Regulators of heart mitochondrial energetic metabolism observed in remote ischemic preconditioning and experimental acute diabetes mellitus

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Background: Measurement of biophysical parameters of heart mitochondria (MIT) membranes may provide valuable information about their role in adaptation processes running in the myocardium. The aim was to elucidate the processes of energetic metabolism, mitochondrial membrane fluidity, pyruvate dehydrogenase activity (PDH) and free oxygen radical (ROS) signalling in myocardial endogenous protection against I/R injury observed in remote ischemic preconditioning (RIP) and experimental acute diabetes mellitus (DM). For the purpose of elucidating the cardioprotective role of pyruvate dehydrogenase regulation, we proposed a protocol using pyruvate dehydrogenase activator - dichloroacetate (DCA) and anoxia induced in in vitro conditions.

Methods: Male Wistar rats (9-11 weeks old, 220±20 g b. wt.) were used for this study. Heart MIT were isolated by means of differential centrifugation and forwarded to biochemical and biophysical investigation. RIP was triggered by three 5-min. cycles of limb ischemia and reperfusion. Acute DM was induced by a single dose of streptozotocin (STZ, 65 mg/kg b.wt.). Experiment was terminated on the 8th day after STZ application. Isolated heart were perfused according to Langendorff (30-min ischemia and 40-min reperfusion).

Results: The results showed that RIP and acute DM preserved ATP synthase activity after I/R injury, but without significant influence on the mitochondrial respiratory function. RIP increased membrane fluidity probably due to inhibition of ROS. We demonstrated the positive effect of DCA on mitochondrial respiratory activity.

Conclusion: Since MIT of streptozotocin acute diabetes hearts show reduced capability to utilize O2, myocardial cells may be experiencing the state of pseudo-hypoxia and exhibit increased expression of genes involved in adaptation to hypoxia. RIP induced endogenous protective mechanisms by increasing the membrane fluidity, thereby improved the energy demand during ischemia. The process of short-term adaptation, such as the RIP induced positive signal is sufficient enough to start the process of myocardial protection against ischemia-reperfusion injury.