

Abstract

Age-Related Features in Systemic Inflammatory Response in Male Wistar Rats with Different Hypoxia Tolerance [†]

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[†] Presented at the 1st International Electronic Conference on Molecular Sciences: Druggable Targets of Emerging Infectious Diseases, online, 01-14 September 2021.

Academic Editor: Clemente Capasso

Published: 31 August 2021

Abstract: Organism's hypoxia tolerance depends on many factors, including age. High newborn organism's tolerance and high level of oxidative stress throughout aging were demonstrated by many studies. However, there is still lack of investigations, reflecting the intensity of systemic inflammatory response in different age organisms in correlation to hypoxia tolerance. The aim of study was to determine the relationship between age-related tolerance to hypoxia, HIF-1 and PHD2 (prolyl hydroxylase domain protein) expression levels and the intensity of systemic inflammatory response in newborn, prepubertal and adult Wistar rats. In case of investigation the tolerance to hypoxia, rats were placed into a decompression chamber at altitude simulation of 11,500 m. It was demonstrated that prepubertal rats are the least tolerant to hypoxia and newborns are the most tolerant. Newborn rats are characterized by high mRNA Hif-1 α expression level in the liver, accompanied by low content of HIF-1 protein and high level of PHD2. The growth in HIF-1 α protein level throughout the age is accompanied by the growth of pro-inflammatory cytokines level. Prepubertal animals are the least hypoxia tolerant and their HIF-1 α mRNA expression level was higher than in adult animals. The PHD2 activity in prepubertal animals was significantly reduced in comparison to newborn rats, and the HIF-1 α protein level was not changed. The lowest tolerance of the prepubertal males to hypoxia correlated with the greatest manifestations of hepatic inflammation and elevated endotoxin, neopterin, and C-reactive protein levels in LPS-induced systemic inflammatory response. The growth of serum HIF-1 α in 3 h after LPS injection was observed only in prepubertal rats. The obtained data should be taken into account during the development of therapeutic strategy for prepubertal children with infectious and inflammatory diseases.

Keywords: hypoxia tolerance; HIF-1; PHD2; age-related differences; systemic inflammatory response; prepubertal age