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Recombinant Full-Length Parathyroid Hormone (1-84)

A Viewpoint by David A. Hanley

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The need for an 'anabolic' therapy for osteoporosis, which would rebuild the osteoporotic skeleton, is obvious. Animal and clinical studies have demonstrated a pronounced anabolic effect with intermittent subcutaneous injections of the parathyroid hormone agents, teriparatide, the biologically active synthetic fragment of parathyroid hormone and, more recently, full-length human parathyroid hormone (PTH[1-84]).[1,2]

Are bisphosphonates or anabolics best for an individual patient at high risk of osteoporotic fracture? With strong clinical trial evidence of prevention of both vertebral and non-vertebral fractures, the 'antiresorptive' or 'anticatabolic' bisphosphonates, particularly alendronate and risedronate, have come to be regarded as first-line therapy for patients with severe osteoporosis (characterised by very low bone density and typical fragility fractures). In the absence of direct head to head comparison clinical trials, it is impossible to be certain that one drug stands out as being superior to the others. In clinical trials, PTH(1-84) or teriparatide and the bisphosphonates appear to show a similar reduction in relative risk of fracture.

Given the 18–24 month maximum duration of therapy with PTH(1-84) or teriparatide, patients with severe osteoporosis might benefit from sequential therapy – stimulation of new bone formation with PTH(1-84) or teriparatide followed by an anticatabolic agent to preserve the bone gains achieved with the anabolic agent. In the case of PTH(1-84), two clinical trials have shown augmentation or maintenance of the bone density gains when PTH(1-84) therapy was followed by alendronate.

Are there substantial differences between teriparatide and full-length PTH(1-84) as osteoporosis therapies? The clinical trials of the two agents utilised very different patient populations, and since age and prior fracture are major contributors to fracture risk, it is not surprising that the teriparatide clinical trial, with a much higher rate of fracturing, also showed a clear prevention benefit for both vertebral and non-vertebral fractures. Although this is only speculation, I would suspect that younger age and lower fracture rate would be the main reasons why prevention of non-vertebral fractures was not seen in the PTH(1-84) clinical trial. In the major clinical trial of PTH(1-84), there was a higher incidence of hypercalcaemia than in the major trial of teriparatide. This difference may be explained by patients with mild hypercalcaemia being allowed to enter the PTH(1-84) study, a higher equivalent dose, possible longer duration of action (absorption), and perhaps there are subtle differences in mechanism of action.

Parathyroid hormone is a welcome addition to the therapeutic armamentarium in osteoporosis management. Cost and ease of use will probably be major determinants of its acceptance in the medical community. However, for the patient in need of an anabolic agent, PTH(1-84) and teriparatide offer a welcome alternative to existing therapies. ▲

References

1. Hodsman AB, Bauer DC, Dempster DW, et al. Parathyroid hormone and teriparatide for the treatment of osteoporosis: a review of the evidence and suggested guidelines for its use. Endocr Rev 2005; 26 (5): 688-703
2. Hodsman A, Papaioannou A, Cranney A. Scientific Advisory Council of Osteoporosis Canada, Clinical Guidelines Committee, Writing Group on the Systematic Review of Parathyroid Hormone for the Treatment of Osteoporosis. Clinical practice guidelines for the use of parathyroid hormone in the treatment of osteoporosis. CMAJ 2006 Jul 4; 175 (1): 48