Zinc: Mechanisms of Host Defense[1–3]

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Abstract

Zinc deficiency in humans decreases the activity of serum thymulin (a thymic hormone), which is required for maturation of T-helper cells. T-helper 1 (Th_1) cytokines are decreased but T-helper 2 (Th_2) cytokines are not affected by zinc deficiency in humans. This shift of Th_1 to Th_2 function results in cell-mediated immune dysfunction. Because IL-2 production (Th_1 cytokine) is decreased, this leads to decreased activities of natural-killer cell and T cytolytic cells, which are involved in killing viruses, bacteria, and tumor cells. In humans, zinc deficiency may decrease the generation of new CD4+ T cells from the thymus. In cell culture studies (HUT-78, a Th_0 human malignant lymphoblastoid cell line), as a result of zinc deficiency, nuclear factor-κB (NF-κB) activation, phosphorylation of IκB, and binding of NF-κB to DNA are decreased and this results in decreased Th_1 cytokine production. In another study, zinc supplementation to humans decreased the gene expression and production of pro-inflammatory cytokines and decreased oxidative stress markers. In HL-60 cells (a human pro-myelocytic leukemia cell line), zinc deficiency increased the levels of TNF-α, IL-1β, and IL-8 cytokines and mRNA. In these cells, zinc induced A20, a zinc finger protein that inhibited NF-κB activation via tumor necrosis factor receptor associated factor pathway, and this decreased gene expression of pro-inflammatory cytokines and oxidative stress markers. We conclude that zinc has an important role in cell-mediated immune functions and also functions as antiinflammatory and antioxidant agent. J. Nutr. 137: 1345–1349, 2007.