Parathyroid hormone decreased fracture rates and increased bone mineral density in postmenopausal women

Neer RM, Arnaud CD, Zanchetta JR, et al. **Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis.** N Engl J Med. 2001 May 10;344:1434-41.

QUESTION

In postmenopausal women with osteoporosis, what is the effectiveness of parathyroid hormone (1-34) (PTH) in decreasing fracture rates and increasing bone mineral density (BMD)?

DESIGN

Randomized {allocation concealed*}†, blinded {clinicians, patients, outcome assessors},*† placebo-controlled trial with median follow-up of 21 months.

SETTING

99 centers in 17 countries.

PATIENTS

1637 postmenopausal women (mean age 69 y) participated. Women were eligible if they were ambulatory, ≥ 5 years had elapsed since menopause, and they had ≥ 1 moderate or ≥ 2 mild atraumatic vertebral fractures on radiography of the thoracic and lumbar spine. Exclusion criteria were illnesses or drugs that affect bone or calcium metabolism, urolithiasis within the previous 5 years, impaired hepatic function, a serum creatinine level > 2 mg/dL, or alcohol or drug abuse. 81% had follow-up radiography.

INTERVENTION

541 women were allocated to PTH, 20 μg/d; 552 to PTH, 40 μg/d; and 544 to placebo, all self-administered subcutaneously once/d.

MAIN OUTCOME MEASURES

New fractures and BMD.

MAIN RESULTS

The study was stopped early by the sponsor. Patients allocated to PTH had fewer new vertebral, new nonvertebral, and fragility fractures than did those allocated to placebo, with no difference between the 40 and 20 μg/d groups (Table). BMD increased with both PTH groups more than with placebo for most skeletal measurements (change ranged from 2.6% to 13.7%).

CONCLUSION

In postmenopausal women with osteoporosis, parathyroid hormone (1-34) decreased new fracture rates and increased bone mineral density.

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*See Glossary.

†Information provided by author.

Parathyroid hormone 20 μg/d (PH-20) and 40 μg/d (PH-40) vs placebo in postmenopausal women with osteoporosis at a median follow-up of 21 months‡

Outcomes	PH-40	PH-20	Placebo	RRR (95% CI)	NNT (CI)
New vertebral fractures	—	5%	14%	65% (45 to 78)	11 (8 to 18)
	4%	—	14%	69% (50 to 81)	10 (8 to 17)
	4%	5%	—	12% (–59 to 51)	Not significant
New nonvertebral and fragility fractures	—	6%	10%	35% (3 to 57)	29 (15 to 438)
	6%	—	10%	40% (10 to 61)	25 (14 to 127)
	5.8%	6.3%	—	8% (–47 to 42)	Not significant

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Neer and colleagues have shown that PTH could be a major advance in treating osteoporosis. Drugs currently approved by the U.S. Food and Drug Administration (FDA) for treating women with osteoporosis (alendronate, risedronate, raloxifene, and calcitonin) decrease bone resorption, whereas PTH stimulates formation of new bone (1–4).

PTH must be given by daily injection and can produce hypercalcuria and transient hypercalcemia. Thus, pending FDA approval, PTH may be valuable for patients who are at high risk for fractures, such as women or men who have had vertebral fractures during treatment with other antiresorptive drugs or who have severe glucocorticoid-induced osteoporosis and vertebral fractures. Treatment should be limited to < 2 years because no long-term effectiveness or safety data exist.

PTH was used alone. Combining PTH with an antiresorptive drug might produce even greater improvements in BMD (5). PTH should at least be followed by treatment with an antiresorptive drug to maintain gains in bone mass.

Is PTH more effective than other approved drugs? The 65% to 69% decreased risk for vertebral fracture with 21 months of PTH use is similar to the 60% to 70% reductions in risk for vertebral fracture seen during the first 1 or 2 years of treatment with risedronate (1), alendronate (2), and raloxifene (6). PTH will be an important advance if trials show that a short course of PTH produces long-term reductions in fracture risk that are greater than can be obtained from long-term use of approved antiresorptive drugs alone.

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