Parathyroid Hormone: A New Treatment Option For Osteoporosis

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**Educational Objectives**
- To outline the basic definition, pathophysiology, treatment, and outcomes of osteoporosis
- To discuss empirical evidence of parathyroid hormone’s effect on osteoporosis
- To discuss the potential value for parathyroid hormone as a new treatment option for osteoporosis in the future

**Abstract**

Current therapies for osteoporosis are limited to antiresorptive agents that act by reducing bone turnover and allowing improved mineralization of new bone. Recombinant human parathyroid hormone (rhPTH) administered in a daily, subcutaneous dose is anabolic for bone, increasing bone volume and replacing lost connectivity. Animal and human clinical trials illustrate dramatic improvements in bone density, architecture, and reduced fracture rates associated with parathyroid hormone (PTH) treatment. PTH’s place in therapy and its optimal dosing regimen remain to be seen.

**Background**

Osteoporosis is the leading metabolic bone disease in adults; it will ultimately afflict about half of all women who reach 65 years of age. The concept of bone remodeling was first proposed by an eighteenth century English surgeon, John Hunter, who recognized that as new bone is laid down in the body, old bone is resorbed. It was not until 100 years later that the term ‘osteoporosis’ was used to describe porous bones. For many years, physicians assumed that this porosity of bones was a natural consequence of aging or immobility. Dr. Fuller Albright, challenged by the observation that bone porosity was more pronounced in older women, made the important connection between estrogen and its ability to promote bone density and strength.1 This was evidenced by the sharp reduction in estrogen at menopause and associated bone loss, and was termed postmenopausal osteoporosis. It was Albright’s mentor, pathologist Jacob Erdheim, who noted that the parathyroid glands were enlarged in patients with osteomalacia, the mineralization defect of bones. When the PTH glands were removed from dogs, the animals had seizures that could be prevented by calcium salt administration. In 1925, the active compound from the parathyroid glands was isolated and named parathyroid hormone.2

The skeleton stores more than 99% of the two to four pounds of calcium in the body. Parathyroid hormone is responsible for keeping the serum calcium level finely tuned so that when blood levels of calcium are low, PTH stimulates the release of calcium from bone into the bloodstream. PTH also increases calcium absorption from the intestines and decreases urinary loss of calcium.3 Regular, continuous doses of PTH promote bone resorption in excess of bone formation and cause severe osteoporosis of hyperparathyroidism.

The mechanism of action of PTH is three-fold. PTH causes an increase the release of calcium from bone, reduced renal clearance of calcium, and an increase in the production of 2-vitamin D-3. Native hormone made by the parathyroid gland chief cells is h(human)PTH-(1-84), a single chain polypeptide with 84 amino acids and a molecular weight of 9425Da. The N-terminal region 1-34 is the biologically active moiety of mineral homeostasis.4 The new anabolic parathyroid hormones contain either the 1-34 fragment, rhPTH(1-34) (LY333334, Forteo)5 or rhPTH(1-84) (Allelix Biopharmaceuticals).6

**Osteoporosis and Bone Remodeling**

Our understanding of osteoporosis has evolved from a primarily quantitative assessment of bone mass and a qualitative analysis of bone architecture, bone turnover, and mineralization. The most recent consensus conference on osteoporosis, sponsored by the National Institutes of Health (NIH), defined osteoporosis as “a skeletal disorder characterized by compromised bone strength predisposing to increased risk of fracture.”7 The negative balance at the basic multicellular unit (BMU) begins in the third decade and progressive skeletal erosion occurs with trabecular thinning and loss of connectivity. With estrogen deficiency at menopause, prolongation of the lifespan of the osteoclast occurs, creating deeper resorptive pits. The reduced mineralization of new bone contributes to the negative qualitative changes.

**Antiresorptive Osteoporosis Therapies**

All current FDA-approved therapies for osteoporosis prevention and/or treatment act by inhibiting bone turnover with a greater suppression of bone resorption than bone formation. The bisphosphonates, alendronate (Fosamax, Merck) and risedronate (Actonel, Procter & Gambel/Aventis) are approved for this use;8 estrogens;9 the selective estrogen receptor modulator (SERM), raloxifene (Evista, Eli Lilly);10 and nasal salmon calcitonin (Miacalcin, Novartis)11 are the other approved antiresorptive agents. These antiresorptive agents reduce the rate of bone turnover so fewer BMUs are activated on the endosteal surfaces of bone. The reduced remodeling slows the rate of bone loss (trabecular and cortical thinning and porosity). By reducing turnover, there is an increase in the mineralization of the existing bone. Although this class of drugs increases bone mineralization, there is no evidence of a positive bone balance or architecturally thickening trabeculae or cortices. In other words, there is no true increase in bone mass. During the course of therapy, these agents will reduce urinary biochemical markers of turnover by 40% to 65%, maintaining an idealized premenopausal bone turnover range. This has often been used as an additional marker for therapeutic efficacy.12

An early anabolic agent, sodium fluoride, was found to increase bone density. Sodium fluoride was used from the 1950s through the 1980s for osteoporosis treatment to prevent fractures.13 Two NIH-
Parathyroid Hormone

Animal Clinical Data

When the skeleton is continuously exposed to exogenous PTH, there is an increase in bone resorption. When PTH is delivered intermit-tently, however, bone formation is stimulated preferential-ly. Selye determined that bovine parathyroid extract, adminis-tered in very small doses, stimulated osteoblast formation in rats and increased bone apposition. In 1974, Niall et al. determined the sequence of the 34-amino acid N-terminal biologically active portion of human parathyroid hormone. Research would no longer be dependent upon bovine or porcine parathyroid gland extracts. Using sequential, short-interval tetracycline labeling, Tam et al. found an increase in dose-dependent stimulation of the bone apposition rate in rats. Intact bovine parathyroid hormone [rbPTH(1-84)] and a synthetic human parathyroid hormone [rhPTH(1-34)] were tested. They confirmed that the 1.34 region of the hormone is responsible for the bone anabolic effect of PTH. They also determined that the anabol-ic effects of PTH that allow it to stimulate the formation of new bone function independent of the resorptive effects of the hormone. Intermittent treatment with PTH increases osteoblast number and bone formation which is thought to be caused by the stimulation of bone-lining cells (osteocytes) on quiescent surfaces of bone, to act as osteoblasts. Daily injections of PTH in mice also decreased osteoblast apoptosis, increasing osteoblast number, bone formation, and bone mass. Daily injections of PTH increased bone apposition rate without an increase in bone resorption, resulting in a net increase in trabecular bone volume. Continuous administration of PTH increased both bone formation and resorption, with a net decrease in trabecular bone volume. Early clinical data using rhPTH(1-34) daily subcutaneous injection in ovariectomized cynomolgus monkeys showed significant bone mineral content increases after six months of treatment relative to placebo. Monkeys were randomized to four groups: 1) sham surgery with vehicle control (Sham), 2) bilaterally ovariectomized (OVX) receiving vehicle, 3) bilaterally ovariectomized receiving 1 mcg/kg PTH(1), or 4) bilaterally ovariectomized receiving 5 mcg/kg PTH(5). Study medication [rhPTH(1-34)] or vehicle was administered daily by subcutaneous injection for 18 months. Compression testing of the third and fourth lumbar vertebrae was performed to obtain yield force and stiffness. Yield force is the maximum load sustained by the specimen for the linear portion of the load-displacement curve. Stiffness was calculated as the maximum slope of the load-displacement curve. The biomechanical indicators of strength (yield force and stiffness) were significantly greater for PTH than for OVX. Yield force and stiffness for PTH1 and PTH5 were significantly greater than for OVX. Yield force for PTH5 was also significantly greater than sham.

Ovariectomy significantly reduced bone strength, whereas rhPTH(1-34) treatment prevented the loss of strength associated with ovariectomy. At the higher dose, rhPTH(1-34) increased strength above levels seen in sham animals. Histomorphometric analysis revealed increased trabecular bone volume and connectivity in both axial and appendicular bone. Active intr trabecular remodeling in vertebral trabecular bone from animals that received 5 mcg/kg/day rhPTH(1-34) is indicated by thickness than normal trabeculae and areas where tunneling appears to have split thickened trabeculae, resulting in an increase in trabecular number.

Human Clinical Trials

Recombinant human parathyroid hormone (rhPTH) (1-34) teriparatide injection is currently under review by the FDA as an anabolic therapy for osteoporosis. It has been shown to increase bone mineral density, connectivity density, biomarkers of turnover and to significantly reduce vertebral and nonvertebral fractures in women and men. The first report of the use of rhPTH(1-34) to treat postmenopausal osteoporosis was by Reeve et al. in 1980 when he reported a four-fold increase in cancellous bone volume after six months of therapy with an average increase of 70% bone volume. These early biopsies showed that trabeculae more than doubled.

In 1997, Lindsay et al. published a study of the effect of (rhPTH) (1-34) teriparatide injection on vertebral bone mass and fracture rate among postmenopausal, osteoporotic women on estrogen. All the women had taken hormone replacement therapy (HRT) for over one year and had been followed for one year to ensure that their bone mineral density (BMD) was stable on HRT. They were randomly assigned to receive either 25 mcg of human parathyroid hormone (1-34) [rhPTH(1-34)] by self-injection plus estrogen or to remain on estrogen alone. HRT was either conjugated equine estrogen (Premarin, 0.625 mg/day) or transdermal estrogen (Estraderm, 50 mcg/day). Bone mass measurements were obtained at six-month intervals during the three-year trial using dual energy X-ray absorptiometry (DEXA). Bone mass in the lumbar spine increased significantly (P<0.001) and continuously throughout the study in the rhPTH(1-34)-treated group. At the end of three years, spine BMD had increased by 13% in the rhPTH(1-34)-treated group, compared with no change in the HRT-alone group. Total hip BMD increased by a modest but significant 2.6% (P=0.05) after three years in the rhPTH(1-34)-treated group, compared to a non-significant decline in the HRT-alone group.

In another study, parathyroid hormone treatment was reported to reverse corticosteroid-induced osteoporosis in 51 postmenopausal women currently taking estrogen and glucocorticoids for more than one year. These women had osteoporosis defined by low bone mass. Subjects were randomly assigned to either 40 mcg of human parathyroid hormone (1-34) [rhPTH(1-34)] plus estrogen (n=28) or to remain on estrogen alone (n=23) for 12 months. The rhPTH1(34) was discontinued at 12 months. BMD testing by DEXA was done at
baseline, 12 months, and 24 months. Lumbar spine BMD increased by 11.8% after 12 months of human parathyroid hormone (1-34) [rhPTH(1-34)] treatment, and was maintained at 11.9% above baseline at 24 months. This included 12 months off rhPTH(1-34) (P<0.001). There were no significant changes in the HRT group. The femoral neck BMD increase of 5.2% was significantly changed from baseline in the rhPTH(1-34) group, but there were no significant differences between treatment groups at this site.31,32

Studies using (rhPTH(1-34) teriparatide injection in 23 men with idiopathic osteoporosis mean age ± SEM, 50 ± 2 years, were randomized to receive 400 IU human parathyroid hormone (1-34) [rhPTH(1-34)] by daily subcutaneous injection (n=10) or vehicle (n=13) for 18 months. Baseline BMD at the lumbar spine or femoral neck was greater than 2.5 SD below the normal young adult mean for men. All men received 1500 mg of calcium and 400 IU of vitamin D daily. BMD was measured by DEXA at six-month intervals. Lumbar spine BMD was significantly increased (P<0.005) by 13.5% above baseline at 18 months in the rhPTH(1-34) group compared to no change in the control group. The lumbar spine bone mineral density mean T-score improved from -3.5 to -2.4. Femoral neck BMD was significantly increased by 2.9% (P<0.05) above baseline at 18 months in the rhPTH(1-34) group, compared to no change in the control group. Bone mineral density at the 1/3 distal radius in the rhPTH(1-34) group declined by 1.2%, a non-significant change compared to baseline.33

The pivotal study assessing the effect of rhPTH(1-34) on vertebral fractures in postmenopausal women was published by Neer and colleagues.34 This was a multicenter, randomized, placebo-controlled trial of 1,637 postmenopausal women with severe osteoporosis who were randomized to 20 or 40 mcg of rhPTH(1-34) or placebo by daily subcutaneous injection. Either two mild vertebral fractures (i.e., a decrease in vertebral height of 20%–25%) or one moderate vertebral fracture (i.e., a decrease in vertebral height of 26-40%) was required for inclusion. The mean duration of observation was 21 months. All patients received 1,000 mg of calcium and between 400 and 1,200 IU/day of vitamin D. Bone density of lumbar spine in the 20- and 40-mcg patient groups increased by 9% and 13%, and femoral neck bone density increased by 3% and 6%, respectively. Total body BMD increased in a dose-dependent fashion with a decrease in radial shaft bone density in the first year of treatment in the 40-mcg dose. Subsequently, the density of the distal radius was not significantly different among the three groups.

New vertebral fractures were reduced from 14% in the placebo group to 5% and 4%, respectively, of women in the 20- and 40-mcg PTH groups. The relative risks for fracture were 0.35 for the 20-mcg dose (95% confidence interval: 0.22–0.55) and 0.31 for the 40-mcg dose (95% confidence interval: 0.19–0.50). No new vertebral fractures were also significantly reduced from 6% in the placebo arm to 3% in each of the parathyroid groups (relative risk: 0.47; 95% confidence interval: 0.25–0.88). The study sponsor, Eli Lilly & Company, chose to terminate the study prematurely because of reports of osteosarcoma developing in a rodent model that was given PTH from birth. In December of 1998, the original study protocol was terminated with follow-up radiographs available on 1,326 of the 1,637 women (81%).

Serious adverse events monitored throughout did not reveal any significant differences among the three groups and specifically there were no cases of osteosarcoma. There were more complaints of headache and nausea in the higher 40-mcg dose. Peak serum calcium levels were monitored four to six hours after injection. Mild hypercalcemia (calcium greater than 10.6 mg per deciliter) occurred in 2%, 11%, and 28% of the placebo group, and in the 20- and 40-mcg dose groups, respectively. Persistent hypercalcemia requiring withdrawal developed in one woman among the 20-mcg dose and placebo groups, and in nine women in the 40-mcg dose group. Although serum 25-hydroxyvitamin D and calcitriol levels were mildly and transiently elevated in the PTH hormone groups, there was no report of significant hypercalcemia. Further investigation into the possible development of bone tumors and hyperparathyroidism, either endogenous or from exogenous therapeutic use, has not corroborated any increased carcinogenic risk.35,36

In another randomized, placebo-controlled fracture endpoint trial of 52 postmenopausal women, Cosman and colleagues reported reduced vertebral fractures in women who received 25-mcg rhPTH(1-34) while receiving hormone replacement therapy.37 After three years, vertebral fractures were reduced from 37.5% in the estrogen-alone group to 8.3% in the combined estrogen and PTH group using a 15% height-reduction criterion for vertebral fracture. In using a 20% height-reduction to fracture criterion, fractures were reduced from 25% in the estrogen-alone group to no fractures reported in the combined group. No hypercalcemia or significant nausea was reported, although the authors did report ‘a large percentage’ of patients having mild discomfort at the injection sites with some erythema lasting less than one hour.

An important component of this trial was continued monitoring of BMD for one year after PTH was discontinued. Bone density measurements remained stable in the women who had previously been treated with the combination of PTH and estrogen, while they continued their estrogen therapy. There was no PTH-alone group. This still begs the question of whether there is PTH withdrawal in a patient who is not continued on any antiresorptive therapy. However, numerous animal studies have been reported in abstract form using either a bisphosphonate, a SERM, or calcitonin antiresorptive therapy after PTH. These studies did show maintenance of the effects of PTH after withdrawal.

Rittmaster and his colleagues treated 66 postmenopausal women with the bisphosphonate alendronate after they had received one year of 50, 70, or 100 mcg of rhPTH(1-84) or placebo.38 Combining all PTH doses, BMD increased from 7.1±5.6% in the lumbar spine, 0.3±6.2% in the femoral neck, and –2.3±3.3% in total body after one year of rhPTH(1-84). All patients received alendronate 10 mg/day in the second year. In patients who were in any PTH group, BMD was increased at all measured sites to 13.4±6.4% at the lumbar spine, 4.4±7.2% at the femoral neck, and 2.6±3.1% for total body. Biochemical markers for both formation and resorption were significantly increased with one year of PTH therapy, but decreased below baseline after one year of therapy with alendronate.

In an alternative dosing combination study with 28-day cycles of 75 mcg rhPTH(1-34) in 30 women with osteoporosis, subjects were randomized to the addition of sequential calcitonin for 42 days immediately following the cycle of rhPTH(1-34) or placebo.39 After three years of these three-month cycles, BMD was not significantly different between the two treatment groups. During the first two cycles, changes in biochemical markers of bone formation (serum total alkaline phosphatase, bone-specific alkaline phosphatase, and osteocalcin) and bone resorption (fasting urinary hydroxyproline and N-telopeptide excretion) were significantly increased over pretreatment values after 28 days of rhPTH(1-34) injections (P<0.05 to P<0.01 for both groups). Even end-of-cycle values remained elevated over the study baseline across time (P<0.01). There were no sig-
nificant differences for any outcome parameter between the two treatment groups. Calcitonin therapy did not appear to attenuate the biomarker elevation.

Biopsy data published by Dempster and colleagues are unraveling the beauty of the true increase in bone seen for the first time with an osteoporosis therapy. In this trial of eight men treated with 40 mcg of rhPTH(1-34) by daily injection for 18 months and eight women on HRT treated with 40 mcg of rhPTH(1-34) for 36 months, trabecular connectivity increased from 2.9 to 4.6 mm³, and cortical thickness as well as cancellous area viewed in three dimensions, were also increased. Because the osteocyte is thought to be the mechanoreceptor for bone, initiating repair as needed, PTH might work in part by preserving the viability of the osteocyte. This could have significant implications for the potential protection against the aging hip and for predisposition to fracture.

The potential for an anabolic agent that truly increases bone volume in an osteoporotic individual is a long-awaited alternative to our current antiresorptive therapies. Many questions remain as to the best way to maximize the efficacy of this potent agent, which will have significant limitations related to its daily subcutaneous administration and high costs associated with recombinant technology. Most studies have been limited to patients with severe osteoporosis, and we await specific guidelines as to the most appropriate patients for initial use of rhPTH(1-34). Clearly, in managing our patients with severe bone loss for whom antiresorptive therapies fall short of bone restoration, we wait expectantly for this new anabolic agent.

References

1. Gordon GS. Fuller Allbright and postmenopausal osteoporosis: A personal appreciati-
2. Li A, J. Colip, AM Hanson and the isolation of the parathyroid hormone, or en-
   ny, pp 1156–1163.
6. Anonymous. ALX 111. ALX 111, PTH, parathyroid hormone (1-84), Allexis, recom-
7. National Institutes of Health Consensus Development Panel on Osteoporosis Pre-
19. Whitfield JF, Morley P, Willick GE. The bone building action of the parathyroid hor-
20. Cosman F, Lindsay R. Is parathyroid hormone a therapeutic option for osteoporo-
25. Jerome CT, Burd DB, Van Biber T, Hock JM, Brommage R. Treatment with human parathyroid hormone (1-34) for 18 months increases cancellous bone volume and im-
27. Lindsay R, Nieves J, Formica C, Henneeman E, Woelfert L, Shen V, Dempster D. Ran-
   domised controlled study of effect of parathyroid hormone on vertebral bone mass and fracture incidence among postmenopausal women on oestrogen with osteo-
28. Lane NE, Sanchez S, Modin GW, Genant HK, Pirisci E, Arnaud CD. Parathyroid hor-
29. Lane NE, Sanchez S, Modin GW, Genant HK, Pirisci E, Arnaud CD. Bone mass con-
   tinue to increase at the hip after parathyroid hormone treatment is discontinued in ghoxiicorticoid-induced osteoporosis: Results of a randomized controlled clinical trial. J Bone Miner Res 2000;15:944–951.
30. Kurland ES, Cosman F, McMahon DJ, Rosen CJ, Lindsay R, Rileskian JP. Parathy-
32. Womers RA, Khesla S, Atkinson EJ, et al. Survival after the diagnosis of hyper-
34. Cosman F, Nieves J, Woelfert L, Formica C, Gordon S, Shen V, Lindsay R. Parathy-
35. Rittmaster, RS, Bolognesi M, Ettinger MP, Hanley DA, Hodsman AB, Kendler DL, Rosen CJ. Enhancement of bone mass in osteoporotic women with parathyroid hor-
   trolled trial to compare the efficacy of cyclical parathyroid hormone versus cyclical parathyroid hormone and sequential calcitomin to improve bone mass in post-
1. The parathyroid hormone maintains calcium homeostasis by all of the following means, with the exception of:
   a. increasing calcium resorption from bone.
   b. reducing renal clearance of calcium.
   c. decreasing hepatic processing of calcium.
   d. stimulating the production of 2-Vitamin D-3.

2. Which statement is correct?
   a. Parathyroid hormone (PTH) given intermittently will increase bone resorption.
   b. The 30-74 region of parathyroid hormone is responsible for its anabolic effect.
   c. Parathyroid hormone given continuously has an anabolic effect on bone.
   d. Intermittent parathyroid hormone stimulates osteocyte production.

3. Intermittent parathyroid hormone therapy has shown to have the following effects on bone:
   a. It will increase thickness of the bone.
   b. It will decrease thickness of the bone.
   c. There is no change in thickness, but bone density increases.
   d. There is no change in thickness, but bone density decreases.

4. Parathyroid hormone is a most promising anabolic agent for:
   a. patients who suffer from hypocalcemia.
   b. patients who suffer from hyperkalemia.
   c. patients who do not respond well to antiresorptive therapies.
   d. patients with multiple, nonvertebral fractures.

5. Which is not a possible FDA-approved treatment option for an osteoporosis patient?
   a. bisphosphonates
   b. hormone replacement therapy
   c. acetylcholinesterase inhibitors
   d. nasal salmon calcitonin

6. According to the NIH, osteoporosis can be defined as:
   a. a skeletal disorder characterized by thinning bones and muscular weakness.
   b. a skeletal disorder characterized by bone mass reduction that alters bone architecture, bone turnover, and mineralization.
   c. a skeletal disorder characterized by compromised bone strength predisposing a person to increased risk of fracture.
   d. a muscular disorder characterized by compromised muscular strength leading to an increased risk of falling and fracture.

7. Current FDA-approved therapies for osteoporosis do NOT act by this mechanism:
   a. increasing mineralization of bone
   b. slowing the rate of trabecular and cortical thinning
   c. increasing bone mass
   d. reducing the rate of bone turnover

8. Two biochemical markers of bone formation are:
   a. serum total alkaline phosphatase and osteocalcin.
   b. serum total alkaline phosphatase and N-telopeptide excretion.
   c. osteocalcin and N-telopeptide excretion.
   d. N-telopeptide excretion and fasting urinary hydroxyproline.

9. Which of the following statements is incorrect?
   a. Niall et al. determined the sequence, used today, of the 34-amino acid N-terminal biologically active portion of human parathyroid hormone.
   b. Neer and colleagues evaluated the effect of parathyroid hormone (1-34) on vertebral fractures in postmenopausal women.
   c. Cosman and colleagues reported reduced vertebral fractures in women who received PTH while receiving hormone replacement therapy.
   d. Early animal data and recent human clinical trials of parathyroid hormone have not shown dramatic improvements in bone density, architecture, or reduced fracture rates.

10. Possible limitations related to treatment with PTH do NOT include:
    a. subcutaneous injection.
    b. recombinant technology.
    c. lack of specific guidelines to determine the most appropriate patients.
    d. lack of improvement in bone density.
Parathyroid Hormone: A New Treatment Option for Osteoporosis

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