Antiresorptives May Decrease Fracture Risk in Older Women

Montreal — Antiresorptive drugs help reduce the risk of low-trauma, nonvertebral fractures among women over 50, according to a Canadian case-control study presented at the annual meeting of the International Bone and Mineral Society.

Women with a prevalent fracture or with frank osteoporosis appeared to have most to gain from these drugs in terms of fracture risk reduction. Dr. Suzanne Morin of McGill University in Montreal, and her colleagues, obtained data from the Canadian Multicentre Osteoporosis Study (CaMos), in which more than 6,000 women over the age of 50 were randomly selected from organizations across Canada for follow-up. They focused on prevalent fractures and developed a standardized interview that addressed demographic risks and medical history. They also conducted measurement of their bone mineral density (BMD).

According to the researchers, an estimated 1 in 100,000 patient-treatment years. This means that continuation of alendronate for 10 years does maintain bone mass and reduces bone remodeling, compared with placebo during years 5-10 had a slight increase, and women on alendronate had a steeper increase in spine bone density, relative stabilization of femoral-neck bone density, and a relative stabilization of spine bone density during the 2-year extension of the trial that was designed to run 3 years. During the 2 years of the extension, women on risedronate had more than a 50% reduction in vertebral fractures, compared with women who stopped therapy. Fewer data are available for ibandronate. In a 3-year study of almost 3,000 women, the incidence of new vertebral fractures in women on oral daily ibandronate (2.5 mg) was 11%, compared with 6% for women in the placebo group (Bone 2005;31:631-4).

There are potential concerns with long-term bisphosphonate therapy, said Dr. Khosla. One important question is whether the continued and potent inhibition of bone turnover could be harmful because of the increased mineralization of bone that has been observed in animal models. There is also concern about the accumulation of microdamage. “Here, the thought is that because bone constantly needs to repair microcracks and microfractures, if you inhibit resorption for long periods of time, these microcracks will accumulate, and you can start to see a paradoxical increase in fractures in various sites because you haven’t repaired the skeleton normally,” said Dr. Khosla.

Animal and human studies do show that bisphosphonate-induced inhibition of bone resorption is associated with increased bone mineralization. Increased bone mineralization does increase bone strength, but only up to a point because bone also becomes too stiff.

However, despite the results of animal studies with high doses of bisphosphonates, there is no evidence in humans for increased accumulation of microdamage. “This is a theoretical concern,” said Dr. Khosla.

Another major concern has been the association between bisphosphonate use and jaw osteonecrosis. “This is a very feared complication of long-term bisphosphonate therapy,” said Dr. Khosla. “This is something that is just coming to (our) attention. I haven’t quite figured out how to deal with it.”

The exposed bone that is the hallmark of jaw osteonecrosis occurs in other conditions, sometimes confounding diagnosis. “Many patients go back from their dentist and say ‘I have jaw osteonecrosis’ when they’ve just had a tooth removed,” said Dr. Khosla. “The estimate is that about 100 patients a year develop jaw osteonecrosis from bisphosphonates, but the number of jaw osteonecrosis patients is more than 100,000. There is a difference in the way that bisphosphonates affect bone compared with other conditions.”

Animal and human studies do show that bisphosphonates, whether given via the oral or IV route, lead to changes in bone turnover. jaw osteonecrosis doesn’t occur with corticosteroids, but it does occur with bisphosphonates. Biphosphonates affect bone turnover, the head, hands, feet, jaw, and can lead to osteonecrosis of the jaw.”

Although data on jaw osteonecrosis associated with oral bisphosphonate use are limited, it’s estimated that the risk is somewhere between 1 in 10,000 and less than 1 in 100,000 patient-treatment years. “This may be an underestimate because of underreporting,” said Dr. Khosla. “The estimate may also be low because the risk is associated with cumulative exposure, and this complication will become more common with more patients on oral bisphosphonates for longer periods.”

It’s clear that the risk of jaw osteonecrosis in patients with cancer, treated with high doses of intravenous bisphosphonates, is higher, said Dr. Khosla. In these patients, the risk is estimated to be 1-10 per 100 patients.

“I think that all we can do as physicians is provide information and factor in the patient’s values. I don’t think as a physician you can completely leave the decision to the patient. They get bewildered.”

—Alison Paikhivala