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Diabetes Health Center

More Evidence Links Fractures to Diabetes Drugs

Avandia, Actos Boost Fracture Risk in Older Women, Study Finds

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July 29, 2010 -- The popular [diabetes drugs](#) Actos and Avandia boost the risk of fracture in older women, according to findings from a new study that echo those of earlier research.

For the new study, researcher William H. Herman, MD, MPH, professor of medicine and epidemiology at the University of Michigan, Ann Arbor, evaluated a large database of managed care patients who had diabetes. He found that those who suffered [fractures](#) were more likely to be taking the class of drugs known as TZDs (thiazolidinediones), such as Actos and Avandia.

The fracture risk he found, Herman tells WebMD, was primarily among postmenopausal women, who already tend to have lower bone density. "Diabetic women over 50 with fractures were 70% more likely to be taking a TZD drug than women without fractures," he says.

The study is published online in the *Journal of Clinical Endocrinology & Metabolism*.

"A lot of the focus [with this class of drugs] has been on cardiovascular risk," Herman tells WebMD. Recently, an FDA advisory panel voted to keep the drug Avandia, linked with a higher risk of death and cardiovascular problems in older patients, on the market, but with stronger warnings.

But Herman notes that the side effect of fractures is also important to examine. "Fractures do have a major impact on quality of life," he says.

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Diabetes Drugs and Fracture Risk: A Closer Look

In the new study, Herman and his colleagues used data from a large study known as TRIAD, identifying 786 cases of fractures and comparing them to 2,657 patients who had diabetes but no fracture history.

Of the 786 patients with fractures, only 54 were women less than 50 years old, while 457 were women 50 and older and 275 were men.

The researchers looked at [prescriptions](#) participants had filled during the 90 days prior to the fracture date or 90 days before a designated study date for those without fractures.

The finding that women with fractures were much more likely to be taking a TZD drug held for both Avandia and Actos, they found. "So it seems to be a class effect," Herman says.

The higher the dose, the higher the fracture risk, they found.

Among the men, only those taking a TZD along with a potent diuretic, called a loop diuretic, were more likely to have a fracture. Taking TZD alone did not appear to increase risk in men.

Loop diuretics have been linked with bone density decreases, Herman says.

Why the TZD drugs boost fracture risk may be due to effects such as the reduction of new bone formation or increased bone breakdown, he says.

The fractures found, he says, "are not typical osteoporosis fractures," which include those of the spine and hip. They found some spine and hip fractures, but also many lower limb, arm, and leg fractures.

The study was funded by the CDC and the National Institute of Diabetes and Digestive and Kidney Diseases. Herman has served as a consultant for GlaxoSmithKline, which makes Avandia.

Diabetes Drugs and Fractures: Diabetes Expert View

The study does add to existing information about diabetes drugs and fracture risks, says David Kendall, MD, chief scientific and medical officer of the American Diabetes Association, who reviewed the study for WebMD.

"This is certainly not the first of these larger studies where I would say this unanticipated event was noted," says Kendall, also an associate professor of medicine at the University of Minnesota, Minneapolis.

"Depending on the study, it appears that people who take TZDs for longer periods of time have about a one-and-a-half to twofold increase in their risk of fractures," he says.

Even so, he says, "These are very effective medicines for some patients. We have to understand there are potential risks. Certainly anyone already considered to be at fracture risk -- a woman with osteoporosis -- or someone who suffers from instability or frequent falls, you should think carefully about the use of the medications. On the other hand, fractures in total [in Herman's study] were generally rare. Far more people didn't have fractures than did have."

In sum, he says, the study finding "is a new piece of information that needs to be taken into consideration when evaluating the potential benefits and risks of your [diabetes treatment](#) regimen."

Diabetes Drugs and Fractures: Industry View

Earlier studies have found the same increased risk for fracture, says Mary Anne Rhyne, a spokeswoman for GlaxoSmithKline, which makes Avandia. "Currently the label for Avandia contains a warning/precaution regarding the risk of fractures with Avandia, usually occurring in the hand, upper arm, or [foot](#), in females. The label further encourages patients to speak with their doctor for advice on how to keep bones healthy."

Ongoing studies may shed more light on the link, Rhyne says.

Takeda Pharmaceuticals, which makes Actos, is conducting a study to examine and better understand the issue of fractures while on the drug, says Elissa Johnsen, a spokeswoman.

The company analyzed the entire database of the Actos clinical trials, she says, and did find increased reports of fracture in women taking Actos compared to comparison groups, but found no increase in fracture risk in men taking Actos. This information is included in the drug's prescribing information, she says.

Diabetes Drugs and Fracture Risk: Take-Home Advice

Those with diabetes on TZD drugs "should not stop these medicines without talking to their doctor," Herman says.

While he found an increased fracture risk with the drugs, he says, it's not known if treating patients with the bone-builder drugs can decrease the risk.

Until more is known, he says, "in a woman over 50 with diabetes and known osteoporosis, these drugs should be used with caution if at all."

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David Kendall, MD, chief scientific and medical officer, American Diabetes Association; associate professor of medicine, University of Minnesota, Minneapolis.

Mary Anne Rhyne, spokeswoman, GlaxoSmithKline.

Bilik, D. *Journal of Clinical Endocrinology & Metabolism*, online July 29, 2010.

Elissa Johnsen, spokeswoman, Takeda Pharmaceuticals North America Inc.

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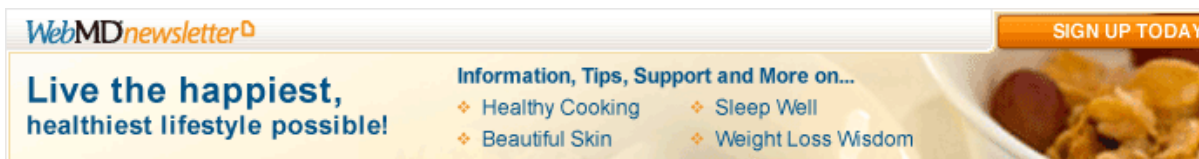
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