

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Thiazolidinediones and the fracture risk

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Case-control studies of patients with fractures have found that subjects with diabetes have at least a twofold higher risk of fracture than subjects without diabetes, with an increased risk of hip, humerus, and foot fractures in elderly diabetic subjects. Risk factors that contribute to increased fracture in diabetic subjects include number of falls, insulin use, functional disability, diabetes duration, and poor vision. In addition, lower bone strength (BMD) might be expected to increase risk for the development of osteoporosis and fracture.

Type 2 diabetic patients are widely prescribed drugs called thiazolidinediones, which increase insulin sensitivity via activation of peroxisome proliferator-activated receptor (PPAR)- $\gamma$  receptors. In animal studies, thiazolidinedione treatment was associated with bone loss in a mouse model and also in ovariectomized rats. Both reduction in bone formation and stimulation of osteoclastogenesis were evidenced [1]. In a recent clinical study [2] on 160 men with type 2 diabetes, BMD was examined in patients on rosiglitazone treatment compared with matched men with type 2 diabetes not on rosiglitazone treatment. It was found that rosiglitazone treatment increases bone loss in men with type 2 diabetes. In another study [3] conducted in obese postmenopausal women, serum total alkaline phosphatase and bone-specific alkaline phosphatase (bsALP) levels were statistically significantly lower 12 weeks after the initiation of rosiglitazone treatment. There were no statistically significant changes in osteocalcin levels or in deoxypyridinoline levels in the rosiglitazone group. At the end of 12 weeks, all patients had statistically significantly decreased IL1- $\beta$  and TNF- $\alpha$  levels compared with baseline. Changes in bsALP levels showed a moderate negative correlation with the changes in the TNF- $\alpha$  levels after rosiglitazone treatment and after diet in the diabetic control group. A similar warning was recently published for pioglitazone which might increase the fracture risk [4]

These convergent observations suggest that thiazolidinediones may induce or increase bone loss and the fracture risk. A watchful eye of clinicians prescribing these drugs is therefore necessary.

1. Lazarenko OP et al. *Endocrinology*. 2007;148:2669-2680.

2. Yaturu S et al. *Diabetes Care*. 2007;30:1574-1576.

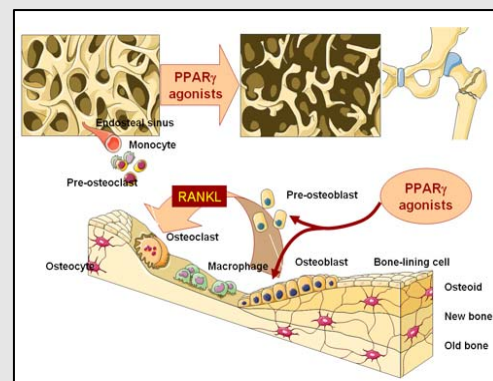
3. Berberoglu Z et al. *J Clin Endocrin Metab*. 2007 doi:10.1210/jc.2007-0431.

4. Hampton T. *JAMA*. 2007;297:1645.

### Thiazolidinediones and the fracture risk

Thiazolidinediones are oral antidiabetic agents used in treatment of type 2 diabetes. These drugs act as PPAR gamma agonists. Long-term treatment with rosiglitazone and pioglitazone was reported to increase the fracture risk.

The primary targets of PPAR gamma agonists are preosteoblasts and osteoblasts whose number is decreased by these drugs. The resulting decrease of bone formation participates in bone loss.



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