Propargylglycine improves diastolic function in old rats via oxidative/ nitrosative stress inhibition and cNOS recoupling.

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Background. Diastolic dysfunction is associated with oxidative and nitrosative stress, which can be enhanced by H2S.

Purpose. The purpose of the study was to determinate the effect of propargylglycine (PAG) – the inhibitor of CSE-dependent way of H2S synthesis, on heart redox-status, cNOS coupling, and diastolic function of old rats. It was shown that H2S levels in the mitochondria and whole heart homogenates obtained from old rats were significantly lower comparing with adult animals.

Methods. To evaluate diastolic function of the heart in vivo experiments, we used pressure-volume (PV) conductance catheter system (Millar Instruments, USA). The level of H2S and oxidative/nitrosative stress markers were determined in heart tissue by spectrophotometric method.

Results. The markers of combined oxidative and nitrosative stress (the rate of ?2•-, •?? generation, pools of H2O2, diene conjugates, malondialdehyde, uric acid, the activity of iNOS, nitrate reductase, and NO3- pools, etc) were increased in the old hearts in line with ?NOS uncoupling. Such changes in heart redox-status resulted in the loss of diastolic relaxation (decrease of the rate of the left ventricle relaxation (dp/dtmin) by 33%, 3-times increase of the end-diastolic pressure (EDP), an increase of the time constant of left ventricular relaxation (Tau g) by 44% and 2-time increase of the end-diastolic stiffness (EDS)). The PAG injection decreased the activity of CSE and, compensatory, increased 3MST (second H2S-synthesized enzyme in cardiovascular system) and increased endogenous ?2S pools 1.9 times. The latest was accompanied with oxidative, nitrosative stress inhibition, cNOS recouplig and cNOS stimulation, which promoted an improvement of the left ventricle relaxation (decrease of EDS by 52% and decrease of EDP by 19%).

Conclusions. Thus, PAG has an ability to improve diastolic function in old rats. This ability is associated with increase of H2S generation, oxidative/nitrosative stress inhibition, cNOS recoupling and increase of constitutive NO-synthesis.