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Nickel and Oxidative Stress: Cell Signaling Mechanisms and Protective Role of Vitamin C

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Abstract

Background: Nickel activates the signaling pathways through oxygen sensing mechanism and the signaling cascades that controls hypoxia-inducible transcriptional gene expressions through oxidative stress. This review emphasizes on the recent updates of nickel toxicities on oxidant and antioxidant balance, molecular interaction of nickel and its signal transduction through low oxygen microenvironment in in-vivo physiological system.

Discussion: Nickel and oxidative stress: Nickel alters intracellular chemical microenvironment by increasing ionized calcium concentration, lipid peroxidation, cyclooxygenase, constitutive nitric oxide synthase, leukotriene B4, prostaglandin E2, interleukins, tumor necrosis factor-α, caspases, complement activation, heat shock protein 70 kDa and hypoxia-inducible factor-1α. The oxidative stress induced by nickel is responsible for the progression of metastasis. It has been observed that nickel exposure induces the generation of reactive oxygen species which leads to the increased expression of p53, NF-kβ, AP-1, and MAPK. Ascorbic acid (vitamin C) prevents lipid peroxidation, oxidation of low-density lipoproteins and advanced oxidation protein products. The mechanism involves that vitamin C is capable to reduce ferric iron to ferrous iron in the duodenum thus availability of divalent ferrous ion increases which competes with nickel (a divalent cation itself) and reduces its intestinal absorption and reduced nickel toxicities.

Conclusion: Reports suggested the capability of ascorbic acid as a regulatory factor to influence gene expression, apoptosis and other cellular functions of living system exposed to heavy metals including nickel.

Keywords: Antioxidant; Cyclooxygenase; Hypoxia inducible factor-1α; Nickel; Oxidative stress; Tumor necrosis factor-α.

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