THERAPY

Once-yearly therapy is enough to stave off glucocorticoid-induced bone loss

A once-yearly infusion of zoledronate is safe and could be more effective than daily or weekly oral bisphosphonate therapy in the treatment of glucocorticoid-induced osteoporosis, according to new research. Bone loss and an increased risk of fracture are well-recognized adverse effects of long-term therapy with glucocorticoids, and are usually prevented by frequent treatment with an oral bisphosphonate such as risedronate. “Glucocorticoid-induced bone loss occurs in patients who often have multiple pathologies and, therefore, require management with multiple drugs,” explains the study’s lead investigator, David Reid. “Treatment with an additional drug that is required to be taken in a fasting state daily or even weekly can be problematic, potentially leading to poor adherence and compliance. To have an effective medication that could be administered

parenterally and very infrequently could be extremely valuable.”

In a multicenter, double-blind, controlled study, 833 patients (mean age 57.1 years) receiving daily oral prednisolone were randomly assigned to receive one intravenous infusion of the potent bisphosphonate zoledronate (5 mg) followed by daily oral placebo, or a placebo infusion followed by 5 mg daily risedronate, for 12 months. To compare the effects of zoledronate and risedronate on bone loss, the researchers measured changes in bone mineral density (BMD) at the lumbar spine, total hip, femoral neck, trochanter and distal radius at regular intervals from baseline to the end of the study period.

At 6 and 12 months, both agents were associated with increases in BMD at all sites, suggesting that zoledronate is not inferior to risedronate in this respect. Interestingly, however, even after 6 months of therapy, improvements in BMD at the lumbar spine, total hip and femoral neck were significantly greater in most patients who had received the single intravenous infusion of zoledronate than in those assigned daily risedronate therapy, and these differences were maintained at 12 months. Zoledronate also performed better than risedronate in reducing fasting serum levels of β -C-terminal telopeptides of type 1 collagen (β CT_x), a marker of bone resorption, and procollagen type 1 N-terminal propeptide (PINP), a marker of bone formation. Moreover, reductions in the bone turnover biomarkers were apparent far sooner in patients treated with zoledronate than with risedronate, occurring as early as 9 days after the start of therapy. This finding is of potential importance, as fractures associated with glucocorticoid-induced osteoporosis have previously been reported as early as 3 months after starting therapy.

Using a semiquantitative assessment method, the investigators found similar

numbers of new vertebral fractures in both groups—just five in the zoledronate group and three in risedronate-treated patients. “Fractures are the ultimate adverse effect of glucocorticoid-induced osteoporosis,” says Reid. “These were very rare in this study compared with previous work in the field, for example where placebo was compared with risedronate, suggesting that both therapies are effective in preventing this problem.” As the authors point out, however, the increased baseline BMD of patients in this study (owing to a lower mean patient age) compared with the BMD of patients in other trials, as well as differences in the methods used to assess fracture, could have contributed to these results. Adverse events, such as influenza-like symptoms and pyrexia, were significantly more frequent in patients receiving zoledronate than in those receiving risedronate, but only during the first 3 days of treatment, after which the rate was similar in both groups. Of seven recorded deaths (four in the zoledronate group and three in the risedronate group), none was attributed to the study drug.

These findings from a large, well-designed study clearly show that an intravenous infusion of zoledronate is as good, if not better, than risedronate for inhibiting bone loss and preventing fractures in patients taking glucocorticoids. “As zoledronate has now been licensed in the US and Europe for the treatment of glucocorticoid-induced osteoporosis,” says Reid, “it will hopefully soon start being used clinically to avoid osteoporosis associated with glucocorticoid use.”

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