BONE

Bisphosphonates in Paget disease of bone

Intensive bisphosphonate treatment does not confer a clinical advantage over treatment of symptoms alone in patients with Paget disease of bone. Findings from a UK study reveal that maintenance of serum alkaline phosphatase levels within the normal range in patients with Paget disease of bone has no substantial impact on fracture incidence, quality of life, bone pain and need for orthopedic surgery.

Bisphosphonates have been widely used in the treatment of Paget disease of bone for over 30 years, but previous studies have focused on short-term effects on biochemical markers of bone turnover rather than on long-term clinical outcomes.

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Alkaline phosphatase is a recognized marker of metabolic activity in Paget disease of bone. To evaluate whether patients with low serum alkaline phosphatase concentrations as a result of bisphosphonate treatment have a favorable clinical outcome compared with patients who receive only symptom-directed treatment, the group of Stuart Ralston (University of Edinburgh, UK) enrolled 1,324 patients with Paget disease of bone (mean age at diagnosis 66 years), who were followed for 2–5 years. Given that bisphosphonates can alleviate pain, the investigators opted

against a placebo-controlled design. The study participants were randomly assigned to one of two treatment groups: around half were administered bisphosphonates irrespective of symptoms to reduce serum alkaline phosphatase concentrations to within the normal range; patients in the control group did not receive treatment for Paget disease of bone unless they experienced bone pain, in which case analgesics or anti-inflammatory drugs were prescribed, followed by administration of bisphosphonates, if the initial treatment was ineffective.

Alkaline phosphatase levels were notably lower in the bisphosphonate treated group compared with the control group after 4 months of treatment and remained reduced over 3 years of follow-up. No differences between the two treatment strategies were detected for quality of life, fracture rate and the need for orthopedic intervention, as well as the occurrence of adverse events. Most surprisingly, the proportion of patients who experienced bone pain was similar in both study groups. “This means that there is no benefit of normalizing alkaline phosphatase levels in patients with established Paget disease of bone,” says Ralston and adds, “treat the patient, not the alkaline phosphatase level.”

The results highlight the fact that further studies are required to improve the effects of current management strategies on quality of life, adverse events and pain in patients with Paget disease of bone. Ralston and colleagues plan to add to their findings by addressing “early

intervention in presymptomatic people who are genetically predisposed to Paget disease of bone.”

Linda Koch

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