Review: Parathyroid hormone increases lumbar spine bone mineral density and decreases vertebral fractures in osteoporosis

Crandall C. **Parathyroid hormone for treatment of osteoporosis.** Arch Intern Med. 2002;162:2297-309.

QUESTION

In patients with osteoporosis, does parathyroid hormone (PTH) increase mineral density (especially of the hip and spine) or reduce the incidence of fractures?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to 2002) and the Cochrane Library, and by reviewing bibliographies of relevant articles.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that evaluated the effectiveness of PTH in patients with osteoporosis.

DATA EXTRACTION

Data were extracted on sample size, demographic characteristics of the patients, details of the interventions, and outcomes. Outcomes included lumbar, total hip, femoral neck, or trochanter bone mineral density and incidence of fractures.

MAIN RESULTS

20 RCTs (2361 patients) met the selection criteria. Types of osteoporosis included postmenopausal osteoporosis (10 RCTs), idiopathic male osteoporosis (2 RCTs), and glucocorticoid-induced osteoporosis (1 RCT). 18 RCTs evaluated human PTH(l-34) administered subcutaneously. Dosages of PTH varied markedly among RCTs. Treatment duration ranged from 6 weeks to 3 years. Comparisons included PTH plus hormone replacement therapy vs hormone replacement therapy alone (5 RCTs), PTH vs placebo (3 RCTs), PTH vs PTH followed by salmon calcitonin (3 RCTs), nafarelin acetate vs nafarelin acetate plus PTH administered intranasally (2 RCTs), PTH plus estrogen vs estrogen (1 RCT), PTH plus alendronate sodium vs alendronate sodium (1 RCT), and PTH plus calcitriol vs calcium (1 RCT). PTH increased lumbar spine bone mineral density in all RCTs at several dosages, for any duration, in different types of osteoporosis, and in combination with multiple agents. PTH also increased femoral neck bone mineral density in 2 RCTs; however, no changes in femoral neck bone mineral density were attributable to PTH therapy in 5 RCTs. At the femoral trochanter, 2 RCTs each reported an increase or no change in bone mineral density with PTH therapy. 3 RCTs reported a detrimental effect of PTH on radius bone mineral density. 2 RCTs (including the largest and highest-quality RCT) reported that PTH decreased the incidence of radiographically detected spinal fractures. 1 RCT (n = 220) that directly compared 3 doses of PTH (15, 30, and 50 µg/wk subcutaneously for 48 wk) reported that increase in lumbar bone mineral density was dose-related (range 0.6% to 8.1%), but there were no changes at the femoral neck with any PTH dosage.

CONCLUSION

In patients with osteoporosis, parathyroid hormone increases lumbar spine bone mineral density and decreases the incidence of vertebral fractures.

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COMMENTARY

PTH is the first Food and Drug Administration–approved agent that stimulates bone formation. According to Crandall's review, many small trials showed that daily subcutaneous PTH increases bone mass and 1 large RCT showed that it reduces fracture risk. The substantial risk reduction with 21 months of PTH resembles that seen with 1 to 2 years of alendronate or risedronate in patients who have osteoporosis (1–4).

Treatment with PTH involves daily self-injections and is expensive. Thus, use of PTH should be limited to patients at high risk for fractures who have ≥ 1 vertebral fracture. The currently approved single 18- to 24-month course of daily PTH may not optimize use of PTH. Less frequent administration and shorter, longer, or repeated courses should be tested in trials to find ways to restore the architecture of bone and, perhaps, reach the previously elusive goal of "curing" patients with severe osteoporosis.

As Crandall points out, the effect of combining antiresorptives and PTH needs study. It makes sense to prescribe an antiresorptive (bisphosphonate or raloxifene) after a course of PTH is finished to minimize the bone loss that eventually resumes after PTH is stopped. 2 controversial questions exist about combinations: 1) Should PTH be used alone or along with antiresorptives? 2) Does PTH effectively build bone in patients who have previously taken alendronate or risedronate? Antiresorptives inhibit bone formation and might attenuate the effect of PTH. Bisphosphonates stay bound to bone and continue to inhibit bone formation for years after treatment stops. Thus, if bisphosphonates inhibit the PTH effect on bone formation, it may be best to give PTH alone before starting bisphosphonates. This would also mean that using PTH in patients who "have not responded" to bisphosphonates may be an ineffective clinical practice. Trials addressing these questions are under way. Stay tuned for answers.

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