Cardioprotective mechanism of S-nitroso-N-acetylcysteine via S-nitrosated betadrenoceptor-2 in the LDLr-/- mice

Wanschel, A.C.B.A¹, Bruni-Cardoso, A¹, Carvalho, H.F¹, Laurindo, F.R², Krieger, M.H¹

¹Department of Anatomy, Cellular Biology and Physiology, State University of Campinas (UNICAMP), Biology Institute, São Paulo, Brazil, ²Vascular Biology Laboratory - Heart Institute (InCor), School of Medicine, University of São Paulo School of Medicine (USP), São Paulo, Brazil.

Previous studies from our group have demonstrated the cardioprotective effect of S-nitroso-N-acetylcysteine (SNAC) on dyslipidemic LDLr-/- mice. The present study was designed to investigate whether SNAC treatment produces cardioprotective effect via an antioxidant role, and to verify the possible anti-apoptotic role of β2-Adrenergic Receptors (β2-ARs) in the cardiac remodeling. Ventricular superoxide (O₂⁻) and hydrogen peroxide (H₂O₂) generation was measured by HPLC methods to allow quantification of dihydroethidium (DHE) products. Ventricular histological sections were stained using terminal dUTP nick-end labeling (TUNEL) to identify nuclei with DNA degradation (apoptosis) and this was confirmed by cleaved caspase-3 protein expression. The findings show that H₂O₂ production and cell apoptosis increased during left ventricular hypertrophy (LVH). SNAC treatment showed reduction of oxidative stress on cardiac remodeling by decreasing H₂O₂ and O₂⁻ production (65% and 52%, respectively), this which was associated with a decrease in the ratio of p-Ser1177 eNOS/total eNOS. Left ventricle (LV) from SNAC treated mice revealed a 4-fold increase in β2-AR expression; β2-ARs-S-nitrosation (β2-AR-SNO) increased 61%, while apoptosis decreased 70%. These results suggest an anti-oxidant role of SNAC on cardio protection, which is associated with the mediation of β2-ARs overexpression and β2-AR-SNO via an anti-apoptotic pathway.

Keywords: β2-adrenergic receptors, apoptosis,

Supported by: FAPESP, CNPq and CAPES