Bisphosphonate

Bisphosphonates are a class of drugs that prevent the loss of bone mass:

Osteoporosis and similar diseases. They are the most commonly prescribed drugs used to treat osteoporosis.

see Paget's disease medical treatment.

They are called bisphosphonates because they have two phosphonate (PO(OH) 2) groups.

Evidence shows that they reduce the risk of fracture in post-menopausal women with osteoporosis.

Bone undergoes constant turnover and is kept in balance (homeostasis) by osteoblasts creating bone and osteoclasts destroying bone. Bisphosphonates inhibit the digestion of bone by encouraging osteoclasts to undergo apoptosis, or cell death, thereby slowing bone loss.

The uses of bisphosphonates include the prevention and treatment of osteoporosis, Paget's disease of bone, bone metastasis (with or without hypercalcaemia), multiple myeloma, primary hyperparathyroidism, osteogenesis imperfecta, fibrous dysplasia, and other conditions that exhibit bone fragility.

Types

Nitrogenous bisphosphonates

Non Nitrogenous bisphosphonates.

Bisphosphonates are pyrophosphate analogues that bind to hydroxyapatite crystals and inhibit bone resorption. They also alter osteoclastic metabolism, inhibit their activity, and reduce their numbers. They are retained in bone until it is resorbed. Oral absorption of all is poor (especially in the presence of food). Bone formed during treatment is lamellar rather than woven.

Etidronate (Didronel®) (AKAEHDP): reduces normal bone mineralization (especially at doses ≥ 20 mg/kg/d) producing mineralization defects (osteomalacia) which may increase the risk of fracture but which tend to heal between courses [1)].

Contraindicated in patients with kidney failure, osteomalacia, or severe lytic lesions of a LE. 5–10 mg/kg PO daily (average dose: 400 mg/d, or 200–300 mg/d in frail elderly patients) for 6 months, may be repeated after a 3–6 month hiatus if biochemical markers indicate relapse.

Tiludronate (Skelid®): unlike etidronate, does not appear to interfere with bone mineralization at recommended doses. Side e ects: abdominal pain, diarrhea, N/V. 400 mg PO qd with 6–8 ounces

Pamidronate (Aredia®): much more potent than etidronate. May cause a transient acute flu-like syndrome. Oral dosing is hindered by GI intolerance, and IV forms may be required. Mineralization defects do not occur in doses <180 mg/course. 90 mg/d IV×3 days, or as weekly or monthly infusions.

Alendronate (Fosamax®): does not produce mineralization defects.

Clodronate (Ostac®, Bonefos®): 400–1600 mg/d PO×3–6 months. 300 mg/d IV×5 days (may be available outside the U.S.).

Risedronate (Actonel®): does not interfere with bone mineralization in recommended doses [2]. 30 mg PO q d with 6–8 oz. of water at least 30 minutes before the first meal of the day.

Cranial base pathology is a serious complication of osteogenesis imperfecta (OI), and may develop despite bisphosphonate treatment. Early initiation of bisphosphonate treatment may delay development of craniocervical junction pathology. Careful followup of cranial base morphology is warranted, particularly in patients with severe OI [3].

1)
Tiludronate for Paget's Disease of Bone. Med Letter. 1997; 39:65–66
2)
Risedronate for Paget's Disease of Bone. Med Letter. 1998; 40:87–88
3)
Arponen H, Vuorimies I, Haukka J, Valta H, Waltimo-Sirén J, Mäkitie O. Cranial base pathology in pediatric osteogenesis imperfecta patients treated with bisphosphonates. J Neurosurg Pediatr. 2015 Mar;15(3):313-20. doi: 10.3171/2014.11.PEDS14113. Epub 2015 Jan 10. PubMed PMID: 25559924.