Pioglitazone: Cardiovascular Effects in Prediabetic Patients

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ABSTRACT

Pioglitazone is the second thiazolidine derivative used clinically in the type 2 diabetes mellitus (DM). In the prediabetic stage, hyperinsulinemia or insulin resistance has been suggested to be closely associated with the oxidative stress. The first thiazolidine derivative used to treat DM, troglitazone, is chemically related to α-tocopherol, a known antioxidant. Troglitazone prevents tissue damage, but has been reported to produce hepatotoxicity. Pioglitazone strongly increases insulin sensitivity, improves glucose and lipid metabolism and showed no evidence of hepatotoxicity. The mechanism of the antidiabetic action of pioglitazone involves activation of insulin receptors and/or high affinity for peroxisome proliferator-activated receptor γ (PPARγ). Hydroxylation of the phenyl and pyridine rings in the chemical structure of pioglitazone may facilitate the scavenging of hydroxyl radicals. The direct antioxidant effect of pioglitazone may contribute to its effect on insulin resistance. The hypoglycemic and hypolipidemic effects of pioglitazone are likely to reduce the expression of TNFα. The reduction in the oxidative stress may lead to the suppression of TGFβ and of collagen accumulation. A decrease in collagen content is likely to improve left ventricular diastolic function and distensibility of the aortic wall. Reduction in the oxidative stress may prevent the proliferation of vascular smooth muscle cells and contribute to the decrease in the aortic wall stiffness.