Abstract

Ventricular arrhythmias are the main cause of death worldwide. An increased incidence of arrhythmias in the heart of mammals is accompanied by a remodeling of the cellular distribution gap between the channels of mainly connexin 43 (Cx43). Recently has been demonstrated significant effect of mitochondria and their association with arrhythmogenesis. Various pathological conditions alter the expression and / or distribution of Cx43, depending on the phosphorylation status. but also on altering the association of hexokinase with mitochondria, which reduces the likelihood of apoptosis activation. Adaptation to intermittent hypobaric hypoxia potentiates endogenous pathways reducing the incidence of ventricular arteries, whereas continuous normobaric hypoxia does not have this effect. Another studied model is cold acclimatization, which has been known for several decades by known effects on human health. However, the heart study of these models in relation to Cx43 is missing. Our goal was to determine the expression of Cx43, phosphorylated Cx43 (p-Cx43) and hexokinase (HK1, HK2) and their distribution in cardiomyocytes. In addition, the expression of Cx43 upstream kinases, protein kinase A, protein kinase G, casein kinase 1 in normoxic and hypoxic left ventricles of rats, along with Cx43 distribution during short ischemia and reperfusion injury was analyzed. Male Wistar rats were adapted to hypoxia (7 000 m, 8 hours/day, 5 weeks or 10% oxygen, 3 weeks), and then special groups of the heart were exposed to short-term ischemia (10 min) and reperfusion (15 min) in vivo. Expression and phosphorylation are assessed by specific antibodies and mass spectrometry. The Cx43 distribution at *end to end* and *side to side* longitudinal junctions were evaluated by quantitative immunofluorescence microscopy. Cx43 on longitudinal sections of the left ventricle and protein expression of Cx43 exposed to cold (6 ± 1° C) for 3 days, 10 days, 5 weeks and then 2 weeks at 24 ± 1° C. Our results indicate significant benefit in changes in expression and Cx43 phosphorylation in signaling pathways that may be responsible for the antiarrhythmic effect associated with adaptation to hypobaric hypoxia. No changes have been demonstrated after normobaric hypoxia and offer the possibility of 5-week acclimation to cold to the cardioprotective pathway.

Key words: Rat, Heart, Cold, Hypoxia, Connexin 43, Hexokinase