA double strand breaks.
Results: Thirty min pretreatment with 160 ng/ml PIF significantly reduced the DOXO-induced cell death and oxidative stress (cell death in DOXO vehicle%: 80±3%). In our longer pretreatment model the 10 ng/ml PIF decreased the elevated cell death and oxidative stress caused by DOXO (cell death in DOXO-vehicle %: 73±7%). We detected higher number of apoptotic nuclei and DNA double breaks in the DOXO treated group, which was improved by both of the PIF pretreatments.
Conclusion: PIF may decrease dose-dependently the doxorubicin-induced cardiac cell damage including cell viability, superoxide level and DNA damages. In the future, we plan to investigate the possible intracellular mechanisms behind this protective effect.

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