Protective effect of a metallothionein inducer on cadmium-induced lung epithelial injury.

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Exposure to cadmium has been reported to cause respiratory disease in humans by inducing oxidative stress-dependent cellular injury. Metallothioneins are intracellular, cysteine-rich, metal-binding proteins that have a detoxifying action on heavy metals such as cadmium in various organs. In addition, expression of metallothioneins is induced by metals with low biological toxicity, such as zinc. Therefore, in this study we examined whether polaprezinc, a chelate compound consisting of carnosine and zinc, can suppress cadmium-induced lung epithelial cell death. We found that cell viability and cytotoxicity were decreased and increased, respectively by cadmium treatment; however, polaprezinc significantly reversed these changes. Moreover, cadmium-dependent endoplasmic reticulum stress responses were suppressed by polaprezinc treatment. Cadmium induced the production of reactive oxygen species (ROS) in A549 cells in a dose-dependent manner and polaprezinc significantly suppressed this cadmium-induced ROS production. Finally, we found that polaprezinc dose-dependently induced metallothioneins using real-time RT-PCR, ELISA, and western blotting analyses. These results indicate that polaprezinc can suppress cadmium-induced lung epithelial cell death and oxidative stress by inducing metallothioneins. We therefore suggest that polaprezinc may have therapeutic effects against respiratory diseases, such as chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis.

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