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ORIGINAL ARTICLE

Protective Effect of Vitamin D3 Against Pb-Induced Neurotoxicity by Regulating the Nrf2 and NF-κB Pathways

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Abstract

Lead (Pb) is a known toxic heavy metal which accumulates in different tissues and causes oxidative stress (OS) and inflammation. The brain tissue is considered as one of the most vulnerable organs to the Pb-induced toxicity. The aim of this study was to investigate the therapeutic effects of vitamin D3 (VD) supplementation against the damages caused by chronic Pb toxicity in the cerebral cortex. Forty Wistar rats were divided into four equal groups and were treated as follows: control group received no treatment, VD group received 1000 IU/kg of VD by intramuscular injection every other day, Pb group received 1000 mg/L of Pb in drinking water, and Pb + VD group received VD and Pb simultaneously. The experiment lasted for 4 weeks and the analyses were conducted 24 h after the last administrations. The obtained results demonstrated that Pb significantly increased cortical lipid peroxidation and reactive oxygen species (ROS) levels. At the same time, there was a significant reduction in glutathione (GSH) content, catalase (CAT), and superoxide dismutase (SOD) activities, as well as a significant increase in the tissue level of inflammatory cytokines. Furthermore, Pb increased the messenger RNA (mRNA) expression level of nuclear factor erythroid 2-related factor 2 (Nrf2) and nuclear factor-kappa B (NF-κB). Anyhow, VD administration during the period of Pb exposure suppressed the OS and inflammation by increasing the antioxidant molecules and decreasing the inflammatory cytokines and consequently repaired Pb-induced cortical tissue damages. Remarkably, these responses were concomitant with the alterations in *Nrf2* and *NF-κB* gene expressions. In conclusion, the present study discloses the potential protective effects for VD against Pb-induced neurotoxicity via anti-inflammatory and antioxidative mechanisms.

Keywords Lead · Vitamin D · Oxidative stress · Inflammation · Brain · Nrf2 · NF-κb

Introduction

Lead (Pb) is a widely used heavy metal with strong toxic effects that have a long biological half-life (Sanders et al. 2009). The extensive application of Pb in a variety of industries has led to constant exposure of humans by inhalation and ingestion of contaminated air, water, and foods (Lidsky and Schneider 2003). It is said that Pb distributes into different tissues upon absorption and results in toxic effects in the nervous system, reproductive organs, kidney, liver, etc. (Sanders et al. 2009; Aglan et al. 2020). The central nervous system is considered as the most affected system by Pb toxicity (Bijoor et al. 2012; Yousef et al. 2019).

Multiple mechanisms are involved in the pathophysiology of Pb poisoning among which the induction of OS and inflammation has recently attracted attention (Flora et al. 2012). The reciprocal interactions between OS

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