Effects of subchronic methylmercury exposure on response to acute hypoxia in mice: role of HIF-1α

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Abstract

Introduction: Methylmercury (MeHg) is a neurotoxic environmental pollutant. Hypoxic response is an adaptive response of organisms to cope with hypoxia, and HIF-1α is a key nuclear transcription factor in response to hypoxia. Acute MeHg exposure can decrease HIF-1α protein in vitro and in vivo, but the impact of subchronic MeHg exposure on hypoxic response has not yet been elucidated.

Methods: Healthy ICR mice were intraperitoneally infected with 0.25, 0.5, and 1.0 mg/kg methylmercury, treated with hypoxia in a 250 ml hypoxia bottle for 15 min, and then recorded the time of death and collected blood, heart tissue, and brain tissue for detection by Western blotting. Analyzing the contents of lactic acid (LA), pyruvate kinase (PK), malondialdehyde (MDA), glutathione (GSH), and Hypoxia-inducible factor-1α (HIF-1α).

Results: According to the mouse survival curve, after methylmercury exposure, the hypoxic survival time of mice in the medium and high dose groups was significantly shorter than that of the normal saline group. The survival rates of mice in the medium- and high-dose groups were 33.3% and 16.7%, which were significantly lower than those in the normal saline group. The detection results of lactic acid and pyruvate kinase showed that the effect of subchronic MeHg exposure on the hypoxic adaptation ability of mice was promoted by low doses and inhibited by medium and high doses. Malondialdehyde content increased and glutathione content decreased with MeHg treatment in a dose-dependent manner; the expression of hypoxia-inducible factor-1α protein decreased after hypoxia treatment, but its expression showed an increasing trend with MeHg treatment; vascular endothelial growth The expression of factor proteins showed an overall upward trend.

Conclusion: Subchronic exposure to methylmercury can aggravate the oxidative damage caused by hypoxia and inhibit the hypoxic response in mice by affecting the expression of HIF-1α. However, cute hypoxia will overexpress HIF-1α protein in the brain tissue of mice with subchronic methylmercury poisoning.

Keywords: Methylmercury; hypoxia; hypoxia response; hypoxia-inducible factor-1α