

Rheumors
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OSTEOPOROSIS

By Norman S. Koval, M.D.

Osteoporosis is a disease process in which the density of bone is decreased to a level so low that it is prone to fracture. Unfortunately, this can often be the first signal that the disease is present. More than 24 million Americans, 80% of whom are women, suffer from this debilitating disease. It is a major public health problem which results in expenditures in excess of 10 billion dollars annually. It is estimated that the annual price tag for the treatment of osteoporosis within the next 30 years will increase to between 30 and 60 billion dollars.

From the time that our bones are first formed they undergo "remodeling", a process in which old bone tissue is broken down or reabsorbed and new bone tissue is formed. Bone is constantly remodeling. It is not an inert substance. New bone is formed at a rate greater than the reabsorption process during the first 30 to 35 years of life. At age 30 to 35, however, bone formation and bone reabsorption are about the same. At this time, bone has reached its peak mass. After age 35, bone reabsorption activity increases and in the years prior to menopause there is a gradual decrease in density. At the menopause, when estrogen (the female hormone produced by the ovaries) levels decline, an accelerated loss of bone occurs which may result in the clinical condition we call **osteoporosis**.

The cause of osteoporosis remains unclear. We do know that there are certain risk factors:

- 1) **sex** - women are at a 4 times greater risk of developing osteoporosis than men,
- 2) **age** - the risk of osteoporosis increases with age,
- 3) **calcium deficiency** - calcium is necessary to help in achieving peak bone mass,
- 4) **race** - Caucasians are at greater risk,
- 5) **sedentary lifestyle** - regular physical activity is known to increase bone mass,
- 6) **body size**, petite women are generally more prone to this disorder than larger framed females. Heavier women may be at less risk because fat cells are a site for estrogen production,
- 7) **family history** - there is an increased incidence in families of having osteoporosis although a specific genetic connection has never been discovered,
- 8) **cigarettes/alcohol** - cigarette smoking as well as alcohol intake reduce the body's ability to absorb calcium, thereby, negatively affecting bone density, and
- 9) **medications** - certain long term use of medications such as corticosteroids, anti-seizure drugs and thyroid hormone can interfere with calcium absorption.

Consequence of Osteoporosis: The most devastating consequence of osteoporosis is bone fracture, usually occurring in either the spine, hip or wrist. There are two types of bone - cortical (compact bone) and trabecular (spongy bone). Cortical bone forms the outer shell of bone and

trabecular bone comprises the interior of bone. The "long bones" of the body (the arms and legs) contain greater concentrations of cortical bone while the "flat bones" (spine and hip) contain a greater concentration of trabecular bone. The trabecular bone density is lost at a much more rapid rate at menopause. Since the back bones are comprised of a high concentration of trabecular bone they are common sites for postmenopausal fractures. These fractures can produce the condition of the Dowager's hump which is a loss of height and bent-over posture, causing the protrusion of the abdomen (pot-belly), difficulty in breathing and pain. As the subject reaches the late 60's and 70's there is an increase of hip fractures. Statistics compiled by the National Osteoporosis Foundation report that a woman's risk of developing a hip fracture is equal to her risk of developing breast, uterine and ovarian cancer combined. Hip fractures may often be deadly. Twenty percent of individuals who survive a hip fracture will die within the first year. Of those individuals who survive a hip fracture, only 25 to 50% maintain their previous level of physical functioning and up to 30% may become totally dependent on others for the activities of daily living.

Making a diagnosis of osteoporosis depends upon the physician having a high index of suspicion, knowing who has risk factors for osteoporosis, and knowing that there are techniques for diagnosing this disorder before fractures occur. Presently, the most sensitive test available for making this diagnosis is known as dual energy x-ray absorptiometry (DEXA). This offers a highly accurate measurement of the hip and spine with a very low dose of radiation exposure. The exposure is one-tenth of the radiation level of a standard chest xray.

The most important treatment for osteoporosis is actually prevention. Education of the female in her teenage years to appropriate diet and exercise is paramount in the prevention approach. Estrogen replacement therapy, calcium supplementation, proper exercise regimen, bisphosphonates, Calcitonin and several investigational agents still early in their development, such as growth hormone and parathyroid hormone, may be used in the treatment of this disease. Medical treatments for this disorder will be discussed by the other contributors to this edition of Rheumors.

The physicians of Arthritis & Rheumatism Associates are dedicated to the education of patients, and physicians alike, as to the gravity of this major public health problem.

RHEUMORS - Q&A

Q. I have been told to take supplemental calcium. What kind should I take?

- A. Most elderly, and many younger patients have insufficient calcium intake. Calcium rich foods such as low fat dairy products, fish, legumes, and green leafy vegetables should, if possible, be part of everyone's daily intake. Supplements may be used if diet alone cannot fulfill daily calcium requirements. Premenopausal women require about 1200 mg of calcium daily and postmenopausal women 1500 mg of calcium daily in the **elemental** form. The most popular and least expensive calcium supplements contain calcium carbonate which is 40% elemental calcium by weight. Popular brands include Tums, Caltrate, and OsCal. In addition, there are many store or local brands. Doses range from 200 mg to 600 mg of calcium per tablet. Often the higher doses with 400 units of Vitamin D are recommended as many calcium poor patients also have insufficient levels of Vitamin D. Since quality and bioavailability (amount of calcium actually available to be absorbed and used by the body) of calcium preparations vary greatly you should consult your physician or pharmacist about the bioavailability of the form of calcium you are taking.

Calcium citrate (Citracal) is 21% elemental calcium by weight and is much better absorbed than calcium carbonate. Calcium citrate also tends to cause less stomach distress. It is, however, more expensive than calcium carbonate. Calcium citrate is available as 200 mg tablets.

--Robert L. Rosenberg, M.D.

Q. How useful are estrogens in preventing osteoporosis?

- A. Estrogen replacement therapy (ERT) is effective in preventing and treating postmenopausal osteoporosis. ERT acts by blocking bone resorption thus allowing the bone producing cells to incorporate more calcium into the bone. Adequate amounts of calcium and Vitamin D are still necessary to allow proper bone formation. ERT should be continued for 10-15 years to gain maximal benefit in the treatment and prevention of osteoporosis. There appears to be little benefit of ERT for those women who are more than 15-20 years from menopause.

While ERT has been safe in the short run, there remains concerns about long term use of ERT, specifically with concern of endometrial and breast cancers. Endometrial cancer risk may be reduced by the addition of progesterone (another female hormone). ERT has other benefits including lowering of blood fats with significant reduction of risk for coronary artery disease as well as elimination of menopausal symptoms such as hot flashes and genital irritation.

ERT may be taken as tablets or twice weekly skin patches. Either method is effective against osteoporosis.

--Robert L. Rosenberg, M.D.

Q Are there exercises to help prevent or treat Osteoporosis?

A Exercise is one of the most important therapies for Osteoporosis. Weightbearing exercise puts important stress on the skeleton which stimulates new bone growth and repair, as well as calcium incorporation. Weightbearing exercises used in treating established Osteoporosis include walking, low-impact aerobics, stair climbing, and other exercises which cause mild gravitational stress on the bones. Swimming has recently also been shown to be of some benefit in preventing and treating Osteoporosis. High impact exercises (jogging, jumping rope, tennis and other sports) are important ways of preventing future Osteoporosis in young people with strong or developing bones, but could risk fractures in patients with established Osteoporosis. The amount of exercise needed is variable, but general recommendations are 15-30 minutes 3 to 5 times per week. In the winter, indoor "mall walking" is an excellent way to pursue this endeavor. Of course, before embarking on any strenuous exercise regimen, one should consult with one's physician.

--Evan L. Siegel, M.D.

Q Are there any special home modifications that should be made for a patient with Osteoporosis?

A Yes. One of the cornerstones of Osteoporosis management is fall prevention. Falls can be devastating in a patient with Osteoporosis, often resulting in painful and debilitating fractures. The home must be looked at carefully with an eye toward safety. All loose rugs or stray wires must be removed or fastened in a safe place. Non-slip mats must be put into showers and baths, with appropriate hand-rails installed. Lighting should be maximized in all areas, and patients with Osteoporosis should never walk in the dark to the bathroom or elsewhere. Snow and ice removal should be arranged for promptly. These and other common sense steps can help prevent long and costly hospitalizations, and even fatal complications of the severe fractures often unnecessarily seen in patients with Osteoporosis.

--Evan L. Siegel, M.D.

Rheuminations

INCLUSION CRITERIA FOR ENTRY INTO A NEW BISPHOSPHONATE ORAL AGENT OSTEOPOROSIS STUDY

We are currently enrolling patients in an osteoporosis third generation bisphosphonate study.

Inclusion criteria follows:

Criteria I

- a. Female, at least 5 years post menopausal, either artificial or natural.
- b. Be less than or equal to 85 years of age.
- c. Meet xray requirements, two or more vertebral deformities or one deformity with low bone mineral density.
- d. Be ambulatory.
- e. Be able to and willing to participate in the Study as evidenced by having signed an informed consent.

If you meet these criteria and are interested in entering our study, contact Donna at the osteoporosis office at 949-1134 or June in our main office at 593-9100.

Points on Joints

BISPHOSPHONATES

Herbert S. B. Baraf, M.D.

Of all the new drug therapies for osteoporosis, none holds more promise than that held by a class of agents called **BISPHOSPHONATES**. The first of these, Etidronate, was originally developed as a water softener and was used to prevent soap scum. By a stroke of good fortune however, Etidronate was found to have significant medical usefulness. Etidronate, marketed under the trade name Didronel, is one of six different bisphosphonate compounds that are of clinical interest in osteoporosis. Thus far, however, none of these drugs has received FDA approval for osteoporosis treatment.

Presently there are only two bisphosphonates available for clinical use in the United States; Etidronate and Pamidronate. Etidronate was initially approved by the FDA more than 15 years ago for the treatment of Paget's Disease, a sometimes serious and fairly rare bone disorder. Pamidronate was made available this year to cancer patients because of its ability to lower elevated serum calcium levels resulting from their cancer's effect on bone. Four additional agents are currently being evaluated in clinical trials. All six of these drugs are actively being studied for their effectiveness in osteoporosis treatment. Thus far, all seem to have promise.

Etidronate (Didronel) is the first of the bisphosphonates to be studied in osteoporosis. It is referred to as a "first generation" agent. It differs from most of the others in its dual ability to inhibit resorption of calcium from bone and deposition of calcium into bone. Of course, in treating osteoporosis only this first effect is desirable. Fortunately, Etidronate is a weaker inhibitor of calcium deposition than it is of calcium resorption. When used for osteoporosis therapy however, it must be given for short periods and then withheld for longer periods so as to selectively inhibit resorption without inhibiting new bone formation.

Pamidronate and tiludronate are among the "second generation" bisphosphonates. Risedronate is a "third generation". Unlike Etidronate, these drugs are more selective in their effect on bone, only demonstrating significant inhibition of bone resorption. They can therefore be given on a more continuous basis.

Etidronate (Didronel), among all of the bisphosphonate compounds, has been studied the longest. Several multicenter studies with this agent have been ongoing and have shown significant improvement in bone density for as long as five years into therapy. Fractures related to osteoporosis seem to occur with less frequency in treated patients. Side effects have been minimal and the drug has been well tolerated. In addition, Etidronate has been shown to inhibit bone loss in patients who require long term cortisone (steroid) treatment. Studies with other bisphosphonates are hoped to show at least the same degree of improvement.

Thus, a number of new drugs, all in the bisphosphonate class, are under development for the prevention and treatment of osteoporosis. These drugs hold considerable promise because of their low toxicity, moderate effectiveness and their ease of administration. As compared to

female hormones (which cannot be given to male osteoporosis patients and have significant side effects for some women) and calcitonin, which is very expensive and must be given by injection, bisphosphonates show some clear advantages.

Once again, a discovery aimed at a mundane task such as eliminating the ring around your bathtub has led to a major medical breakthrough - an important treatment for osteoporosis.

Rheuminations

CALCITONIN

By Emma DiIorio, M.D.

Osteoporosis is a condition in which a person's bone mass decreases, leaving these bones more susceptible to fracture. We can reduce one's risk of osteoporotic fractures by increasing bone mineral density and by preventing bone loss. This can be achieved with various substances. One of these substances is calcitonin.

Calcitonin is a hormone that is made and secreted by the thyroid gland. Calcitonin prevents bone resorbing cells, known as osteoclasts, from resorbing bone. Calcium levels in the blood control calcitonin release, so that the intake of dietary calcium increases calcitonin production and decreases bone resorption.

Synthetic salmon calcitonin is 40-50 times more potent than human calcitonin. Clinical studies using calcitonin in the treatment of osteoporosis have shown effective responses, ranging from slowing of further bone loss to a striking increase in bone mass. At present the only route of administration approved in the United States is by subcutaneous injection (similar to insulin administration). Intranasal administration is currently undergoing clinical trials in the United States. To see if you are a candidate for this treatment, your physician will obtain a baseline measurement of your bone mass. Once treatment has begun, annual measurements of bone mass are done to see if the drug has been effective in either increasing bone mass or preventing further bone loss.

Calcitonin is also as effective as estrogens in preventing bone loss in postmenopausal women. It can easily serve as an alternative in the prevention of osteoporosis in women who are unable or unwilling to take estrogens.

Beyond its beneficial effects on bone mass, calcitonin has analgesic effects. It provides pain relief to patients with acute osteoporotic fractures. The analgesic effects begin within a few weeks of the start of treatment.

Calcitonin is a relatively innocuous medication. The most common side effects are nausea, vomiting, gastric discomfort, metallic taste, facial flushing, and skin hypersensitivity. Most of these symptoms decrease or disappear with continued use. It is best to administer the drug at bedtime and to take Benadryl thirty minutes before injection to decrease gastrointestinal side effects.

In summary, calcitonin is the treatment of choice in patients with severe osteoporosis, especially in patients with osteoporotic fractures and in steroid related osteoporosis. It also serves as an alternative to estrogen therapy and is effective in the prevention of osteoporosis.

Rheuminations

DEFLAZACORT

By Emma DiIorio, M.D.

Steroid medications such as Prednisone are used for the treatment of a variety of disorders including rheumatoid arthritis and polymyalgia rheumatica. Steroid medications have many adverse effects, including hypertension, diabetes, cataracts, and cause significant loss of calcium from bone, leading to osteoporosis.

Deflazacort, a new derivative of Prednisone, is thought to cause less of this troublesome bone loss and yet be as effective as Prednisone. We are currently conducting a two-year randomized double blind study comparing Prednisone to Deflazacort in patients with rheumatoid arthritis and polymyalgia rheumatica. The primary goal of this study is to confirm the relative bone-sparing effect of Deflazacort. We are actively enrolling patients with established rheumatoid arthritis or polymyalgia rheumatica currently on Prednisone, or in whom the initiation of Prednisone is being contemplated.

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