Therapeutic Potential of Dihydroartemisinin in Mitigating Radiation-Induced Lung Injury: Inhibition of Ferroptosis through Nrf2/HO-1 Pathways in Mice

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Abstract

Background: Radiation-induced lung injury (RILI) is a common consequence of thoracic radiation therapy that lacks effective preventative and treatment strategies. Dihydroartemisinin (DHA), a derivative of artemisinin, affects oxidative stress, immunomodulation, and inflammation. It's uncertain, nevertheless, whether DHA reduces RILI. In this work, we looked into the specific mechanisms of action of DHA in RILI. Methods: The mice were irradiated with 20 Gy 6 MV irradiation dose followed by administration of DHA and Brusatol for 30 days. Pathologic changes in the lungs were observed thereafter. TNF-α, TGF-β, glutathione peroxidase (GPX4), Nuclear factor erythroid 2-related factor 2 (NRF2), and heme oxygenase-1 (HO-1) expression in lung tissues were detected. In addition, mitochondrial ultrastructural changes in lung tissues were also observed, and the GSH content in lung tissues was assessed. Results: DHA attenuated radiation-induced pathological lung injury and inflammatory cell infiltration. Additionally, it decreased the synthesis of inflammatory substances like TNF-α and TGF-β. DHA additionally stimulated the Nrf2/HO-1 pathway. DHA inhibited cellular ferroptosis and upregulated GPX4 and GSH levels. The Nrf2 inhibitor Brusatol reduced DHA's inhibitory effect on ferroptosis. Conclusion: DHA modulated the Nrf2/HO-1 pathway to prevent cellular ferroptosis, hence reducing RILI. Therefore, DHA could be a potential drug for the treatment of RILI.

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