METABOLIC BONE DISEASES

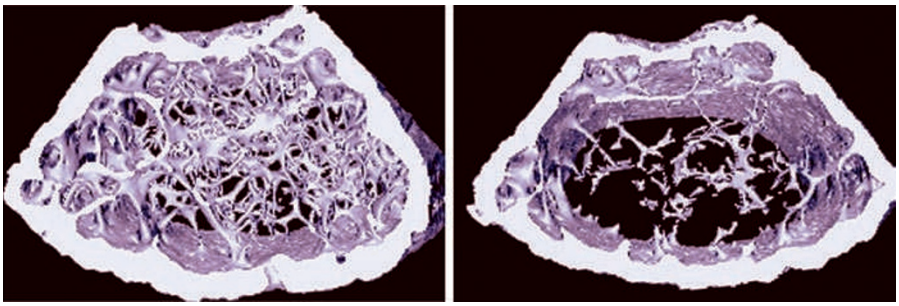
Teriparatide or alendronate for glucocorticoid-induced osteoporosis therapy?

A synthetic form of human parathyroid hormone, teriparatide, is more efficacious than a bisphosphonate for the treatment of glucocorticoid-induced osteoporosis (GIO), according to a multinational study led by Kenneth Saag in the USA. The results, now published in *Arthritis & Rheumatism*, extend the group's previous findings and show that 36 months of teriparatide injections produce considerably greater increases in spine and hip bone mineral density (BMD) than alendronate in patients taking glucocorticoids for at least 3 months.

Glucocorticoids are frequently prescribed for the treatment of autoimmune inflammatory disorders such as rheumatoid arthritis and systemic lupus erythematosus. Prolonged use of these agents, however, is associated with bone loss and an increased risk of osteoporotic fracture. The severe health and economic consequences of such fractures, both to individuals and to society, underscores the importance of prompt and effective management of patients with GIO.

The combination of an oral bisphosphonate, such as the antiresorptive agent alendronate, with vitamin D and calcium supplements comprises the mainstay of therapy for GIO. In an 18-month extension of their previous study, Saag and colleagues now show that teriparatide, a bone anabolic drug, could be more efficacious than alendronate in this setting.

In a double-blind, contolled trial, 428 patients with GIO were randomly assigned to receive 20 μg teriparatide injections per day plus oral placebo or 10 mg per day oral alendronate plus injectable placebo, combined with calcium and vitamin D supplements, for a total of 36 months. In all, 123 patients in the teriparatide group and 118 of those on alendronate completed the trial.



The researchers found that the change in lumbar spine BMD from baseline (the primary outcome measure) was significantly increased with terpirartide compared with alendronate (11.0% versus 5.3%; $P<0.001$). Changes in hip BMD (5.2% for teriparatide versus 2.7% for alendronate; $P<0.001$) and femoral neck BMD (6.3% and 3.4%, respectively; $P<0.001$) were also significantly different between the two groups. In addition, the incidence of new vertebral fractures was lower in the teriparatide group compared with the alendronate group; but no differences were observed between the two groups in the number of nonvertebral fractures.

The investigators also found that serum levels of bone formation markers in the teriparatide group were strikingly higher than baseline throughout the study period. By 18 months, however, these markers began to drop towards baseline levels, which could imply a lack of long-term effect with the agent. Similarly, levels of C-terminal telopeptide of type I collagen (a marker of bone resorption) were also considerably higher than baseline, but only for up to 6 months of therapy. As expected, alendronate was associated with a decrease in all markers of bone turnover.

"These results are impressive," says Johannes Bijlsma, Head of the Department of Rheumatology and Clinical Immunology at the University Medical Center Utrecht in the Netherlands "and they are in line with our knowledge of the pathophysiology of GIO, where reducing osteoblast activity is more important than stimulation of bone resorption". Bijlsma suggests that "an interesting way to take these results forward would be to try and figure out whether the combination of teriparatide and alendronate, preferably in a specific sequence, would be an effective therapeutic approach. For example, using teriparatide in the first 6 months (when bone loss is maximal), followed by 1 year of alendronate, then another period of teriparatide and so on". Given the clear effects of the agent on markers of bone turnover, Bijlsma further suggests that "treatment choices and periods could be guided by serum levels of markers of bone formation and resorption".

Saag and colleagues hope that their results will enhance the future therapeutic management of patients with GIO. "Our findings were submitted to the FDA, and to European and Canadian regulatory agencies, and teriparatide is now approved in the US for the treatment of men and women with GIO at high risk for fracture."

Negin Nassabeh

Original article Saag, K. G. *et al.* Effects of teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis. *Arthritis Rheum.* **60**, 3346–3355 (2009)