Methylmercury-induced ferroptosis may be attenuated by vitamin K in PC12 cells

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ABSTRACT:

Introduction: As a ubiquitous environmental pollutant, methylmercury (MeHg) induces toxic effects in the nervous system, one of its main targets. However, the exact mechanism of its neurotoxicity has not been fully elucidated. Ferroptosis may be related to methylmercury toxicity and methylmercury-induced ferroptosis may be attenuated by vitamin K.

Methods: Rat adrenal pheochromocytoma PC12 cells with neuron-like characteristics were selected and treated with different concentrations of MeHg (0, 1, 2.5, 5, 10 μM) for 6 h. CCK8 was used to detect cell viability, FerroOrange fluorescent probe was used to detect the level of free ferrous ions in cells, microplate method was used to detect the level of reduced GSH in cells, SLC7A11 and GPX4 protein expression were detected by western blotting, and the changes of Lipid ROS content in cells were detected by flow cytometry. In the vitamin K intervention experiment, the MeHg group was treated with 5 μM MeHg for 6 h, the vitamin K+ MeHg group was pretreated with 80 μM vitamin K for 1 h, and then co-treated with 5 μM MeHg for 6 h, the changes of intracellular Lipid ROS content were detected by flow cytometry, and the expression of FSP1 protein was detected by western blotting.

Results: MeHg decreased the viability of PC12 cells in a dose-dependent manner, while the level of free ferrous ions in cells was significantly increased, the content of Lipid ROS in cells was also significantly increased, the expressions of FSP1, SLC7A11 and GPX4 decreased, and the level of reduced GSH in cells was significantly reduced when treated with 10 μM. After vitamin K intervention, cell viability is increased in a dose-dependent manner compared to the MeHg group, and intracellular Lipid ROS content is significantly reduced after treatment with 80 μM vitamin K.

Conclusion: MeHg can induce ferroptosis in neuron-like cells, and vitamin K intervention can alleviate MeHg-induced cytotoxicity and ferroptosis, its exact mechanism is worthy of further investigation.

Keywords: methylmercury; vitamin K; ferroptosis; FSP1