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Drugs to Build Bones May Weaken Them

By TARA PARKER-POPE

New questions have emerged about whether long-term use of bone-building drugs for osteoporosis may actually lead to weaker bones in a small number of people who use them.

The concern rises mainly from a series of case reports showing a rare type of leg fracture that shears straight across the upper thighbone after little or no trauma. Fractures in this sturdy part of the bone typically result from car accidents, or in the elderly and frail. But the case reports show the unusual fracture pattern in people who have used bone-building drugs called bisphosphonates for five years or more.

Some patients have reported that after weeks or months of unexplained aching, their thighbones simply snapped while they were walking or standing.

“Many of these women will tell you they thought the bone broke before they hit the ground,” said Dr. Dean G. Lorich, associate director of orthopedic trauma surgery at NewYork-Presbyterian/Weill Cornell and the Hospital for Special Surgery. Dr. Lorich and his colleagues published a study in The Journal of Orthopaedic Trauma last month reporting on 20 patients with the fracture. Nineteen had been using the bone drug Fosamax for an average of 6.9 years.

Last year, The Journal of Bone and Joint Surgery published a Singapore report of 13 women with low-trauma fractures, including 9 who had been on long-term Fosamax therapy.

The doctors emphasize that the problem appears to be rare for a class of drug that clearly prevents fractures and has been life-saving for women with severe osteoporosis. Every year, American adults suffer 300,000 hip fractures.

Merck, which makes Fosamax, says it will study whether the unusual fracture pattern is really more common in bone-drug users. Arthur Santora, Merck’s executive director for clinical research, noted that the fracture accounted for only about 5 or 6 percent of all broken hips, while drugs like Fosamax reduced the risk for the other 95 percent.

The fracture pattern did not emerge in placebo-controlled studies of bone drugs. But those studies have lasted only three to five years, although follow-up studies of the drug users have lasted longer. Now that the fracture pattern has been identified, researchers expect more doctors to publish reports.

“I have several similar patients myself,” said Dr. Susan M. Ott, associate professor of medicine at the University of Washington. “Prior to these recent articles, there were a few cases here and a few cases there, but they are kind of starting to add up.”

Bones are in a constant state of remodeling — dissolving microscopic bits of old bone, a process called resorption, and rebuilding new bone. After age 30 or so, a woman’s bones start to dissolve faster than they can be rebuilt, and after menopause she may develop thin, brittle bones that are easily broken. Bisphosphonates, including Fosamax, Procter & Gamble’s Actonel and GlaxoSmithKline’s Boniva, slow this process.

But some experts are concerned that microscopic bone cracks that result from normal wear and tear are not repaired when the bone remodeling process is suppressed. A 2001 study of beagles taking high doses of bisphosphonates found an accumulation of microscopic damage, though there was no evidence that their bones were weaker.

Last September, the medical journal Bone reported on a study of 66 women, financed by Eli Lilly, that showed an association between Fosamax use and an accumulation of microdamage in bones.

In January 2006, the medical journal Geriatrics published an unusual autobiographical case report. Dr. Jennifer Schneider, a 59-year-old physician from Tucson, wrote that she was riding a New York City subway when the train

lurched. “I felt a crack and I fell,” she recalled in an interview. “I knew I’d fractured my femur.”

Dr. Schneider, who had been taking Fosamax for seven years, said she had had pain in her thigh, but X-rays and scans had not found a problem.

In recent years, another rare side effect has been associated with bone drugs: osteonecrosis of the jaw, in which a patient’s jawbone rots and dies. Most victims are cancer patients taking a potent intravenous form of the drug, but a small number of cases from ordinary users have been reported.

Notably, studies suggest there is little extra benefit in taking the bone drugs more than five years. Dr. Lorich says that doctors should monitor the bone metabolism of long-term users and that some patients may want to consider taking time off the drugs. When fractures do occur, surgeons need to be alerted about long-term drug use, because the fracture may require more aggressive treatment and be slower to heal.

Dr. Ott says the focus should be on using bone drugs only in patients with a fracture risk of at least 3 percent over the next 10 years. (An online fracture risk tool is at www.shef.ac.uk/FRAX.)

“Too many of these people are not getting adequate treatment that definitely is beneficial,” Dr. Ott said. “My major caution is that the bisphosphonates should not be used in people who don’t have a high risk of fracture.”

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