CME CREDIT

TAKE-HOME POINTS FROM LECTURES BY CLEVELAND CLINIC AND VISITING FACULTY

Osteoporosis: Which current treatments reduce fracture risk?

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ABSTRACT

Randomized controlled trials showed that several antiosteoporosis drugs decrease the incidence of fractures, which is a better measure of efficacy than are changes in bone mineral density or serum markers of bone turnover. With effective agents available, physicians should make osteoporosis treatment a priority, especially for patients at high risk, such as those who have already had a fracture.

HOW DO WE KNOW that treating osteoporosis is worthwhile? Many studies found that various agents could increase bone mineral density; however, the true goal is to prevent fractures. Therefore, although we can assess an individual patient's risk or response to therapy by measuring bone mineral density or biochemical markers of bone resorption, the only way to prove that a drug is effective is to perform randomized controlled trials that show that patients who take the drug have fewer fractures than do patients who do not take the drug.

Such data are at hand, giving clinicians and patients several options for prevention and treatment.

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HALF OF ALL 50-YEAR-OLD WOMEN WILL HAVE A FRACTURE

Preventing and treating osteoporosis ought to be a priority because it is extremely common and causes considerable suffering. Nearly half of all 50-year-old women will have an osteoporotic fracture before they die.[1] A 50-year-old woman's risk of dying of complications of a fracture, such as pneumonia or pulmonary embolism, is approximately the same as her risk of dying of breast cancer.

Risk factors for osteoporosis include advanced age, corticosteroid use, cigarette smoking, family history, thin body habitus, and of particular importance, previous fractures. I urge you to consider treatment for any woman who has had an osteoporotic fracture: in the MORE study,[2] 20% of the patients in the placebo group who had a previous vertebral fracture had another vertebral fracture within 36 months, even though they were taking calcium and vitamin D supplements.

Fracture reduction is the gold standard of efficacy

PREVENTING AND TREATING OSTEOPOROSIS

Drugs approved by the Food and Drug Administration for preventing osteoporosis are estrogen, raloxifene (a selective estrogen receptor modulator, or SERM), and alendronate and risedronate (bisphosphonates); those approved for treating osteoporosis are calcitonin, raloxifene, alendronate, and risedronate. An essential part of the regimen with any of these agents is an adequate intake of calcium and vitamin D.

Calcium and vitamin D

Although calcium and vitamin D are frequently given to osteoporotic patients, no

study has shown conclusively that they reduce fracture risk by themselves. Studies that did demonstrate an effect[3,4] may have been confounded by the presence of vitamin D insufficiency.

Still, optimizing calcium and vitamin D intake through diet or supplementation is the basis for prevention and treatment of osteoporosis. It may help to think of calcium and vitamin D as the cement powder we may use to set a fence post. The only way the cement powder will hold the post is if we add water. In osteoporosis, calcium and vitamin D are like cement powder, and the drugs that have been approved are the water.

Calcium supplements should provide 500 to 1,000 mg of elemental calcium per day, either as calcium carbonate (eg, Os-Cal, Tums, taken with food) or calcium citrate (eg, Citracal, taken without regard to food). Vitamin D supplements should provide 400 to 800 units/day.

Estrogen replacement therapy

Most of the data on the efficacy of estrogen in osteoporosis are from case-control and cohort studies,[5,6] in which women taking estrogen had a 20% to 60% lower incidence of hip fractures and a 50% lower incidence of spine fractures than did women not taking estrogen. A major drawback of these studies is that they were not randomized: patients self-selected estrogen therapy.

Only alendronate definitely reduced hip fracture risk

One small prospective study[7] evaluated the effect of transdermal estrogen on spine fracture reduction in 75 women with osteoporosis. Estrogen significantly reduced the number of new spine fractures, but the number of patients who had fractures was not statistically different between the active treatment group and the placebo group. A large prospective, randomized study sponsored by the National Institutes of Health is underway to determine the effects of estrogen on the bones, heart, and breasts.

A variety of preparations is available. A typical regimen is conjugated equine estrogen (Premarin) 0.625 mg/day. In women with a uterus, medroxyprogesterone acetate (eg, Provera, Cycrin, Amen) 5 to 10 mg is also taken on the first 12 days of the month.

Raloxifene: A selective estrogen receptor modulator

An ongoing prospective, randomized study[2] of more than 7,700 women with osteoporosis showed that raloxifene (Evista), a selective estrogen receptor modulator (SERM), given for 3 years reduced the incidence of spine fractures by 30%. Treatment did not significantly reduce nonvertebral or hip fractures. Dosage is 60 mg/day.

Nasal salmon calcitonin

The effect of nasal salmon calcitonin (Miacalcin) on fracture reduction was evaluated in a 5-year prospective, randomized study[8] of more than 1,200 women. The drug reduced the risk of spine fracture by 36% in women receiving 200 IU. The study has been criticized, however, because it did not demonstrate a dose-response relationship, more than 60% of the patients withdrew from the study, and the investigators did not use intention-to-treat as the basis of their statistical analysis.

Bisphosphonates

The bisphosphonates currently used to treat osteoporosis include etidronate, alendronate, and risedronate; however, only alendronate and risedronate are FDA-approved for this indication at present.

Etidronate (Didronel) has been shown to decrease spine fractures after 2 years of therapy, but this effect was lost after 3 years.

Alendronate (Fosamax) reduced vertebral, nonvertebral, and hip fractures by about 50% in prospective studies involving more than 10,000 women.[9,10] It is the only medication that has unequivocally been shown to reduce the risk of hip fracture in prospective studies. The dosage is 5 to 10 mg/day, taken with a full glass of water at least 30 minutes before the first food, medication, or beverage of the day. Because alendronate can irritate the esophagus, patients should remain upright after taking the drug to avoid possible reflux.

Risedronate (Actonel), in two separate studies involving nearly 2,500 women,[11,12] decreased spine fractures by 40% to 50%. However, neither study showed that risedronate reduced hip fractures. In another large study[13] evaluating the effect of risedronate on

hip fractures in 9,000 women over age 70, about 5,000 women ages 70 to 79 with femoral neck T scores less than −2.5 had no significant reduction in hip fracture risk when taking 2.5 mg/day or 5.0 mg/day. Combining the two dosage groups gave a significant reduction of 39%. Risedronate did not reduce hip fractures in 4,000 women over age 80.

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