1 year of alendronate after 1 year of parathyroid hormone (1-84) treatment increased bone mineral density in osteoporosis

Black DM, Bilezikian JP, Ensrud KE, et al. **One year of alendronate after one year of parathyroid hormone (1-84) for osteoporosis.** N Engl J Med. 2005;353:555-65.

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

QUESTION

In postmenopausal women with osteoporosis, does 1 year of alendronate after 1 year of parathyroid hormone (1-84) (PTH) maintain or increase bone mineral density (BMD)?

METHODS

Design: Randomized controlled trial (The Parathyroid Hormone and Alendronate [PaTH] study).

Allocation: {Concealed}†.*

Blinding: Blinded {clinicians, patients, data collectors, data analysts, and outcome assessors}†.*

Follow-up period: 24 months.

Setting: 4 clinical centers in the U.S.

Patients: 238 postmenopausal women 55 to 85 years of age (mean age 70 y) who had osteoporosis defined as a T score for BMD < −2.5 at the femoral neck, total hip, or spine; or a T score < −2 at 1 of these sites and ≥ 1 of the following: age ≥ 65 years, history of postmenopausal fracture, and maternal history of hip fracture. Exclusion criteria included bisphosphonate treatment > 12 months or for shorter intervals in recent periods.

Intervention: 1 year of PTH, 100 µg/d subcutaneous injection followed by 1 year of alendronate, 10 mg/d (PTH1–AL2) (n = 59); 1 year of PTH followed by 1 year of placebo (PTH1–Plac2) (n = 60); 1 year of PTH plus alendronate followed by 1 year of alendronate (PTH1+AL1–AL2) (n = 59); or 2 years of alendronate (AL1–AL2) (n = 60).

Outcomes: Change from baseline in areal BMD at the lumbar spine, femoral neck and total hip, and the distal one third of the radius; volumetric BMD in trabecular bone at the spine and hip; and volumetric BMD in cortical bone at the hip.

Patient follow-up: 94% (intention-to-treat analysis).

MAIN RESULTS

At 24 months, BMD at the lumber spine increased in all 4 groups (P < 0.001); the greatest increase was in the PTH1–AL2 group (Table). BMD at the femoral neck and total hip increased in all groups except for the PTH1–Plac2 group (Table). Decrease in BMD at the distal one third of the radius occurred in the PTH1–AL2 and the PTH1–Plac2 group, but not in the other 2 groups (Table). Volumetric BMD in trabecular bone at the spine and the hip increased in all 4 groups, with the greatest increase in the PTH1–AL2 group (Table). Small decreases in volumetric BMD in cortical bone at the hip occurred in all 4 groups (Table). Groups did not differ for clinical fracture and adverse events.

CONCLUSION

In postmenopausal women with osteoporosis, 1 year of alendronate maintains the increase in bone mineral density observed after 1 year of parathyroid hormone treatment.

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*See Glossary.

†Information provided by author.

PTH followed by alendronate (AL) (PTH1–AL2), PTH followed by placebo (PTH1–Plac2), PTH plus AL followed by AL (PTH1+AL1–AL2), and 2 years of AL (AL1–AL2) in osteoporosis at 24 months

Disease sites	Mean change in bone mineral density from baseline			
	PTH1–AL2	(PTH1+AL1–AL2)	AL1–AL2	PTH1–Plac2
Lumbar spine	12%	8%	8%	4%
Femoral neck	4%‡	3%	3%	1%
Hip	4%‡	3%	3%	0
Distal one third of radius	−2%§	−1%§	0‖	−4%
Trabecular bone at spine	31%	11%	6%¶	14%
Trabecular bone at hip	13%	11%	4%¶	4%¶
Cortical bone at hip	−3%	−1%¶	−2%	−3%

‡Increase was significant for PTH1–AL2 vs other 3 groups (P < 0.01). §Decrease was significant for PTH1–AL2 vs PTH1-Plac2 (P = 0.04). ‖Decrease was significant for PTH1–AL2 vs AL1-AL2 (P < 0.001). ¶Not statistically different from baseline values.

COMMENTARY

In this well-designed study, Black and colleagues reported that the increases in BMD observed after 1 year of PTH were lost if therapy was stopped but could be maintained if treatment with PTH was followed by the introduction of alendronate.

When applying these findings to patient care, it is important to consider that the clinically relevant questions of PTH effects in women previously treated with bisphosphonates and how to manage these women after PTH treatment cannot be answered. Furthermore, no fracture data exist and the results may not be applicable to other antiresorptive therapies.

Black and colleagues also addressed whether combination therapy (PTH plus alendronate for 1 y) followed by alendronate for 1 year was superior to other regimens. With the caveat that this study did not include a group treated with PTH alone for 2 years, there was no apparent advantage to combination therapy. Indeed, the effect on BMD may be slightly lower with combination therapy. This suggests that, when prescribing osteoporosis medications, we should use "serial monotherapy": 1 agent at 1 time (1). This approach may enhance drug effectiveness and patient compliance. Long-term adherence is necessary for fracture protection, yet even with once-weekly bisphosphonate regimens, only 50% of patients are still taking the medication at 1 year (2).

This study shows that PTH can increase BMD and is best used as a single agent. When PTH is stopped, bone loss ensues. The degree of fracture reduction, the BMD response to PTH after bisphosphonate therapy, and the BMD response to antiresorptives other than to alendronate after PTH treatment requires further study.

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References

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