Parathyroid Hormone - Current Status

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Parathyroid Hormone (PTH) or its analogues, given by subcutaneous injection once daily, are anabolic agents that directly stimulate osteoblastic bone formation, resulting in substantial increases in trabecular bone density in women with postmenopausal osteoporosis.

It promotes new bone formation, leading to increased BMD. Teriparatide (Rdna Origin) is a biological product containing a portion of human PTH. It acts as endogenous PTH, thus regulating calcium and phosphate metabolism in bone and kidney. It works primarily to stimulate new bone by increasing number and activity of osteoblasts (bone-forming cells). Its additional physiological actions include regulation of bone metabolism, renal tubular reabsorption of calcium and phosphate, and intestinal calcium absorption. When administered with calcium and vitamin D, it increases BMD and decreases risk of fractures in patients with osteoporosis.

Although in primary hyperparathyroidism bone catabolism prevails on bone anabolism, PTH remains a potent stimulator of osteoblasts and its anabolic properties can be seen when it is given at a low dose and intermittently. Intermittent PTH can stimulate bone formation to a greater extent and earlier than bone resorption, thus creating the so called "anabolic window"(1).

Teriparatide is reserved for treating women at high risk for fracture, including those with very low BMD (T-score worse than -3.0) with a previous vertebral fracture. PTH improves BMD and reduces the risk of new vertebral (65%) and nonvertebral (54%) fractures in 2 Years. Patients intolerant to or unresponsive to antiresorptive therapy are the candidates for terparatide. Because PTH improves microarchitecture, mass of bone, it might produce better long-term protection against fracture, when given first and followed by antiresorptive therapy (2,3,4).

In RCTs, daily subcutaneous injections of teriparatide stimulated bone formation and improved bone density in postmenopausal women, regardless of whether they were receiving ET (5). In postmenopausal women with prior vertebral fracture, 19 months of teriparatide treatment (20 µg/d) significantly increased bone density in the spine by 8.6% and in the femoral neck by 3.5% compared with placebo. The incidence of new vertebral fractures was reduced by 65% and new nonvertebral fragility fractures by 53%. Teriparatide is also indicated for the treatment of glucocorticoid-induced osteoporosis and male osteoporosis (6).

Teriparatide is able to reduce the risk of a new fracture in patients with prevalent vertebral fractures, but the same effect is also seen on the incidence of the first fracture in women without fractures at baseline. Moreover PTH produces a continuous increase of bone mineral density, particularly in the cancellous bone. A positive effect of PTH has been described also on fracture healing, consisting both by a shortened time for fracture repair and by improving all the parameters of callus formation and development. In elderly patients with osteoporosis and fractures PTH treatment may reduce the healing time, improve clinical outcomes and reduce the time of immobilization together with the risk of complications of fracture.

When PTH therapy is stopped, substantial bone loss occurs within the first year. However, in RCTs using, alendronate after discontinuing PTH therapy has shown to maintain or improve BMD. Thus, recommendation can be made for treatment with antiresorptive therapy following a course of PTH (7). Teriparatide should not be administered to postmenopausal women with hypercalcemia, bone metastases, disorders that predispose them to bone tumors such as Paget's disease, or those who received prior skeletal irradiation.

From the PG Deptt. of G. Medicine,*Gyan & Obst and **Pharmacology & Therapeutics, Govt Medical College, Jammu J&K- India

Correspondence to : Dr Annil Mahajan, Professsor, PG Department of G Medicine, Govt Medical College, Jammu J&K-India.
Teriparatide 20 microg daily subcutaneously. Dosage requirement of daily subcutaneous injection and high cost the drug may limit its use. However, recently, Weekly s.c. administration of teriparatide at a dose of 56.5 microg has been shown to provide another option of anabolic treatments in patients with osteoporosis at higher fracture risk. It reduce the risk of new vertebral fracture significantly in comparison to placebo but dropout and adverse effects were more in teriparatide group. Thus, currently no recommendations can be given for such different regimens (8). Safety beyond two years is not known and FDA has labeled a black box warning about osteosarcoma. No doubt, it is appealing to consider simultaneous combination therapy with antiresorptive and osteoanabolic drugs as potentially more beneficial than monotherapy with either class, given that their mechanisms of action differ. But simultaneous combination therapy with PTH and an antiresorptive drug does not appear to provide any advantages over monotherapy. Data are inadequate to make definitive recommendations regarding combination or serial antiresorptive and anabolic drug therapy (9,10).

Postmenopausal women with severe osteoporosis receiving glucocorticoid (GC), who are treated with teriparatide for up to 18 months, show a reduced incidence of clinical fractures during the third year (11).

Indian experience with the drug is scanty and in one the preliminary Indian study teriparatide has been shown to be an effective and safe drug in increasing the BMD. Percentage of increase in lumbar spine BMD, is significantly higher in teriparatide group compared to that in control group (6.58% vs. 1.06%). Administration of teriparatide result in a significant increase in all the bone biomarkers in teriparatide group compared to control group patients at 3 and 6 months over baseline (12).

No doubt cost remains a constraint still, teriparatide provides yet another new therapeutic option for reducing the risk of osteoporosis in postmenopausal women.

References