



Drug Information Office / Jordan University of Science and Technology

New Data Linking Bisphosphonates and Atrial Fibrillation

Bisphosphonates are widely prescribed and highly effective at limiting the bone loss that occurs in many disorders characterized by increased osteoclast-mediated bone resorption, including senile osteoporosis in men and women, glucocorticoid-associated osteoporosis, and malignancies metastatic to bone. Although they are generally well tolerated, potential adverse effects may limit bisphosphonate use in some patients.¹

Recent studies have linked the use of intravenous and orally administered bisphosphonates with subsequent development of atrial fibrillation. Patients with cancer who receive intravenous bisphosphonate therapy may be at particular risk for this adverse event because they receive higher doses of these drugs than do patients treated for other indications.²

HORIZON Pivotal Fracture Trial reported that atrial fibrillation has recently been a concern with bisphosphonate use. In this study, a statistically significant increase (relative risk, 1.3% vs 0.5%) in the incidence of serious atrial fibrillation (defined as events leading to hospitalization or disability or judged to be life-threatening) was noted in patients receiving yearly IV zoledronic acid vs placebo.¹

Last year, a meta-analysis including newer studies was published, which showed that the use of bisphosphonates was linked with a greater risk of AF requiring hospitalization. However, this finding may have been due to the IV bisphosphonates, since that route of administration is associated with a stronger release of inflammatory cytokines. Previous studies that examined oral and IV bisphosphonates separately have reported contradictory findings. Therefore, the researchers performed a systematic review and meta-analysis of published studies to evaluate this.³

They identified five randomized controlled trials, which compared IV zoledronic acid and oral alendronate and risedronate vs placebo. They also identified four observational studies that examined IV zoledronate and pamidronate, as well as oral alendronate, clodronate, etidronate, ibandronate, and risedronate. There were a total of 135 347 patients.³

They find that both oral and IV bisphosphates were associated with a significantly increased risk of new-onset AF. The risk was greater with the IV drugs.³

Although this meta-analysis was large enough to capture rare events, it has several limitations. They did not have detailed information about baseline cardiovascular risk factors and concomitant medication use, and the original studies were too small to see effects from individual drugs. As well, the randomized trials used in the analysis were not specifically designed to determine risk of AF with bisphosphonates.³

The conclusion, prospective randomized data are needed to further evaluate the risk of AF with bisphosphonate therapy and to determine whether the association is a 'class' effect or is dependent on specific drugs.

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