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CHEST: Bisphosphonates May Increase Risk of Atrial Fibrillation

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PHILADELPHIA, Oct. 27 -- For patients who have osteoporosis, the use of bisphosphonates appears to increase the risk of serious atrial fibrillation, according to a meta-analysis.

The risk of atrial fibrillation leading to hospitalization or death was 68% greater in patients taking alendronate (Fosamax) or zoledronic acid (Reclast, Zometa) than in those taking placebo (OR 1.66, 95% CI 1.23 to 2.24), Jennifer Miranda, M.D., of the University of Miami in Florida, reported at the American College of Chest Physicians meeting here.

Patients taking the osteoporosis medications tended to be more likely to have atrial fibrillation of any severity, but the difference did not reach statistical significance (OR 1.19, 95% CI 0.97 to 1.47).

Action Points

- Explain to interested patients that this meta-analysis found that the use of two commonly used osteoporosis medications was associated with an increased risk of atrial fibrillation, resulting in hospitalization or death.
- Point out that the FDA has not recommended modifying prescribing practices for bisphosphonates.
- Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.

"In patients with increased risk factors, clinicians should be more cautious when choosing treatment for osteoporosis and weigh the risks against the benefit of decreased fracture risk," Dr. Miranda said.

The gastrointestinal side effects of bisphosphonate therapy have been well documented, according to Dr. Miranda, but little is known about potential cardiovascular risks.

Atrial fibrillation has been reported previously as an adverse event in clinical trials involving alendronate and zoledronic acid. (See: [Osteoporosis Drug Elevates Atrial Fibrillation Risk](#) and [Once-a-Year IV Drug Scores for Postmenopausal Osteoporosis](#))

Those studies, combined with post-marketing reports, alerted the FDA to the potential link, prompting an ongoing safety review.

The agency did not recommend, however, that physicians modify their prescribing practices or use of bisphosphonates.

To explore the connection with atrial fibrillation, Dr. Miranda and colleagues performed a literature search and identified three randomized controlled trials comparing bisphosphonates with placebo that reported atrial fibrillation as an adverse event.

Two of the studies evaluated zoledronic acid and one examined alendronate.

The researchers did not find any evidence of publication bias.

The studies comprised 16,322 patients with a mean age range of 69 to 74.5. Most of the patients (76% to 100%) were female.

Mean body mass index ranged from 24.7 to 25.3 kg/m² and mean bone mineral density at the femoral neck ranged from 0.53 to 0.65 g/cm².

Overall, 3% to 4% of patients taking bisphosphonates had atrial fibrillation; it was classified as serious in 1% to 2%.

The odds of having any degree of atrial fibrillation were not significant for any of the individual studies or in the pooled analysis.

Dr. Miranda said that the mechanism behind the link between bisphosphonates and atrial fibrillation remains unclear and needs to be elucidated in further studies along with the population most at risk and the impact of the association.

Detailed cardiovascular risk factors were not consistently reported across studies, she said.

"It was interesting that the incidence of new atrial fibrillation was not significantly different but the incidence of more complicated or symptomatic events related to atrial fibrillation that caused hospitalization was," commented David Gutterman, M.D., of the Medical College of Wisconsin in Milwaukee, past chair of the health and science policy committee of the ACCP.

"So it makes one wonder whether or not the heart rate was much faster in those on bisphosphonates, and that might be why they develop more symptoms [of atrial fibrillation]," he said.

Dr. Miranda acknowledged that the study was limited by the exclusion of foreign-language studies and the small number of studies reporting atrial fibrillation as an adverse event.

Dr. Miranda made no financial disclosures.

Primary source: CHEST 2008

Source reference:

Miranda J, et al "A meta-analysis of the risk of atrial fibrillation in bisphosphonate users" *CHEST* 2008; 134: s1002.

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