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HYPOXIA INDUCED MYOCARDIAL PROTECTION INVOLVES CYTOSKELETAL PROTEINS

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Acute systemic hypoxia induces delayed protection of tissue from hypoxic injury. The known mechanisms of delayed myocardial protection are based on induction of some proteins possess vasoactive, metabolic and antioxidant properties. However, role of cytosceletal proteins in delayed cardioprotection is unclear. At the same time, hypoxia/ischemia causes injury and/or translocation of membrane-associated proteins, among of them dystrophin is known as most sensitive to oxygen deprivation. In male Wistar rats role of dystrophin in delayed cardioprotection were studied. Hypoxic preconditioning was performed by whole body hypoxia séance (10% O_2 in N_2 during 3 h). In 24 h hearts were isolated and tested for ischemic injury by 30 min ischemia and 40 min reperfusion in Langendorff mode. Expression of protein in both heart ventricles and in subcellular fractions of cardiomyocytes was assessed by Western blotting. It was shown that hypoxic preconditioning led to induction of dystrophin in both left and right ventricles; in the last ones the expression levels prevail. In the ischemic hearts, dystrophin redistributed from membrane-cytosolic to myofibrillar fraction in control as well as in preconditioned group. After post-ischemic reperfusion, dystrophin translocation was intensified in control hearts, but in preconditioned hearts subcellular distribution of dystrophin restored to normal. Hypoxic preconditioning improved contractile function of reperfuzed hearts, and reduced appearance of reperfusion arrhythmias. Application of K_{ATP}-channel inhibitor glybenclamide abolished the restoration of membrane pool of dystrophin in preconditioned hearts, as well as cardioprotective effects. These results evidenced that hypoxic preconditioning induces dystrophin synthesis, which may prevent lack of this protein in case of subsequent hypoxic/ischemic injury. Besides, K_{ATP}-channel activation following the hypoxic preconditioning mediates restoration of membrane pool of dystrophin during reperfusion, and prevents cytosceletal damage of cardiomyocytes. Thus, in addition to known mechanisms, hypoxic preconditioning protects myocardium by induction and redistribution of cytosceletal proteins.