Table 75-5). No reduction in nonvertebral or hip fractures was found. The U.S. Food and Drug Administration (FDA) advisory panel is reviewing an association with cancer.

Denosumab

The receptor activator of nuclear factor-κB (RANK) and its ligand (RANKL) are mediators of osteoclast activity. Compared with placebo, denosumab, an antibody to RANKL, produced a relative increase in bone mineral density at the spine of 9.2% and hip of 6.0% over 3 years, and it reduced fractures by 68% at the spine, 40% at the hip, and 20% at nonvertebral sites. Denosumab is approved for postmenopausal women and men with osteoporosis, for men with prostate cancer on androgen deprivation therapy, and for postmenopausal women with breast cancer on aromatase inhibitors. It is given as a subcutaneous 60-mg injection every 6 months.

Estrogen Agonists-Antagonists

Estrogen agonists-antagonists were previously called selective estrogen receptor modulators (SERMs) because they have some estrogen-like and anti–estrogen-like benefits. Raloxifene is approved for the prevention and treatment of osteoporosis. The Multiple Outcomes of Raloxifene Evaluation (MORE) trial found that bone mass was increased by 4% at the spine and 2.5% at the femoral neck over 3 years. This increase was associated with a 50% reduction in vertebral fractures. No reduction in nonvertebral or hip fractures was seen (see Table 75-5). Treatment was associated with improved lipid status, as shown by decreased total and low-density lipoprotein cholesterol.

Raloxifene is not associated with endometrial hyperplasia, and patients should not have bleeding or spotting. They do not have breast tenderness or swelling. Raloxifene reduces the risk for invasive breast cancer in postmenopausal women with osteoporosis and in women at high risk for invasive breast cancer. Patients have the same small risk of deep vein thrombosis or pulmonary embolus that is found with hormone therapy. Raloxifene does not relieve postmenopausal symptoms and may exacerbate hot flashes. Studies have not found a significant impact on cardiovascular disease. Raloxifene can be given with or without food in a daily oral dose of 60 mg per day.

Hormone Therapy

Investigators of the Women's Health Initiative, a large, randomized, placebo-controlled, multicenter trial evaluating hormone therapy, reported a 36% reduction in hip and vertebral fractures after 5.2 years. In addition to improvements in bone mass, benefits include an improved lipid profile, decreased colon cancer incidence, and decreased menopausal symptoms. However, because of the potential risks of hormone therapy (i.e., cardiovascular events, breast cancer, deep vein thrombosis, pulmonary embolus, and gallbladder problems), it should be used only for prevention or management of menopausal symptoms, and other agents should be used for the treatment of osteoporosis.

Parathyroid Hormone

Recombinant human PTH (1-34), or teriparatide, is an osteoanabolic agent that increases spinal bone mineral density by 9.7% and hip bone mineral density by 2.6% in 18 months. It is associated with a 65% reduction in vertebral fractures and a 53% reduction in nonvertebral fractures. Teriparatide is taken for up to 2 years as a subcutaneous, 20-μg daily dose for postmenopausal women and men at high risk for fracture. After therapy, patients benefit from antiresorptive therapy to prevent bone loss. Recombinant human PTH (1-84) is approved for use in Europe.

Alternative Therapies

Medical Therapies

Strontium ranelate is an approved agent for the treatment of osteoporosis in Europe, but it is not FDA approved in the United States. The mechanism of action is not fully understood, but strontium is thought to stimulate osteoblast proliferation and inhibit osteoclast formation. Inhibition of the protease cathepsin K appears to prevent bone resorption with no major impact on bone formation. Another promising osteoanabolic therapeutic target is the inhibition of sclerostin, a potent inhibitor of bone formation, with an antibody.

Combination therapy has been examined with two antiresorptive agents or an antiresorptive and osteoanabolic agent together. Overall, studies with combination therapy have suggested minor improvements in bone mass over therapy with single agents. Because studies have not shown greater fracture reduction, this type of combination therapy with two antiresorptive agents or an antiresorptive plus an osteoanabolic usually is not recommended. However, it is recommended to follow osteoanabolic therapy using teriparatide with an antiresorptive therapy such as a bisphosphonate to maintain the gain.

Vertebroplasty and Kyphoplasty

Vertebroplasty involves injection of cement (i.e., polymethylmethacrylate) into a compressed vertebra to prevent the vertebral body from further collapse. Kyphoplasty introduces a balloon into the vertebral body to expand it, followed by cement placement inside the vertebral body. This approach expands the vertebral body and may increase height. Some studies suggest a significant reduction in pain early on, but the long-term pain reduction may be similar to that of placebo. Ongoing studies are needed to determine whether differences in outcomes can be found between vertebroplasty and kyphoplasty. These procedures are recommended only for patients with significant pain from vertebral fractures and are not routinely performed in asymptomatic patients with vertebral osteoporosis.

SUGGESTED READINGS

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