Expression and activity of mitochondrial creatine kinase and hexokinase are enhanced in the left ventricle of rats adapted to chronic intermittent hypoxia

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Purpose: Creatine kinase (CK) and hexokinase (HK) play a key role in energy homeostasis of cardiomyocytes. Mitochondrial sarcomeric CK (mtCKs) and two hexokinase isoforms (HK1 and HK2) highly support mitochondrial oxidative phosphorylation by increasing the availability of ADP for complex V of the respiratory chain. Besides the mtCKs, there are two cytosolic CK isoforms (CKM and CKB) present in cardiomyocytes that help to maintain energy homeostasis.

Aim: We determined CK and HK isoforms expression, enzyme activity and HK colocalization with mitochondria in more ischemic tolerant chronically hypoxic rat hearts and normoxic controls.

Methods: Male Wistar rats were adapted to chronic intermittent hypobaric hypoxia (IHH) (7000 m, 8 h/day). Real Time-PCR, Western blot and quantitative immunofluorescence technique were used to assess the expression of CK and HK isoforms and changes in HK isoforms localization with respect to mitochondrial compartment.

Results: IHH increased CK activity by 30%, which was consistent with elevated protein expression of mitochondrial mtCKs (by 30%) and cytosolic CKB (by 50%). After adaptation to IHH, HK activity increased by 20%, whereas protein expression of HK1 and HK2 nearly doubled. Colocalization of HK1 with mitochondria increased significantly (p<0.03), but HK2 did not reached statistical significance (p=0.06) in hypoxic rats.

Conclusion: Up-regulation of mtCKs and HK isoforms and increased colocalization of HK1 may stimulate the respiratory chain and help to maintain energy homeostasis of chronically hypoxic myocardium. Our results suggested that CK and HK enzymes can participate in the induction of ischemia more resistant phenotype in rat hearts adapted to IHH.

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