Pharmacological therapy of Osteoporosis

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The diagnosis of pediatric osteoporosis requires a history of recurrent low trauma long-bone fractures and low bone mineral density (Z-score < -2) OR a low trauma vertebral fracture alone. Younger patients have the potential to regain bone mineral and reshape vertebral bodies without drugs as they grow if skeletal risk factors can be reduced. None of the osteoporosis drugs used in adults have been FDA-approved for use in children. However, if fragility fractures occur and spontaneous recovery is unlikely, pharmacological therapy is used on a compassionate basis. The ideal treatment would be an anabolic agent like teriparatide but there is a black box warning against its use in pediatrics due to concerns for osteosarcoma. Bisphosphonates inhibit bone resorption by osteoclasts on the bone surface. Reducing bone turnover alone reduces fracture risk. In younger patients, reduced bone resorption during periods of growth can also produce net gains in bone mineral and size.

The optimal bisphosphonate agent and dose are debated. Intravenous agents appear to be more effective than oral agents in reducing vertebral fractures.

- ***Pamidronate (PAM):*** has been used most extensively in doses of 4–9 mg/kg/year divided every 2–4 months for initial therapy.
- ***Zoledronic acid (ZOL):*** newer, more potent drug can be infused more rapidly and less frequently. Typical doses are 0.05–0.1 mg/kg/year divided every 3–6 months.

Duration of therapy: Depends upon the underlying condition.

- Treatment can be discontinued in patients whose underlying disease or risk factors resolve once they are clinically stable for 6–12 months.
- Children with persistent risk factors for bone fragility generally need continuous BP treatment until final height is reached to avoid fractures.
- A "drug holiday" is ***not*** recommended for patients with persistent risk factors or in patients with primary osteoporosis like osteogenesis imperfecta (OI) until adult height is attained.
- The dose is reduced by 50% dose after 2–4 years of therapy to prevent over-suppression of bone turnover.

Side effects: Infusions are generally well tolerated without serious adverse effects.

- A brief acute-phase reaction (including myalgia, bone pain, fever, nausea, and/or vomiting) is common during the first few days after the first dose.
- Transient hypocalcemia, hypophosphatemia, or hypomagnesemia may occur 3 to 5 days after bisphosphonate administration.
- Atypical femur fractures are rare; one retrospective study concluded that the risk of AFF was related to severity of OI and not to bisphosphonate treatment.
- Avascular necrosis of jaw has not been reported in pediatrics.

References:

1. Ward LM, Konji VN, Ma J. *The management of osteoporosis in children.* Osteoporos Int. 2016;27(7):2147–79.
2. Grover M, Bachrach L. *Osteoporosis in children with chronic illnesses: diagnosis, monitoring, and treatment.* Curr Osteoporos rep 2017; 15: 271–282.

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