

UPDATE ON OSTEOPOROSIS MEDICATION

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Recent reports that the most popular anti-osteoporosis drug causes an unusual type of fracture have left people scrambling for options. But is the concern justified?

The concern: Some people who have taken alendronate (Fosamax) for several years have incurred an unusual type of leg fracture with minimal provocation. Breaks at the hip (not below it) account for the bulk of femur fractures, but these people are fracturing the shaft of the femur just below the hip.

The facts: The incidence of these sub-hip fractures is low. A review of trials involving all bisphosphonates, alendronate's drug class, found only 12 such fractures in 10 women, a rate of 2.3 per 10,000 women per year.

Sub-hip femur fractures afflict women not on bisphosphonates too. Sub-hip femur fractures account for 2-4% of all hip/upper femur fractures, with only one-third of those occurring in women taking the drugs.

Between 1986 and 2005 the average annual yearly number of hip fractures was about 95.7 per 10,000 women and 41.4 per 10,000 men. But within that time there was an increase of fractures in both sexes until 1995, after which the rate declined. The reduction after 1995 coincides with widespread use of bisphosphonates.

Hip fracture risk: Twenty to twenty-five percent of people die in the year following their hip fracture. The risk is greatest in the first three months, usually from pulmonary embolism (blood clot in the lung) or surgery complications. The risk tapers with time but still exceeds that for non-hip fracture people for three years after the fracture. Reduced mobility leads to pneumonia, worse diabetes, heart attacks, stroke and skin infections.

So people must decide if they want to stop a drug that prevents a common type of fracture in order to avoid the side effect of a rare fracture, both of which have the same potentially devastating health effects.

The mechanism: Why would a drug to prevent fractures cause unusual fractures? Bisphosphonates retard bone loss due to aging and medications. To some extent they stimulate bone calcium deposition. But the bone that bisphosphonates builds is not entirely normal – Increased calcium shows up on bone scans as an improvement, but the underlying bone matrix, to which calcium binds, is slightly more brittle than normal bone.

Bone is basically a protein lattice to which calcium and phosphate are attached. In osteoporosis both the lattice-matrix and calcium disappear, leaving something akin to Swiss cheese. We don't yet have a drug that fills in the holes with perfectly normal protein matrix and mineral.

Other side effects. Bisphosphonates have other side effects. They may cause erosion of the esophagus in people who have reflux or do not take the drug according to directions. They drive calcium into bone and may cause low blood calcium levels if you do not get enough from your diet and supplements. They (rarely) induce bone erosion (osteonecrosis) in the jaw. They may cause severe allergic reactions, gastrointest-tinal upset, with nausea, vomiting, heartburn, mouth sores, diarrhea, loss of appetite or pain, psychological issues like insomnia, depression or agitation, chest pain, irregular heartbeat, bleeding, gum and teeth problems, vaginitis or flu-like symptoms. Do they cause these side effects in everyone? No, but they increase their risk.

The reason that doctors still prescribe them is that these drugs do drastically reduce the overall risk of hip and spine fractures. Fosamax was the original drug, and risidronate (Actonel), ibandronate (Boniva, used monthly), zoledronic acid (Reclast, used yearly) and amidronate (Aredia, used only to lower high calcium levels in cancer patients) followed.

Alternatives: There are other medication alternatives, like raloxifene (Evista) and calcitonin nasal spray (Miacalcin). Calcium (about 800mg/day from food and supplements) and vitamin D (with a goal level of 35-100 ng/ml) are necessary but not sufficient to make strong bone. Lifestyle makes a difference. Daily, heavy, weight-

bearing exercise tells bone to stay strong – This could take the form of weight lifting, moving around an obese body, carrying heavy packages, or doing heavy lifting. The best diet is one that contains enough protein and calories to make protein matrix.

The new bisphosphonate: Zoledronic acid (Reclast and Zometa) is the newest approved bisphosphonate. Its advantage is its once a year administration by injection. Taking it by vein avoids irritation and ulceration of the

esophagus, but it is not free of the other bisphosphonate side effects. It may cause severe bone, muscle, back, head or joint pain which may start weeks or months after receiving the injection. It interacts with a variety of medications.

Theoretically this bisphosphonate's side effects might persist longer than those of the others, because it hangs around in the body so long. For some it works well. Others have side effects for months.