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Use of Thiazolidinediones and Fracture Risk

N°55 – November 2008

Preclinical and clinical studies indicate that thiazolidinediones may exert unfavorable effects on bone, resulting in reduced osteoblastic bone formation and accelerated bone loss. An increased fracture risk seems to be related to the use of both rosiglitazone and pioglitazone, indicating a possible class effect of thiazolidinediones. However, it remains unclear whether thiazolidinedione use is associated with peripheral fracture sites only and whether this effect is sex-specific. In this large population-based study [1], the authors explored the association between thiazolidinedione use or use of other oral antidiabetic drugs and the risk of fractures in women and men aged 30 to 89 years. Case patients with fracture aged 30 to 89 years with an incident fracture diagnosis between January 1994 and December 2005 and control subjects who were matched to case patients on age, sex, calendar time, and general practice were studied. The odds ratios (ORs) of having a fracture associated with the use of rosiglitazone, pioglitazone, other oral antidiabetic agents, or insulin were assessed.

There were 1020 case patients with an incident low-trauma fracture and 3728 matched controls. After adjustment for age, body mass index, other antidiabetic drugs, comedication, and comorbidities, the ORs for users of 8 or more thiazolidinedione prescriptions (corresponding to approximately 12-18 months of therapy) compared with nonuse was 2.43. Rosiglitazone (OR, 2.38) and pioglitazone (OR, 2.59) were used more frequently by case patients with fracture (predominantly hip and wrist fractures) than by controls. The association was independent of patient age and sex and tended to increase with thiazolidinedione dose. No materially altered relative fracture risk was found in association with the use of other oral antidiabetic drugs.

This analysis provides further evidence of a possible association between long-term use of thiazolidinediones and fractures, particularly of the hip and wrist, in patients with diabetes mellitus.

1. Meyer C et al. *Arch Intern Med.* 2008;168: 820-825

Use of thiazolidinediones and fracture risk

A large population-based study was performed in order to address the question of whether thiazolidinedione use is associated with peripheral fracture sites only and whether this effect is sex specific.

Administration of pioglitazone or rosiglitazone for more than 18 to 24 months (more than 8 prescriptions) was associated with an increased occurrence of proximal and distal fractures of the upper and lower limbs.

This analysis provides further evidence of a possible association between long-term use of thiazolidinediones and fractures, particularly of the hip and wrist, in patients with diabetes mellitus.

Fracture Site	Participants, No. (%)		Adjusted OR (95% CI)
	Case Patients	Control Subjects	
Hip/femur			
No TZD use	261 (95.3)	977 (96.3)	1 [Reference]
Current TZD use			
1-7 Rx	3 (1.1)	9 (0.9)	1.40 (0.31-6.30)
≥ 8 Rx	8 (2.9)	12 (1.2)	4.54 (1.28-16.10)
Humerus			
No TZD use	207 (93.2)	757 (94.4)	1 [Reference]
Current TZD use			
1-7 Rx	2 (0.9)	12 (1.5)	0.28 (0.04-1.92)
≥ 8 Rx	7 (3.2)	18 (2.2)	2.12 (0.62-7.26)
Wrist/forearm			
No TZD use	277 (92.0)	1028 (93.0)	1 [Reference]
Current TZD use			
1-7 Rx	5 (1.7)	25 (2.3)	0.74 (0.23-2.35)
≥ 8 Rx	14 (4.7)	22 (2.0)	2.90 (1.19-7.10)

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