

Skeletal and hormonal effects of magnesium deficiency. J

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Rude RK1, Singer FR, Gruber HE.

Author information:

1USC Keck School of Medicine, Los Angeles, CA, USA

Abstract

Magnesium (Mg) is the second most abundant intracellular cation where it plays an important role in enzyme function and trans-membrane ion transport. Mg deficiency has been associated with a number of clinical disorders including osteoporosis. Osteoporosis is common problem accounting for 2 million fractures per year in the United States at a cost of over \$17 billion dollars. The average dietary Mg intake in women is 68% of the RDA, indicating that a large proportion of our population has substantial dietary Mg deficits. The objective of this paper is to review the evidence for Mg deficiency-induced osteoporosis and potential reasons why this occurs, including a cumulative review of work in our laboratories and well as a review of other published studies linking Mg deficiency to osteoporosis. Epidemiological studies have linked dietary Mg deficiency to osteoporosis. As diets deficient in Mg are also deficient in other nutrients that may affect bone, studies have been carried out with select dietary Mg depletion in animal models. Severe Mg deficiency in the rat (Mg at <0.0002% of total diet; normal = 0.05%) causes impaired bone growth, osteopenia and skeletal fragility. This degree of Mg deficiency probably does not commonly exist in the human population. We have therefore induced dietary Mg deprivation in the rat at 10%, 25% and 50% of recommended nutrient requirement. We observed bone loss, decrease in osteoblasts, and an increase in osteoclasts by histomorphometry. Such reduced Mg intake levels are present in our population. We also investigated potential mechanisms for bone loss in Mg deficiency. Studies in humans and our rat model demonstrated low serum parathyroid hormone (PTH) and 1,25(OH)(2)-vitamin D levels, which may contribute to reduced bone formation. It is known that cytokines can increase osteoclastic bone resorption. Mg deficiency in the rat and/or mouse results in increased skeletal substance P, which in turn stimulates production of cytokines. With the use of immunohistochemistry, we found that Mg deficiency resulted in an increase in substance P, TNFalpha and IL1beta. Additional studies assessing the relative presence of receptor activator of nuclear factor kB ligand (RANKL) and its decoy receptor, osteoprotegerin (OPG), found a decrease in OPG and an increase in RANKL favoring an increase in bone resorption. These data support the notion at dietary Mg intake at levels not uncommon in humans may perturb bone and mineral metabolism and be a risk factor for osteoporosis.