Drugs for bone disorders

Osteoporosis is a progressive loss of bone mass and skeletal fragility. Patients with osteoporosis have an increased risk of fractures, which can cause significant morbidity. Osteoporosis occurs in older men and women but is most pronounced in postmenopausal women.

Osteomalacia is softening of the bones that is most often attributed to vitamin D deficiency.
[Note: Osteomalacia in children is referred to as rickets].

Bone remodeling

Bone is continuously remodeled, with about 10% of the adult skeleton replaced each year. The purpose of bone remodeling is to remove and replace damaged bone and to maintain calcium homeostasis.
Osteoclasts are cells that break down bone, a process known as bone resorption. Following bone resorption, **osteoblasts** or bone-building cells synthesize new bone. Crystals of calcium phosphate known as hydroxyapatite are deposited in the new bone matrix during the process of **bone mineralization**.Lastly, bone enters a resting phase until the cycle of remodeling begins again. Bone loss occurs when bone resorption exceeds bone formation during the remodeling process.

Treatment of osteoporosis

1-**Bisphosphonates (***alendronate , ibandronate and zoledronic acid).*

Mechanism of action: Bisphosphonates decrease osteoclastic bone resorption mainly through an increase in osteoclastic apoptosis (programmed cell death) and inhibition of the cholesterol biosynthetic pathway important for osteoclast function. The decrease in osteoclastic bone resorption results in a small increase in bone mass and a decreased risk of fractures in patients with osteoporosis.
Adverse effects:
1-Diarrhea, abdominal pain, and musculoskeletal pain.
2- Associated with esophagitis and esophageal ulcers. To minimize esophageal irritation, patients should remain upright after taking oral bisphosphonates.
3-Osteonecrosis of the jaw has been reported with bisphosphonates but is usually associated with higher intravenous doses .
4-Uncommon, bisphosphonates may be associated with atypical fractures. The risk of atypical fractures may increase with long-term use of bisphosphonate therapy.
2-**Selective estrogen receptor modulators**
Lower estrogen levels after menopause promote proliferation and activation of osteoclasts, and bone mass can decline rapidly.
Raloxifene is a selective estrogen receptor modulator approved for the prevention and treatment of osteoporosis. It has estrogen-like effects on bone and estrogen antagonist effects on breast and endometrial tissue. It is an alternative for postmenopausal osteoporosis in women who are intolerant to bisphosphonates. In addition, it decreases the risk of invasive breast cancer and also reduces levels of total and low density lipoprotein cholesterol.

Adverse effects include hot flashes, leg cramps, and a risk of venous thromboembolism similar to estrogen.

3-**Calcitonin**

Salmon *calcitonin* is indicated for the treatment of osteoporosis in women who are at least 5 years postmenopausal. The drug reduces bone resorption, but it is less effective than bisphosphonates.
A unique property of *calcitonin* is the relief of pain associated with osteoporotic fracture.
It is available in intranasal and parenteral formulations.
Because of a potential increased risk of malignancy with *calcitonin*, this agent should be reserved for patients intolerant of other drugs for osteoporosis.

4-**Denosumab**

Is a monoclonal antibody that targets receptor activator of nuclear factor kappa-B ligand and inhibits osteoclast formation and function. *Denosumab* is approved for the treatment of postmenopausal osteoporosis in women at high risk of fracture. It is administered via subcutaneous injection every 6 months.

Adverse effects

Increased risk of infections, dermatological reactions, hypocalcemia, osteonecrosis of the jaw, and atypical fractures.

5-**Teriparatide**

Is a recombinant form of human parathyroid hormone that is administered subcutaneously daily for the treatment of osteoporosis. *Teriparatide* is the first approved treatment for osteoporosis that stimulates bone formation. Other drugs for osteoporosis inhibit bone resorption. *Teriparatide* promotes bone formation by stimulating osteoblastic activity. *Teriparatide* has been associated with an increased risk of osteosarcoma in rats. The safety and efficacy of this agent have not been evaluated beyond 2 years.

Drugs induced osteoporosis

1-Corticosteroids
2-Anticonvulsants
3-Aromatase Inhibitors.
4-Proton Bump Inhibitors
5- Medroxyprogesterone Acetate
6-Thiazolidinediones

Osteomalasia treatment

1-Vitamin D supplements: Vitamin D helps the body absorb calcium, which is necessary for healthy bones.
2-Calcium and phosphorus supplements: Taking supplements of calcium and phosphorus along with vitamin D can help to increase bone density and strength.
3-Treatment of underlying condition.