BONE

Thiazolidinediones increase fracture risk

Patients with type 2 diabetes mellitus (T2DM) treated with thiazolidinediones to improve glycemic control could be at an increased risk of fractures, according to a prospective study published in the *Archives of Internal Medicine*. The findings also indicate that pioglitazone treatment may pose a greater risk for fractures than use of rosiglitazone.

Patients with T2DM have an increased risk of fractures. The reasons for the increase are not fully understood, but evidence exists that women with T2DM who take the thiazolidinedione rosiglitazone have an increased risk of fractures. In addition, use of thiazolidinediones can accelerate bone loss and decrease bone formation. Dormuth *et al.* wanted to find out whether the thiazolidinediones rosiglitazone and pioglitazone have different effects on fracture risk and if fracture risk is also increased in men who are treated with these drugs.

The researchers explored the association between thiazolidinedione use and peripheral fracture risk in 84,339 patients (mean age 59 years) with T2DM who began treatment with a thiazolidinedione (rosiglitazone or pioglitazone) or a sulfonylurea agent between 1998 and 2007. Sulfonylurea treatment was used as a comparator to that of thiazolidinediones because agents of either of these drug classes are usually prescribed as second-line therapy for T2DM.

Risk of peripheral fractures was 28% higher in men and women treated with thiazolidinediones than in those treated with sulfonylureas, after adjustment

for potential confounders. When exposure to each agent was evaluated separately in women, pioglitazone use was associated with a 77% increased risk of peripheral fractures, whereas rosiglitazone use did not significantly increase peripheral fracture risk. In men, the peripheral fracture risk associated with thiazolidinedione use was not significantly higher than that for sulfonylurea use. But in a subgroup analysis, pioglitazone use was associated with increased peripheral fracture risk in men, but rosiglitazone use was not. Nevertheless, the researchers concede that overlapping confidence intervals for this subgroup analysis in men preclude firm conclusions.

The findings fuel the debate concerning the harm versus benefit of thiazolidinedione treatment for T2DM, and Dormuth and co-investigators stress the need for large observational studies to further define the fracture risk associated with the use of these agents.

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Original article Dormuth, C. R. *et al.* Thiazolidinediones and fractures in men and women. *Arch. Intern. Med.* 169, 1395–1402 (2009).