Abstract:

Abstract This study explored the role of gasotransmitters in lead-induced nephrotoxicity. Long-term exposure of rats to lead resulted in its accumulation in kidney. The accumulated metal impaired kidney function and structure. Lead intoxication resulted in oxidative stress, inflammation and apoptosis in kidney. In addition, it resulted in nitric oxide (NO) overproduction and decrease in hydrogen sulfide (H2S) level and heme oxygenase (HO-1) concentration in kidney. Inhibition of NO overproduction by L-N(G)-nitroarginine methyl ester (L-NAME) and increasing of H2S level by sodium hydrosulfide (NaHS) and CO level by carbon monoxide-releasing molecule-A1 (CORM-A1) inhibited lead-induced impairment of kidney function and structure. These agents inhibited lead-intoxication induced oxidative stress, inflammation, apoptosis, nitrosative stress and reduction of H2S level and HO-1 concentration. Also, concomitant treatment with these agents inhibited lead intoxication-induced increase in protein expressions of inducible NO synthase (iNOS), tumor necrosis factor-alpha (TNF-α), interleukin-1beta (IL-1β) and caspase-3 as well as decrease in protein expressions of HO-1 and cystathionine-β-lyase (CSE) in kidney. The NO donor, L-arginine and the H2S and CO biosynthesis inhibitors, trifluoro-DL-alanine and zinc deutroporphyrin, respectively produced opposite effects and aggravated the toxic effects of lead. These results demonstrate, for the first time, that gasotransmitters play an important role in lead-induced nephrotoxicity.

Published In:

Toxicol Lett., 310, 39-50