Thiazolidinedione Use Linked to Increased Fracture Risk

BY MITCHEL L. ZOLER

NEW YORK — Treatment with a thiazolidinedione, either pioglitazone or rosiglitazone, has been linked to an increased rate of bone fractures, particularly in women, in several recently published reports.

Although a definitive link between these drugs and an increased fracture risk has not yet been proven, the evidence amassed so far is suggestive enough to prompt caution in the treatment of patients with type 2 diabetes (T2D), Dr. Robert G. Josse said at a meeting sponsored by the American Diabetes Association.

“In those with a higher fracture risk, consider other hypoglycemic therapy,” advised Dr. Josse, professor of medicine and nutritional sciences at the University of Toronto and medical director of the department of medicine at the osteoporosis center at St. Michael’s Hospital in Toronto.

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In another study, published last May, randomized 30 postmenopausal women with polycystic ovarian syndrome but without diabetes to treatment with either 30 mg pioglitazone daily or placebo. The women treated with pioglitazone had significantly lower lumbar spine and femoral neck density, compared with the controls.

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When the analysis broke the study population down by gender, a statistically significant 2.2-fold increased fracture risk was seen in women treated with a TZD, but absolutely no increased risk was seen in men.

Additional analysis by sex showed that, in women, TZD treatment was linked with significant reductions of bone mineral density in the lumbar spine and hip. The two observational studies also showed a significant link between TZD use and fracture risk in women, but not in men.

The two short-term, randomized studies included a study with 50 healthy postmenopausal women without osteoporosis, patients with diabetes who were randomized to treatment with 8 mg rosiglitazone daily or placebo for 14 weeks. Despite the brief period of treatment, the women in the rosiglitazone-treated group had a statistically significant reduction in their total hip bone mineral density, compared with the placebo group (J. Clin. Endocrinol. Metab. 2007;92:1051-10).

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The TZD-treated women also showed significantly decreased blood levels of bone-turnover hormones and enzymes.

Dr. Josse reported receiving research support from, and serving on the speakers bureau and advisory panel for, several companies including Agen Inc., Eli Lilly & Co., Procter & Gamble Co., and Sanofi-Aventis.