Teriparatide: A Potential Drug For Osteoporosis.


Introduction

Osteoporosis can be defined as a systemic skeletal disease characterized by low bone mass, microarchitectural deterioration of bone tissue, and increased bone fragility and susceptibility to fracture. It most commonly affects older populations, primarily postmenopausal women. The goal of pharmacological treatment is to maintain or increase bone strength, to prevent fractures throughout the patient's life, and to minimize osteoporosis-related morbidity and mortality by safely reducing the risk of fracture. The medications that have been used most commonly to treat osteoporosis include calcium and vitamin D, estrogen (with or without progestin), bisphosphonates, selective estrogen receptor modulators (SERMs), and calcitonin.

Parathyroid hormone (PTH) has recently emerged as a popular osteoporosis treatment. PTH increases bone mass, which results in greater bone mineral density (BMD). As a PTH derivative, teriparatide has proved effective in increasing bone formation, augmenting bone mass, and reducing fracture rates.

Pharmacodynamics

A strain of *Escherichia coli*, modified by recombinant DNA technology, is used to manufacture teriparatide. The drug contains recombinant human PTH (rhPTH 1-34) and has a sequence that is identical to that of the 34N-terminal amino acids (the biologically active region) of the 84-amino acid human PTH. PTH can initiate bone turnover by the stimulation of osteoclasts. This stimulation results in net resorption of bone or directly activates bone formation by initiating osteoblastic activity.

Pharmacokinetics

Teriparatide is absorbed extensively after subcutaneous injection. Its absolute bioavailability is approximately 95%, and its half-life in serum is approximately one hour when it is given by subcutaneous injection. The metabolism and excretion of teriparatide have not yet been formally studied, but the peripheral metabolism of PTH is believed to occur by nonspecific enzymatic mechanisms in the liver, followed by excretion via the kidneys.

Adverse effects

The FDA has issued a black-box warning because of the drug's association with an increased incidence of osteosarcoma (a malignant bone tumor) in male and female rats. This effect is dose dependent and also on the duration of treatment. The other adverse effects are headache, asthenia, neck pain, hypertension, angina pectoris, syncope, nausea, constipation, dizziness, depression, insomnia, vertigo, hyperuricemia, and hypercalcemia. There is no literature on dermatological and respiratory adverse effects.

Drug Interactions

Teriparatide has no significant drug-drug interactions. But when co-administered at 40mcg teriparatide with intravenous furosemide (20-100), there results a small elevation in serum calcium levels. Teriparatide causes an increase in serum calcium which may predispose patients to digitalis toxicity.

Uses

Treatment of Osteoporosis. Dose-20mcg subcutaneous daily.

Clinical trials

In a study, PTH was a potent stimulator of skeletal dynamics in men with idiopathic, low-bone turnover osteoporosis. In another study it was found that treatment of postmenopausal osteoporosis with PTH decreased the risk of vertebral and nonvertebral fractures; increased vertebral, femoral, and total-body BMD; and was well tolerated. Some have demonstrated that weekly injections of PTH stimulated bone formation in the cortical and trabecular bone, resulting in positive effects on bone mass and bone structure. In other study it was shown that that long term, intermittent treatment with PTH led to the formation of a substantial amount of new bone.

Conclusion

The novel PTH analog, Teriparatide is the newest option for the treatment of postmenopausal osteoporosis. It is effective when used as a single agent and in conjunction with bisphosphonates like...
alendronate to increase bone density. It is well tolerated with the most common adverse being dizziness and leg cramps. Teriparatide has a place in therapy as an alternative treatment for osteoporosis, but no current studies have demonstrated its safety or efficacy after two years of use.

References