KYNURENIC ACID AGAINST SIMULATED ISCHEMIA/REOXYGENATION-INDUCED CARDIAC CELL DAMAGE: THE POSSIBLE ROLE OF MITOPROTECTION

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Acute myocardial infarction (AMI) is a life-threatening condition that belongs to the leading causes of death worldwide. Analysis of agents which potentially increase the tolerance of cardiac cells against the harmful effects of ischemia/reperfusion supports the development of new treatment strategies. In this study, we aimed to investigate the potential mitoprotective effect of kynurenic acid (KYNA) and its possible involvement in the agent's previously uncovered cardiocytoprotective effect against simulated ischemia/reoxygenation (SI/R)-induced damage of H9c2 cardiomyoblasts. H9c2 cells were exposed to 6 hours of ischemia, followed by 2 hours of reoxygenation. 64 μM KYNA treatment was performed throughout the SI/R protocol for the investigation of the potential mitoprotective effects of KYNA. The rate of oxidative stress was measured on both cellular (DHE staining) and mitochondrial (MitoSox) levels at the end of the experiment. Mitochondrial function was analyzed via the detection of potential alterations in the mitochondrial membrane potential (JC-1 staining) and investigations on the efficiency of mitochondrial respiration (high resolution respirometry; Oroboros O2k). Alterations in the structure and distribution of mitochondria were investigated via immunocytochemistry and electronmicroscopic morphometry. Our results demonstrated that SI/R caused an increase in the level of both cellular and mitochondrial oxidative stress. SI/R-induced depolarization of mitochondrial membranes was observed compared to the normoxic control groups. SI/R-induced functional damage of mitochondria affected the baseline respiration and decreased the activity of respiratory complexes. Alterations both in the distribution and structure of mitochondria were detected as well. All the above-mentioned SI/R-induced harmful effects were attenuated by the applied KYNA treatment. Our data suggest that attenuation of mitochondrial damage might be involved in the cytoprotective effect of KYNA against SI/R induced cardiac cell damage.

Keywords: mitochondria, mitoprotection, kynurenic acid, ischemia/reperfusion

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