

Abstract

Cardiovascular diseases represent the most important health risk factors because they are responsible for more than 50% of total mortality. Among them, the ischemic heart disease is leading cause of mortality. From the whole spectrum of different cardioprotective phenomena we have selected: 1) adaptation to chronic normobaric hypoxia (CNH) as the traditional experimental model in our laboratory area and 2) protective effect of exercise which in recent years represents promising and clinically relevant protective mechanism.

The whole thesis is based on two studies. Aim of the first study was to characterize the expression of the main pro-inflammatory cytokine, TNF- α , in hearts of rats adapted to CNH. Chronic TNF- α inhibition by infliximab was used for discovering of certain role of TNF- α in CNH. We showed that increased myocardial level of TNF- α during adaptation to CNH was contributed via its receptor TNFR2 and nuclear factor κ B-dependent activation of protective redox signalling with increased antioxidant defence. This adaptive pathway participates on the infarct size-limiting effect of CNH. Aim of the second study was find out whether exercise training and CNH could play synergy in cardiac protection in rats model. We reported that CNH and exercise reduced infarct size but their combination provided the same degree of protection as CNH alone. High ischemic tolerance of the CNH hearts persists after exercise, possibly by maintaining the increased antioxidant capacity despite attenuating TNF- α -dependent protective signalling.

In conclusion, TNF- α is involved in the cardioprotective mechanism afforded by CNH, and regular exercise training of rats during their adaptation to CNH conferred the same infarct size-limiting effect as CNH alone. All these findings significantly contribute to the actual information about the cardioprotective mechanisms of adaptation to CNH and physical training.

key words: ischemia, reperfusion, cardiac protection, chronic hypoxia, exercise, tumor necrosis factor alpha