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Bone Health & Osteoporosis

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ABSTRACT: *Osteoporosis is a reduction in bone mass which leads to increased susceptibility to bone fracture, accounting for well over one million fractures each year in the United States. With the rapid aging of the population, the suffering and health care costs associated with osteoporosis are expected to increase dramatically. Experts agree that prevention is the most effective method of dealing with osteoporosis. The two approaches to prevention are maximizing peak bone mass at skeletal maturity and reducing the rate of age and menopause-related bone loss. Adequate calcium intake has been shown to have a strong influence on attaining peak bone mass and reducing the rate of bone loss. Unfortunately, studies have shown that a large proportion of the population does not even meet the current RDA levels for calcium. The data for women is especially alarming: after age 11, no age group of females achieved even 75% of the RDA for calcium. Supplementing the diet with calcium and other nutrients important for bone health, along with regular exercise and a healthy lifestyle, is essential in reducing the risk of osteoporosis. Microcrystalline hydroxyapatite (MCHC) is an excellent source of bioavailable calcium and other nutrients that are important for maintaining bone health.*

Osteoporosis is a metabolic bone disorder characterized by decreased bone mass, enhanced bone fragility, and increased susceptibility to bone fractures.[1,2] It is a major health problem affecting more than 25 million individuals in the United States and is responsible for well over one million bone fractures each year.[1,3,4] The annual financial costs of osteoporosis in the U.S. alone – based on hospitalization costs and acute and long-term care – are estimated to exceed ten billion dollars.[5] And with the rapid aging of the population, these costs are expected to increase dramatically.

The bone loss that precedes the osteoporotic fracture is a symptomless process, so osteoporosis may go undetected until bones become so brittle that even the slightest trauma causes a fracture.[1] The spine is the most common region of fracture, with one third of women 65 years and older having sustained spinal vertebrae fractures, leading to loss of height, kyphosis ("dowager's hump"), and chronic back pain.[1,4,6] By extreme old age, one of every three women and one of every six men will have had a hip fracture which, by any measure, is the most devastating of all osteoporotic fractures.[4,7]

The good news is that recent scientific evidence suggests that much of this suffering may be avoidable. The agreement among qualified experts is that the severity of age-related bone loss may be reduced in patients at risk if adequate amounts of calcium are ingested throughout their lifetime. In fact, the Food and Drug Administration concludes that "maintenance of an adequate calcium intake throughout life may optimize peak bone mass at skeletal maturity and help to slow the rate of bone loss later in life, and may help to reduce the risk of osteoporosis."[5]

RISK FACTORS FOR OSTEOPOROSIS

Two major factors that influence the risk of development of osteoporosis are the level of bone mass achieved at skeletal maturity (peak bone mass) and the rate at which bone loss occurs in later years. The more bone mass available before age-related bone loss ensues, the less likely it will decrease to a level at which fractures occur.[8]

Research studies point to a number of risk factors that may have a strong influence on peak bone mass and the rate of bone loss, and thus the development of osteoporosis (Table 1).[1,4,8,9] Some of these factors include: inadequate nutritional intake, lack of physical activity, smoking, excessive alcohol consumption, and prolonged use of corticosteroids.

In addition to diet and lifestyle factors, genetic and ethnic factors significantly influence many aspects of calcium and skeletal metabolism.[1,4,8-10] Caucasian and Asian women tend to have lower bone density than African and Hispanic women and, consequently, are more likely to suffer from osteoporotic fractures. The same holds true for thin, smaller boned women. Evidence also suggests there may be a link between mother and daughter; mothers with low bone mineral content tend to have daughters with low bone mineral content. Whether this link is a function of heredity or the influence of the mother's habits, or both, remains uncertain.

Table 1. Major Risk Factors for Osteoporosis in Women

- Family history of osteoporosis
- White or Asian
- Small body frame
- Postmenopausal
- Hysterectomy
- Inadequate calcium intake
- Excess protein in the diet
- Inadequate exercise
- Smoking
- Excessive alcohol consumption
- High caffeine intake
- Long-term glucocorticoid therapy
- Long-term use of anticonvulsants, antacids
- Hyperparathyroidism, thyrotoxicosis, Cushing's syndrome, type 1 diabetes

What does appear certain is that regular exercise, lifetime maintenance of an adequate nutritional status with regard to calcium and other nutrients important for bone health, and a healthy lifestyle are essential for maximizing peak bone mass and for minimizing the rate of bone loss that occurs with aging, and thus reducing the risk of osteoporosis.[6,9,11]

OSTEOPOROSIS: IT'S NEVER TOO EARLY OR TOO LATE TO THINK ABOUT PREVENTION

Experts agree that prevention is likely to remain the most effective method of dealing with osteoporosis.[1,4] The two approaches to prevention are maximizing peak bone mass at skeletal maturity and reducing the rate of age and menopause-related bone loss:[10,12]

• Maximizing Peak Bone Mass

Bone mass is continually acquired during the first three decades of life, typically peaking between the ages of 30-35. Although the rate of bone loss has received more attention in the study of the pathogenesis of osteoporosis, it is becoming increasingly clear that insufficient accumulation of skeletal mass by young adulthood predisposes a person to fractures later in life as age-related bone loss ensues.[4]

Studies have shown that maximizing calcium intake during the growth years and up to age 25-30 can greatly affect an individual's peak bone mass.[8,13-17] Children and young adults who do not get adequate calcium may have suboptimal bone density by the time they reach their third and fourth decades. This not only creates a greater risk for fractures at a young age but it increases the chance for developing osteoporosis later in life.

According to a study done on identical twins at the Indiana State University School of Medicine, calcium supplementation significantly enhanced the rate of increase in bone mineral density in prepubertal children already receiving the RDA for calcium. "If the gain persists, it would probably result in an increase in peak bone mass that would reduce the risk of osteoporotic fractures later in life," stated the researchers.[15] Another study done at the Pennsylvania State University College of Medicine showed that calcium supplementation of 500 mg/day for a group of 12-year old girls resulted in significant gains in total body and spinal bone density when compared to the control group.[16]

• Reducing Bone Loss in Postmenopausal Women

Bone continuously remodels through the processes of bone resorption and bone formation. This remodeling process functions by the interaction of two types of cells: osteoclasts, which resorb bone, and osteoblasts, which form new bone. Bone remodeling is in balance until the fourth decade of life when resorption becomes slightly greater than formation and a small, continuous loss of bone mass results. Bone turnover depends on parathyroid hormone (PTH); an increased serum PTH stimulates bone turnover and increases bone loss when the balance between bone resorption and formation is negative.

Bone loss occurs with age in both sexes; however, the pattern differs significantly between men and women.[1,9] In women, bone loss begins prior to menopause (35-45 years), with a pronounced acceleration of bone loss occurring rapidly for about 5-10 years following menopause, at which point the rate of bone loss becomes relatively stable.[2,9,18] Over their lifetimes, women lose about 35% of their cortical bone mass and 50% of their trabecular bone mass whereas men lose about two-thirds of these amounts.[2,4] Cortical bone predominates in the shafts of long bones, while trabecular bone is concentrated in the vertebrae, the pelvis and other flat bones, and in the ends of long bones.

There is now substantial evidence that an inadequate intake of calcium is a risk factor for bone loss.[18] A study reported in the *New England Journal of Medicine* by Reid et al. demonstrated a 43% reduction in bone loss in postmenopausal women who supplemented their regular diets with 1,000 mg of calcium for two years compared to postmenopausal women receiving placebos.[19] Their results confirmed an earlier two-year calcium supplementation study also reported in the *New England Journal of Medicine* which indicated that healthy postmenopausal women can significantly reduce bone loss by increasing their calcium intake to at least 800 mg/day.[20]

Dr. Robert Heaney of Creighton University states, "The growing body of controlled trials, all showing a benefit of calcium, vitamin D, or both, constitutes persuasive evidence that some portion of age-related bone loss in elderly women in Europe and North America is due to insufficient intake of calcium (and vitamin D) and that some portion of osteoporotic fractures could be prevented by ensuring higher intakes of both nutrients."[21]

CALCIUM—WHAT ARE THE RECOMMENDED LEVELS?

The Recommended Daily Allowance (RDA) for calcium is currently set at 800 mg for individuals 1-10 years old and 25 years and older and 1,200 mg for those 11-24 years old and for pregnant or lactating women. However, these levels are well below the level of intake that many experts recommend.[10,21-25] The authors of a study of recent intervention trials of calcium supplementation recommended that the RDA during childhood should be 1,250 mg and 1,450 mg during adolescence,[22] while others have recommended a calcium intake of up to 1,800 mg/day during adolescence.[10] Such an increase in calcium intake during adolescence could play an important role in the attainment of optimal peak bone mass.

Regarding the calcium intake for older individuals, many experts recommend an intake of 1,500 to 2,000 mg/day to minimize bone loss in some patients.[21,23,24] The National Institutes of Health (NIH) Consensus Conference on Optimal Calcium Intake recommends calcium intakes of 1,200 to 1,500 mg for 11-24 year olds, 1,000 mg for those 25-50 years, and 1,500 mg for those over 65.[3] In addition, the NIH recommends a calcium intake of 1,500 mg/day for women over 50 years who are not receiving hormone replacement.

While the RDA levels of calcium may be a source of debate, the real issue is the fact that a large proportion of the population isn't even meeting the current RDA levels.[4,9,26] According to data obtained from the USDA's 1987-88 Nationwide Food Consumption Survey, the mean per capita daily consumption of calcium for the U.S. population was 737 mg.[26] The data for women as a group was even worse: after age 11, no age group of females achieved even 75% of the RDA for calcium. And between the ages of 12 to 29, when calcium requirements reach their peak because of rapid skeletal growth, women consumed <60% of the RDA for calcium. Therefore, the challenge for the health-care professional is to educate patients on the importance of lifetime maintenance of adequate calcium intake.

CALCIUM ABSORPTION

Intestinal absorption of calcium declines with age in both sexes and, overall, the body is less able to adapt to an insufficient calcium supply.[1,4,9,27] Consequently, there is a need to address factors that affect calcium absorption, particularly when dealing with the elderly population. For instance, large quantities of dietary fiber can interfere with calcium absorption, as can diuretics, alcohol, certain medications such as corticosteroids, and vitamin D deficiency. Hypochlorhydria, a condition of low gastric acid production, can also hinder calcium absorption. Patients encountering any of these factors may need closer nutritional attention.

VITAMIN D

Vitamin D plays an essential role in maintaining a healthy mineralized skeleton.[28] The main physiologic function of vitamin D is to maintain serum calcium and phosphorus concentrations within the normal range to maintain essential cellular functions and to promote mineralization of the skeleton.[28-31] Vitamin D acts primarily to increase serum calcium by stimulating intestinal absorption of calcium. Vitamin D insufficiency results in reduced calcium absorption, a rise in circulating parathyroid hormone, and increased bone resorption.[28,30] The elderly often have a low level of vitamin D deficiency owing to less efficient skin synthesis of vitamin D, less efficient intestinal absorption, and reduced sun exposure and vitamin D intake.[28-30]

Vitamin D deficiency can result in secondary hyperparathyroidism, a condition that accelerates bone resorption and thus exacerbates osteoporosis.[28,29,32] Vitamin D deficiency is associated with increased risk of hip fracture,[28] and several studies have demonstrated that an increase in calcium intake of 800-1000 mg/day with supplementation of 400-800 units of vitamin D daily will decrease the risk of vertebral and nonvertebral fractures and increase bone mineral density.[28,31-33]

MAGNESIUM

Although decreased bone mass is the hallmark of osteoporosis, qualitative changes in bone matrix are also present, which could result in fragile or brittle bones that are more susceptible to fracture. There is growing evidence that magnesium may be an important factor in the qualitative changes of the bone matrix that determine bone fragility.[34,35] Magnesium influences both matrix and mineral metabolism in bone by a combination of effects on hormones and other factors that regulate skeletal and mineral metabolism, and by direct effects on bone itself. Magnesium depletion affects all stages of skeletal metabolism adversely, causing cessation of bone growth, decreased osteoblastic and osteoclastic activity, osteopenia, and bone fragility.[34,35]

Magnesium plays important roles in calcium metabolism through its involvement in normal activity of the hormones controlling calcium utilization.[36] Adequate serum magnesium levels are necessary for proper calcium metabolism since hypomagnesemia can result in hypocalcemia and peripheral resistance to the effects of vitamin D. Thus, adequate calcium intake may not ensure proper bone health if magnesium status is abnormal.[34,36] Because of the effect of magnesium deficiency on calcium metabolism, it may also be implicated as a risk factor for osteoporosis.[37,38] Disorders such as chronic alcoholism, diabetes mellitus, and malabsorption syndromes in which magnesium deficiency is prevalent are also associated with a high prevalence of osteoporosis.[37]

Large numbers of individuals may be at risk for magnesium deficiency. Dietary intake studies consistently show intakes of magnesium to be below the RDA in many age groups and surveys have shown that 39% of American women between 15 and 50 years of age receive less than 70% of the RDA.[34,36,39] Because high calcium intake intensifies magnesium deficiency, patients who take calcium supplements to an extent that the Ca:Mg ratio of 2:1 is substantially exceeded are likely to have relative or absolute magnesium deficiency.[39] Calcium supplementation without magnesium may reduce the efficiency of magnesium absorption from the diet and further aggravate the consequences of diminished estrogen, resulting in less movement of magnesium into bone and greater activity of demineralizing parathyroid hormone.[40]

TRACE MINERALS

Trace minerals, particularly zinc, copper, manganese, fluoride, boron, and silicon, are being studied for their roles in bone health. Zinc is needed for osteoblastic activity, collagen synthesis, and alkaline phosphatase activity; copper for cross-linking collagen and elastin; manganese for the biosynthesis of mucopolysaccharides in bone matrix formation; fluoride for osteoblastic activity; and boron and silicon for healthy bone formation.[41] Many other trace minerals are present in bone, such as strontium, molybdenum, vanadium, and chromium, which likely play important roles in bone health that are not completely understood.

Studies have shown that trace mineral deficiencies can impair bone formation and resorption. In a two-year clinical study, postmenopausal women who received calcium supplements together with zinc, copper, and manganese experienced a gain in bone mineral density while women receiving calcium alone, trace minerals alone, or a placebo experienced increasingly greater losses in bone mineral density.[42]

IPRIFLAVONE

Ipriflavone (7-isopropoxyisoflavone) is a derivative of naturally occurring isoflavones and is active in bone metabolism.[43-45] In vivo and in vitro studies in different experimental models have demonstrated the inhibitory effect of ipriflavone on osteoclast recruitment and function (bone resorption) and a stimulatory effect on osteoblastic activity (bone formation).[43-49] Studies in humans have confirmed the inhibitory effect of ipriflavone on bone resorption in conditions of high bone turnover, such as Paget's disease of bone.[43]

Numerous double-blind, placebo-controlled studies have shown a positive effect of ipriflavone in reducing bone mineral loss and increasing bone density in postmenopausal women with osteopenia or established osteoporosis at a dose of 600 mg/day.[43,44,49-52] All patients received an oral calcium supplement of 1 g/day in addition to ipriflavone or placebo. One of the researchers, Dr. Donato Agnusdei, stated that "long-term treatment with ipriflavone may be considered safe, and may increase bone density and possibly prevent fractures in elderly patients with established osteoporosis."[51] Another study evaluating the effects of ipriflavone combined with vitamin D showed that the combined therapy was more effective in reducing bone loss than either therapy alone or control.[45]

All clinical trials confirm a very good tolerance of ipriflavone with a frequency of adverse reactions equal to that observed during administration of a placebo. Despite its structural similarity with some naturally occurring phytoestrogens, ipriflavone has been shown to be devoid of any estrogenic activity in animals and in humans and does not appear to modify secretion or metabolism of endogenous estrogens.[44,48]

COMPREHENSIVE BONE NOURISHMENT: MCHC

Microcrystalline hydroxyapatite concentrate (MCHC) is an excellent source of bioavailable calcium.[27,53-56] MCHC is derived from whole bone and is complete with the minerals and organic matrix found in raw bone. In addition to calcium and the organic components (mostly collagen protein and mucopolysaccharides), MCHC contains phosphorus, magnesium, fluoride, zinc, silicon, manganese, and other trace minerals in the same physiological proportions found in healthy bone. The many features of MCHC are outlined in Table 2 below.

Table 2. Features of MCHC

- Excellent source of bioavailable calcium
- Microcrystalline structure provides a large surface area which is thought to help facilitate mineral absorption
- Contains intact organic bone matrix, collagen protein, and mucopolysaccharides
- Provides a full complement of minerals that are important for healthy bone formation and metabolism such as phosphorus, fluoride, magnesium, silicon, iron, zinc, copper, and manganese

A recent study published in *Osteoporosis International* evaluated the effectiveness of two forms of calcium supplements – calcium carbonate and MCHC – in preventing further bone loss in postmenopausal osteoporosis.[55] In a comparison of a historical untreated group with the present treatment groups, the calcium carbonate supplement was shown to reduce the rate of bone loss by about half, while the MCHC was shown to nearly halt it. Another study of osteoporotic post-menopausal women, with the complication of primary biliary cirrhosis, showed that MCHC supplementation not only helped reduce bone loss but it actually helped increase cortical bone thickness by 6.1%.[53] Conversely, calcium gluconate halted the bone loss but did not restore bone, and the group receiving no supplementation continued to show accelerated loss of bone.

Not only has MCHC been shown to be effective in minimizing bone loss, but it has also been shown to positively affect bone healing. The effectiveness of MCHC on the healing of a standardized bone defect in rabbits was evaluated as compared with a control group and two other forms of calcium supplements: bone mineral (MCHC without the organic constituents) and calcium carbonate.[57] The results showed that treatment with MCHC, but not the other two calcium supplements, resulted in significant improvements in the pattern and quality of bone healing.

These results indicate that MCHC has a beneficial effect on the process of bone healing but that this effect is lost if the organic components of the compound are destroyed or if pure calcium carbonate treatment is substituted. The researchers postulated that "specific osteogenic substances may be present in the organic fraction of MCHC, resulting in its observed superiority over simple mineral supplementation."

GUIDELINES FOR DETERMINING THE PURITY OF MCHC

All MCHC products are not the same. The source of the bone extract as well as the processing procedures are of utmost importance in determining the quality of MCHC. Some sources of MCHC may contain high levels of lead and other contaminants, or be adulterated with cartilage and tendons. Certain processing procedures, such as high-heat and excessive grinding, can result in a product that is nothing more than bone meal. These products lack the full complement of minerals, organic factors, and the microcrystalline structures that are characteristic of true MCHC. How can you be sure that what you are providing to your patients is pure, authentic MCHC? Guidelines for determining the identity and purity of MCHC products may prove helpful to the clinician wanting to provide an exceptional product to his or her patients, and are presented in Table 3.

Table 3. MCHC Purity Guidelines

1. The results of a Certificate of Analysis should be requested from the supplier. This analysis will indicate the protein and mineral content of the MCHC, as well any microbial contamination. Analysis of authentic MCHC will show the same constituent ratios typically found in bone: 25% protein (mostly collagen), 25% elemental calcium, and 12% phosphorus, with the remainder comprised of fat and other minerals.

2. The results of a collagen analysis will indicate the purity and non-adulteration of MCHC. Type I collagen is the predominant type of collagen found in bone, along with small amounts of type V collagen. Properly processed MCHC should contain approximately 20% collagen, the majority of which should be type I. Poorly processed bone, such as bone meal, yields a product with only 0% to 7% type I collagen. The presence of other types of collagen would indicate that the raw material used to make the MCHC contained cartilage, tendons, muscle, marrow, or ligaments.

3. The results of an x-ray diffraction analysis should be requested. This analysis will confirm the microcrystalline structure of the MCHC.

4. A certificate proving the material is approved for human consumption is very important. MCHC may be available in different grades of varying quality. A reliably pure form of MCHC is imported from New Zealand where cattle are free-range and raised in a pesticide-free environment. A Certificate of Edible Origin from the Ministry of Agriculture and Fisheries accompanies MCHC imported from New Zealand. This certificate is required for import into the U.S. and provides assurance of high-grade MCHC.

5. The results of a heavy metal analysis conducted by a third party laboratory should be requested. Heavy metal contamination with lead, arsenic, aluminum, mercury, strontium, and other metals is a concern with regard to some forms of calcium supplements and MCHC is no exception. According to an analysis conducted on 70 brands of calcium supplements sold in the U.S. and Canada, 25% exceeded the FDA's total tolerable daily intake of 6 µg of lead for children age 6 and younger. In high quality MCHC, lead should not be present in levels higher than 1 µg per gram of product.

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