

Diabetes Drug Avandia Could Weaken Bones

Mouse study suggests it boosts production of bone-eroding cells



By Amanda Gardner
December 2, 2007

Avandia, a drug used by millions of diabetes patients, may contribute to bone loss, according to a new study conducted in mice.

Experts fear that, over the long term, Avandia (rosiglitazone) may speed osteoporosis, the thinning of the bones that can lead to dangerous and even fatal fractures.

The findings appear in the Dec. 2 online issue of Nature Medicine.

"Our study suggests that long-term rosiglitazone usage in the treatment of type II diabetes may cause osteoporosis due to both increased bone resorption and decreased bone formation," said study senior author Ron Evans, a professor at the Salk Institute for Biological Studies in La Jolla, Calif. "Because Avandia is effective in controlling glucose and restoring the body's sensitivity to insulin, we do not recommend that people stop their treatment. You must balance the benefits against the complications."

"Anyone who is already at risk for osteoporotic fractures should consider an alternative anti-diabetic drug," added Paul Brandt, an associate professor of neuroscience and experimental therapeutics at Texas A&M Health Science Center College of Medicine, in College Station. "There are many alternatives," he said.

"It may [also] be possible to blunt some of Avandia's effects with anti-osteoporosis drugs such as bisphosphonates, raloxifene, vitamin D and calcium," Brandt added.

Earlier this year, Avandia and four other diabetes drugs from the same class were given a "black box" warning by the U.S. Food and Drug Administration. That warning advises users of an increased risk of heart failure while on the drug.

The black box message is the FDA's strongest label warning.

With an estimated 3.5 million or more U.S. patients taking Avandia, the public health impact from the point of view of both heart failure and bone degradation could be substantial, experts say.

Avandia affects a key cellular protein called the peroxisome proliferator-activated receptor (PPAR-gamma). In their study, the California team discovered that, in mice, activating this receptor also stimulates the production of osteoclasts, cells whose key function is to degrade bone.

Proper bone health is maintained by a balance between osteoclasts and osteoblasts, the cells that build bone up.

If either side is out of whack, so to speak, bones become thinner, more fragile and prone to fracture.

The current results are particularly disturbing in light of prior studies, the experts said.

"It was previously known that Avandia mediates bone loss by inhibiting bone formation," Evans explained. "Our work identified an additional mechanism, in which Avandia promotes bone resorption. These are the two parts of the checks-and-balance system that maintains bone in good shape. The drug weakens both sides of the balance mechanism, leading to an increased risk for osteoporosis."

"Previous research showed that Avandia reduced osteoblasts," Brandt added. "Combine the two, and you're going to get thinning of the bone."