# Review: Human parathyroid hormone reduces fractures and increases bone mineral density in severe osteoporosis

Cranney A, Papaioannou A, Zytaruk N, et al. **Parathyroid hormone for the treatment of osteoporosis: a systematic review.** CMAJ. 2006;175:52-9.

**Clinical impact ratings:** GIM/FP/GP ★★★★★★☆ Geriatrics ★★★★★☆☆ Rheumatology ★★★★★☆☆

## QUESTION

In patients with severe osteoporosis, how effective and safe is human parathyroid hormone (hPTH)?

## METHODS

**Data sources:** 5 databases and references of relevant studies and reviews.

**Study selection and assessment:** Randomized controlled trials (RCTs) ≥ 1 year in duration that compared hPTH with placebo or an active comparator in postmenopausal women with osteoporosis or corticosteroid-induced osteoporosis or men with osteoporosis. 12 RCTs met the selection criteria: 9 in postmenopausal women ($n$ = 2709) and 3 in men ($n$ = 543). 10 RCTs evaluated hPTH(1-34) and 2 evaluated hPTH(1-84). Quality assessment of individual studies included allocation concealment, blinding, and follow-up.

**Outcomes:** Fractures, bone mineral density (BMD), back pain, quality of life (QOL), and adverse events.

## MAIN RESULTS

Among postmenopausal women with previous fractures, 1 placebo-controlled RCT found a relative risk reduction (RRR) in new vertebral fractures of 65% (95% CI 45 to 78) with 20 µg/d of hPTH(1-34) and 69% (CI 50 to 81) with 40 µg/d, and an RRR of 53% (CI 12 to 75) in nonvertebral fractures with 20 µg/d. Another RCT comparing hPTH(1-34), 40 µg/d, with alendronate, 10 mg/d, showed a lower rate of nonvertebral fractures with hPTH (4.1% vs 14%, $P$ = 0.042). Most RCTs showed an increase in lumbar spine and femoral neck BMD (Table) and little or no difference in distal radius BMD, although 2 of 3 RCTs in men showed a significant decrease in distal radius BMD with hPTH(1-34) (−1.2% [25 µg/d] to −0.8% [40 µg/d] vs 0.5% [placebo] to 1.0% [alendronate]). 1 RCT that assessed QOL found no difference between hPTH (1-34) and placebo. 3 RCTs reporting back pain found a reduction with hPTH(1-34). Adverse effects of hPTH included hypercalcemia (9 RCTs) and transient hypercalciuria (6 RCTs).

## CONCLUSION

In patients with severe osteoporosis, human parathyroid hormone reduces risk for new vertebral and nonvertebral fractures in postmenopausal women with previous fractures and increases bone mineral density of the lumbar spine and femoral neck.

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**Human parathyroid hormone (hPTH) vs placebo or active comparator for severe osteoporosis at 11 months to 2 years***

| Population | Number of trials | Comparisons | BMD results | |
|---|---|---|---|---|
| | | | LS | FN |
| Postmenopausal women | 6 | hPTH(1-34 vs placebo or active comparator | 6.1% to 14.3% vs 1.1% to 8.9%† | 2.5% to 5.1% vs −1.3% to 3.5%† |
| | 1 | hPTH(1-84) vs placebo | 7.8% vs 0.9% | No difference |
| | 1 | hPTH(1-84) vs alendronate | No difference | 0.93% vs 2.45%‡ |
| Postmenopausal women with corticosteroid-induced osteoporosis | 1 | hPTH(1-34) + HRT vs HRT | 13% vs 1.2% | 4.7% vs 0% |
| Men | 1 | hPTH(1-34) vs placebo | 14% vs 0% | 2% vs 0% |
| | 1 | hPTH(1-34) vs calcium + vitamin D | 9.0% vs 0.5% | 2.9% vs 0.3% |
| | 1 | hPTH(1-3s4) vs hPTH + alendronate or alendronate | 18% vs 7.9% | 9.7% vs 6.2% |

*BMD = bone mineral density; LS = lumbar spine; FN = femoral neck; HRT = hormone replacement therapy. Results favor hPTH unless otherwise noted.
†Range of mean percentage change for the 6 individual trials.
‡Favors alendronate.

## COMMENTARY

Teriparatide (hPTH[1-34]) is the only U.S. Food and Drug Administration (FDA)–approved therapy for osteoporosis that increases bone mass and reduces fracture risk by stimulating osteoblast activity and promoting bone formation, as opposed to bisphosphonates and other agents that inhibit bone resorption. hPTH(1-84) also increases bone mass and reduces vertebral fracture risk, but the fracture data have not been published and hPTH(1-84) is not FDA-approved.

The review by Cranney and colleagues shows that daily administration of hPTH for 12 to 18 months increases bone mass and, among postmenopausal women, reduces vertebral and nonspine fracture risk. The review appropriately points out the limitations of the existing literature—namely, that few trials have fracture endpoints or long-term follow-up, the effects of hPTH on hip fracture are unknown, and the extent and consequences of hPTH-related hypercalcemia and hypercalciuria are not well studied.

The existing data suggest that bisphosphonates or other types of antiresorptive therapy should be given after and not concurrently with hPTH (1, 2). Other studies have suggested that adding PTH to existing bisphosphonate therapy somewhat blunts and delays the anabolic response (3). Contrary to early predictions that it would be particularly useful for patients with low bone turnover, the antifracture efficacy of hPTH seems to be independent of pretreatment bone turnover (4).

Despite the growing evidence that hPTH therapy is safe and effective, there is no clear consensus on how or when to use it in clinical practice. hPTH therapy must be administered by daily subcutaneous injections and is substantially more expensive than bisphosphonates. Thus, it should be reserved for very-high-risk persons with low bone mass and multiple fractures. Formal cost-effectiveness analyses are needed. Future trials should define the optimal duration of hPTH treatment and the utility of repeated cycles of administration.

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***References***

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