**EXPRESSION OF Flk-1 AND CYCLIN D2 mRNA IN MYOCARDIUM WITH DOXORUBICIN-INDUCED CARDIOMYOPATHY**

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**Objectives.**To evaluate the cytoprotective reactions in rat myocardium induced by doxorubicin (Dox) in cardiomyocytes.
**Background.** Cytotoxic agent Dox is widely used in treatment of oncological diseases with cardiomyopathies development. Cyclin D2 promotes the induction of DNA synthesis in postnatal cardiomyocytes and their proliferation, so it is important to estimate expression of cyclin D2 mRNA in cardiomyocytes after Dox exposure. The intracellular regeneration reactions were evaluated as expression of Flk-1 associated with the PI3K-Akt pathway.
**Methods.** Anthracycline cardiomyopathy was reproduced in Wistar male rats by Dox hydrochloride (Pharmachemi BV, Netherlands, 7 mg/kg, single). Expression of cyclic D2 mRNA in myocardium was evaluated by RT-PCR on a CFX96 Touch thermophycore (Bio-Rad Laboratories, USA) with amplification kit containing the SYBR Green I and SynTaq fluorescent probe DNA polymerase. Expression of VEGFR2/KDR/Flk-1 was evaluated immunohistochemically using rabbit polyclonal antibody E3712 diluted 1:50 (Spring Bioscience, USA). The sections were analyzed in Leica DM 4000B. Flk-1-positive cardiomyocytes were counted at a magnification of 400 times (test area 61171.56 μm2).
**Results.** Amount of cyclic DNA mRNA, related to the mRNA of the 18S ribosomal subunit, in control was 1.00±0.06. After 3 days, the amount of cyclin D2 mRNA decreased (p<0.05) vs control. At 14 days, the expression of cyclin D2 mRNA significantly (p<0.01) increased, indicating on the increase in the proliferative activity of cardiomyocytes at a later time after exposure. After 3 days after Dox administration, the index of Flk-1-positive cardiomyocytes significantly (p<0.001) increased vs control (from 13.6±1.45 to 94.3±0.76); after 14 days, this index was also significantly (p<0.001) increased.
**Conclusion.** The obtained results indicate that cytoprotective reactions in the myocardium are induced after Dox administration.