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TI - CARDIOMYOCYTE DNA CONTENT AND ITS LINK TO CSE/ H2S SYSTEM IN THE HEART OF
EXPERIMENTAL DIABETIC RATS.
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AB - One of the most common complication of diabetes mellitus (DM) is diabetic
cardiomyopathy, which is associated with the development of inflammation,
fibrosis and the induction of apoptosis. Hydrogen sulfide (H2S) has recently been
shown to play an important role in the regulation of cardiac and vascular
function. The role of the H2S system in the mechanisms of diabetic heart
development remains uncertain. The aim of this work was to evaluate the effect of
modulators of H2S system on the level of DNA fragmentation and H2S concentration
in heart of rats with experimental diabetes mellitus. The experiment was
performed on 40 white laboratory male rats (180-250 g), randomly divided into 4
groups (n=10): healthy (control), diabetes mellitus induced by streptozotocin
(STZ), diabetes mellitus + propargylglycine, inhibitor of cystathionine gamma
lyase (STZ + PPG), diabetes mellitus + NaHS, exogenous H2S donor (STZ + NaHS).
The experimental DM was induced by a single intraperitoneal injection of
streptozotocin (40 mg/kg). The animals from two groups (3rd and 4th groups)
starting from 14th to 28th day after the injection of STZ were administered
modulators of H2S system i/p once per day. D, L-propargylglycine was dosed at 50
mg/kg body weight, while NaHS · H2O - at 3 mg/kg body weight. H2S content in
hearts was evaluated by spectrophotometry (Wilinski, 2011). DNA content was
determined by flow cytometry (Partec PAS, Germany). The development of DM in rats
was accompanied by a significant decrease in myocardial H2S concentration by

36.6% ($p<0.05$) compared with control. The administration of proparglyglycine led to an increase in H2S deficiency (29.4%, $p<0.05$) compared to the STZ group. The administration of NaHS resulted in a decrease in H2S deficiency (by 23.5%, $p<0.05$) compared to the STZ group. Flow cytometry showed that DM was accompanied by an increased apoptotic activity (increased number of myocardiocytes in the SUB- G0G1 phase by 11.4%, $p<0.05$), polyploidization (increased proportion of cells in the G2M phase by 32.1%, $p<0.05$) and proliferation (29.8% increase in S-phase cells, $p<0.05$) of heart cells compared with controls. The introduction of propargylglycine led to an increase in apoptosis (14.4%, $p<0.05$) compared with the STZ group. Whereas NaHS administration decreased the degree of apoptosis (12.3%, $p<0.05$), polyploidization (14.4%, $p<0.05$) and proliferation compared (26.2%, $p<0.05$) with untreated diabetes. Correlation analysis showed that impaired H2S metabolism is an important factor of disregulation of cell cycle in diabetic heart: a reliable inverse relationship was registered (r=-(0,69-83), $p<0.01$) between H2S level and the indicators of apoptosis activity, proliferation and polyploidization. Disintegration of the H2S/CSE system is associated with an increase in apoptosis activity, polyploidization, and proliferation of myocardiocytes in experimental DM. Modulation of H2S metabolism is a potential direction for the prevention of the development of cardiovascular complications of diabetes.
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