

Osteoporosis : Prevention and Treatment

Osteoporosis is a skeletal disease characterized by loss of bone mass and architectural integrity, leading to increased fragility of bones and subsequent risk for fracture. Osteoporosis is often undetected until a fracture occurs. The spine, hip, and wrist are the most common sites for fractures. The lifetime risk of a 50-year-old woman for osteoporotic fracture approaches 40%. Hip fractures are more worrisome, as the subsequent mortality rate is approximately 25% for those greater than 65 years of age. The other common site for fracture, the wrist, causes additional morbidity. While the medical consequences of osteoporosis need for long-term care placements as disability limits the ability for self-care.

Several interventions to reduce fracture risk can be recommended to the general population. These include an adequate intake of calcium and vitamin D, lifelong participation in regular weight-bearing and muscle-strengthening exercise, avoidance of tobacco use, identification and treatment of alcoholism, and treatment of other risk factors such as impaired vision.

Providing adequate daily calcium and vitamin D is a safe and inexpensive way to help reduce fracture risk. Controlled clinical trials have demonstrated that the combination of supplemental calcium and vitamin D can reduce the risk of fracture.

All individuals should be advised to obtain an adequate intake of dietary calcium (at least 1,200 mg per day, including supplements if necessary). Lifelong adequate calcium intake is necessary for the acquisition of peak bone mass and subsequent maintenance of bone health.

The skeleton contains 99 percent of the body's calcium stores; when the exogenous supply is inadequate, bone tissue is resorbed from the skeleton to maintain serum calcium at a constant level. National Osteoporosis Foundation (NAS) recommendation that women older than age 50 consume at least 1,200 mg per day of elemental calcium.

Intakes in excess of 1,200 to 1,500 mg per day have limited potential for benefit and may increase the risk of developing kidney stones or cardiovascular disease.

Men and women age 50 and older typically consume only about 600 to 700 mg per day of calcium in their diet. Increasing dietary calcium is the first-line approach, but calcium supplements should be used when

an adequate dietary intake cannot be achieved. Vitamin D plays a major role in calcium absorption, bone health, muscle performance, balance and risk of falling.

Many elderly patients are at high risk for vitamin D deficiency, including patients with malabsorption (e.g., celiac disease) and chronic renal insufficiency, housebound patients, chronically ill patients and others with limited sun exposure. Serum 25 (OH)D levels should be measured in patients at risk of deficiency and vitamin D supplemented in amounts sufficient to bring the serum 25(OH)D level to 30 ng/ml (75nmol/L) or higher.

Regular Weight- Bearing Exercise

Regular weight-bearing and muscle-strengthening exercise should be recommended to reduce the risk of falls and fractures. Among its many health benefits, weight-bearing and muscle-strengthening exercise can improve agility, strength, posture and balance, which may reduce the risk of falls. In addition, exercise may modestly increase bone density.

Full Prevention

In addition to maintaining adequate vitamin D levels and physical activity, as described above, strategies to reduce falls include, but are not limited to, checking and correcting vision and hearing, evaluating any neurological problems, reviewing prescription medication for side effects that may affect balance and providing a checklist for improving safety at home. Wearing undergarments with hip pad protectors may protect an individual from injuring the hip in the event of a fall. Hip protectors may be considered for patients who have significant risk factors for falling or for patients who have previously fractured a hip.

Avoidance of Tobacco Use and Excessive Alcohol Intake

Patients should be advised to avoid tobacco smoking. The use of tobacco products is detrimental to the skeleton as well as to overall health.

Pharmacological Therapy

All patients being considered for treatment of osteoporosis should also be counseled on risk factor reduction. Patients should be counseled specifically on the importance of calcium, vitamin D and exercise as part of any treatment program for osteoporosis. Prior to initiating treatment, patients should be evaluated for secondary causes of osteoporosis and have BMD measurements.

Who should be considered for Treatment?

Postmenopausal women and men age 50 and older presenting with the following should be considered for treatment:

- A hip or vertebral (clinical or morphometric) fracture
- T-score ≤ -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes.
- Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) and a 10-year probability of a hip fracture $\leq 3\%$ or a 10-based on the US-adapted WHO algorithm.

Drugs for Osteoporosis

Options for the prevention and/or treatment of postmenopausal osteoporosis include, in alphabetical order; bisphosphonates (alendronate, alendronate plus D, ibandronate, risedronate, risedronate with 500 mg of calcium carbonate and zoledronic acid), estrogen agonist/antagonist.

The anti-fracture benefits of FDA-approved drugs have mostly been studied in women with postmenopausal osteoporosis. There are limited fracture data in glucocorticoid-induced osteoporosis and no fracture data in men.

Bisphosphonates

Alendronate. Alendronate sodium is approved by the FDA for the prevention Alendronate is also approved for treatment to increase bone mass in men with osteoporosis and for the treatment of osteoporosis in men and women taking glucocorticoids. Alendronate is now available as a generic preparation in the US. Alendronate reduces the incidence of spine and hip fractures by about 50 percent over three years in patient with a prior vertebral fracture. It reduces the incidence of vertebral fractures by about 48 percent over three years in patients without a prior vertebral fracture.

Ibandronate. Ibandronate sodium is approved by the FDA for the treatment of postmenopausal osteoporosis. The oral preparations are also approved for the prevention of postmenopausal osteoporosis. Ibandronate reduces the incidence of vertebral fractures by about 50 percent over three years. It also reduces the non-vertebral fractures significantly.

Risedronate. Risedronate sodium is approved by the FDA for the prevention and treatment Risedronate reduces the incidence of vertebral fractures by about 41-49 percent and non-vertebral fractures

by about 36 percent over three years, with significant risk reduction occurring after one year of treatment, in patients with a prior vertebral fracture.

Zoledronic Acid. Zoledronic acid is approved by the FDA for the treatment of osteoporosis. Zoledronic acid is also indicated for the prevention of new clinical fractures in patients who have recently had a low-trauma hip fracture.

Side effects and administration of bisphosphonates:

Side effects are similar for all bisphosphonate medications and include gastrointestinal problems such as difficulty swallowing, inflammation of the esophagus and gastric ulcer. There have been reports of osteonecrosis of the jaw (particularly following intravenous bisphosphonate treatment for patients with cancer) and of visual disturbances, which should be reported to the healthcare provider as soon as possible.

Calcitonin

Salmon calcitonin is the treatment of osteoporosis in women who are at least five years postmenopausal. It is delivered as a single daily intranasal spray that provides 200 IU of the drug. Subcutaneous administration by injection also is available. Oral calcitonin has been approved by the FDA for the treatment of osteoporosis.

Estrogen/ Hormone Therapy (ET/HT)

Estrogen/hormone therapy is approved by the FDA for prevention of osteoporosis, relief of vasomotor symptoms and vulvovaginal atrophy associated with menopause. Women who have not had a hysterectomy require HT, which contains progestin to protect the uterine lining.

Estrogen Agonist/Antagonist (formerly known as SERMs)

Raloxifene is approved by the FDA for both prevention and treatment of osteoporosis in postmenopausal women. Raloxifene reduces the risk of vertebral fractures by about 30 percent in patients with a prior vertebral fracture and by about 55 percent in patients without a prior vertebral fracture over three years.

Parathyroid Hormone

Teriparatide is approved by the FDA for the treatment of osteoporosis in postmenopausal women at high risk for fracture. It is an anabolic

(bone-building) agent administered by daily subcutaneous injection. The safety and efficacy of teriparatide has not been used for a maximum of two years. It is common practice to follow teriparatide treatment with an antiresorptive agent, usually bisphosphonate, to maintain or further increase BMD.

Combination therapy

Combination therapy (usually a bisphosphonate with a non-bisphosphonate) can provide additional small increases in BMD when compared with monotherapy; however, the impact of combination therapy on fracture rates is unknown.

Calcitriol. This synthetic vitamin D analogue, which promotes calcium absorption, has been approved by the FDA for managing hypocalcemia and metabolic bone disease in renal dialysis patients. It is also approved for use in hypoparathyroidism, both surgical and idiopathic and pseudohypoparathyroidism. No reliable data demonstrate a reduction of risk for osteoporotic fracture.

Other bisphosphonates (etidronate, pamidronate, tilubronate):

These medications vary chemically from alendronate, ibandronate, risedronate and zoledronate but are in the same drug class. At the time of publication, none is approved for prevention or treatment of osteoporosis. Most of these medications are currently approved for other conditions including Paget's disease, hypercalcemia of malignancy and myositis ossificans.

Sodium fluoride, Strontium ranelate

Monitoring Effectiveness of Treatment: It is important to ask patients whether they are taking their medications and encourage continued and appropriate compliance with their osteoporosis therapies to reduce fracture risk. It is also important to review their risk factors and encourage appropriate calcium and vitamin D intakes, exercise, fall prevention and other lifestyle measures. Serial central EXA BMD testing is important component of osteoporosis management.

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