Abstract

Recently, they are examined various means for activating the endogenous signalling pathways leading to increased resistance of the myocardium from ischemic/reperfusion (I/R) injury. One of them is the adaptation to chronic hypoxia, which has been shown to reduce the incidence and severity of ventricular arrhythmias, improves the recovery of postischemic contractile function of the heart and particularly reduces the extent of myocardial infarction. Since the function of the heart depends on the maintenance of membrane integrity of cardiomyocytes there are very important phospholipase A_2 (PLA_2) which are involved in the repair of cellular membranes. Also they are an important component of the protective signalling pathways because they cleave membrane phospholipids to produce lipid signalling molecules. Elucidate the role of PLA_2 and the precise mechanism of action of signalling pathways leading to cardioprotection could be important for the prevention and treatment of cardiovascular diseases. Therefore, in this thesis we examined the influence of continuous normobaric hypoxia (CNH) to the relative representation of cardiac PLA_2 (secretory – $sPLA_2$IIA, calcium-independent – $iPLA_2$, cytosolic – $cPLA_2\alpha$ and its phosphorylated form – p-$cPLA_2\alpha$), and proteins involved in the activation and phosphorylation of $cPLA_2\alpha$ (protein kinase Cα – PKCα, extracellular signal regulated kinases 1 and 2 – ERK 1/2, the protein with a molecular weight 38 kDa – p38 and their phosphorylated forms) in the homogenate of left ventricle of rat myocardium. The Western blot revealed that after adaptation to CNH the relative representation of $sPLA_2$IIA was unchanged, however there is an increase in $iPLA_2$ and $cPLA_2\alpha$. Likewise, there was an increase in all studied phosphorylated forms (p-$cPLA_2\alpha$, p-PKCα, p-ERK 1/2 and p-p38), although the relative representation of proteins PKCα, ERK 1/2 and p38 was unchanged. From these results it is apparent that the $cPLA_2\alpha$ could be involved in the signalling pathway of cardioprotection induced by CNH. Therefore, in the next phase of the research it was analyzed the influence of a specific inhibitor $cPLA_2\alpha$ (pyrrophenone) on cardiomyocytes isolated from the left ventricle of myocardium from normoxic and CNH adapted rats. Testing of viability and release of lactate dehydrogenase from cardiomyocytes after simulated acute I/R damage did not prove the involvement of $cPLA_2\alpha$ in cardioprotection, we will need to perform further experiments to explain its role.