Gaby’s Literature Review

Strontium for Osteoporosis: How Much and for How Long?

In the Treatment of Peripheral Osteoporosis (TROPOS) study, 5091 postmenopausal women (mean age, 77 years) with osteoporosis who were not receiving any antosteoporosis medications were randomly assigned to receive, in double-blind fashion, 2 g per day of strontium ranelate (680 mg per day of elemental strontium) or placebo for five years. After five years, the incidence of nonvertebral fractures was 15% lower in the strontium group than in the placebo group (p = 0.032), as compared with a 16% reduction in incidence during the first three years of the study. After five years, the incidence of new vertebral fractures was 24% lower in the strontium group than in the placebo group (p < 0.001), as compared with a 39% reduction in incidence during the first three years. The apparent loss of efficacy with respect to fracture prevention occurred even though bone mineral density of the lumbar spine and hip increased progressively in the strontium group during the entire study, and the difference in bone mineral density between the strontium and placebo groups became progressively more pronounced during the entire study.

Comment: Strontium has two different actions in bone. First, it is incorporated in small amounts into the hydroxyapatite crystal lattice, where it remains bound for years or decades and may improve bone quality. This effect probably occurs with “nutritional” doses (i.e., 1–3 mg per day, the amount present in a typical diet), since strontium derived from the diet and drinking water is known to be incorporated into bone and to persist there for decades. Second, strontium stimulates bone formation, inhibits bone resorption, and increases bone mineral density. These effects apparently require pharmacological doses of strontium and are thought to be mediated by adsorption of strontium onto the crystal surface. Unlike strontium incorporated into the crystal lattice, strontium adsorbed onto the crystal surface is rapidly cleared from the body after high-dose strontium is discontinued.

Administration of large doses of strontium to experimental animals has been reported to cause mineralization defects resembling rickets and to inhibit the synthesis of 1,25-dihydroxyvitamin D (the biologically active form of vitamin D). Hypomineralization and abnormal crystal formation has been observed with strontium in doses equivalent to about 800 mg per day for humans. It has been suggested that the deleterious effects on bone that resulted from strontium supplementation were due to the concomitant feeding of a calcium-deficient diet. However, strontium-induced bone changes have occurred in rats even when the diet contained 0.5% calcium, which is the estimated calcium requirement for growing rats. The possibility that long-term use of high-dose strontium can cause mineralization defects in humans is supported by the fact the reduction in fracture incidence relative to placebo in the study cited above diminished with time, even though the increase in bone mineral density relative to placebo became progressively more pronounced with time. Similar results were seen in a previous study of high-dose strontium.

The available evidence indicates that high-dose strontium therapy for up to five years reduces the incidence of fractures, but the benefit appears to diminish after the first year of treatment. Until longer-term safety data are available, it would seem inadvisable to administer high-dose strontium indefinitely. For patients at high risk of sustaining an osteoporotic fracture, a reasonable approach would be to administer high-dose strontium for one year and then to consider a dosage reduction.

DHEA Reverses Increases Bone Mass in Women

Fifty-five men and 58 women (aged 65–75 years) were randomly assigned to receive, in double-blind fashion, 50 mg per day of dehydroepiandrosterone (DHEA) or placebo for one year. Thereafter, all participants received 50 mg per day of DHEA for an additional year. All participants received daily 640 IU of vitamin D and 700 mg of calcium. In women, mean lumbar spine bone mineral density (BMD) increased by 1.9% (p = 0.0003 compared with baseline) during the first year in the DHEA group and increased by 0.8% in the placebo group (p = 0.03 for the difference in the change between groups). After two years, mean spine BMD increased by a total of 3.6% in the DHEA group. Hip BMD did not change. In men, there were no differences in BMD between DHEA and placebo.

Comment: DHEA is an androgen produced in women primarily by the adrenal glands and to a lesser extent by the ovaries. It is metabolized in part to estrogen and testosterone. In addition, DHEA appears to have physiological actions that are unrelated to its function as a precursor hormone, including stimulation of osteoblasts. The results of the present study indicate that DHEA can increase bone mass in elderly women, although it was not effective in men.

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