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Adaptive changes of rat heart mitochondrial respiration: response of remote ischemic preconditioning

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Introduction: Myocardium heavily depends on the oxidative generation of energy that requires involvement of functional mitochondria. These organelles were recently shown to participate also in the mechanisms of cardioprotection induced by ischemic preconditioning. Based on the previous findings of increased myocardial resistance to ischemia, it could be assumed that mitochondria and functional alterations in the respiratory chain might also be involved in the mechanisms of remote ischemic preconditioning (RIP). In RIP, the increased cardiac resistance to ischemia is achieved by brief episodes of ischemia with subsequent reperfusion performed in distant organs or places. Hence, on the contrary to ischemic preconditioning, a direct restriction of oxygen supply to cardiac mitochondria is missing. The aim of this pilot study was to reveal whether, and in what way are cardiac mitochondria and respiratory chain involved in the mechanism of cardioprotection.

Methods: For this purpose, 13-week-old male Wistar rats were divided into 2 groups: control group without RIP (n=21) and the group with RIP (n=21). Protocol of RIP consisted of 3 cycles of ischemia and reperfusion, 5 min of duration each. Not-preconditioned and preconditioned hearts were subjected to the testing of ischemia-reperfusion injury (T-IRI): 30 minute ischemia followed by 40 minutes of reperfusion according to Langendorff. Parameters of oxidative phosphorylation (OXPHOS) in the isolated cardiac mitochondria were determined by the method of high resolution respirometry using Oxygraph-2k (Oroboros Instruments, Austria).

Results: Mitochondrial respiration was stimulated by ADP (state III) using glutamate + malate and malate + octanoylcarnitine as substrates. After ischemic phase of T-IRI the hearts without RIP exhibited a decrease by 26.7% whereas the hearts with RIP showed an increase by 40.4% in the rate of O2-consumption in comparison with the hearts in baseline preischemic phase of T-IRI. Reperfusion phase of T-IRI was characterized by a decrease in state III respiration in the group of hearts without RIP (65.9 %) and with RIP (35.6%). Interestingly, a decrease in O2-consumption induced by reperfusion was less pronounced when malate + octanoylcarnitine as a substrate was used instead of glutamate + malate.

Conclusion: Our results revealed that the positive effect of remote preconditioning i.e., the increased or better preserved state III O2 consumption, became manifested only during the ischemic and reperfusion phase of T-IRI. Grants: VEGA 2/0101/12, APVV 0102-11, KEGA 003 UK-4/2012.