Effect of peroxisome proliferator-activated receptor γ on inflammatory markers

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Letter to Editor

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Introduction

In a recent study published in "ARYA atherosclerosis," Pourmoghaddas et al. reported that administration of pioglitzone in non-diabetic patients with metabolic syndrome had no positive effect on inflammatory markers including high sensitive C-reactive protein, interleukin-10 (IL-10), and tumor necrosis factor-α (TNF-α).[1]

Peroxisome proliferator-activated receptors (PPARs) are ligand-activated transcription factors which involved in some physiological processes including energy balance, lipid metabolism, and glucose control.[2] They improve glycemic control and enhances insulin sensitivity in diabetic patients.[2,3] These drugs also improve the lipid profile of patients at risk of developing atherosclerosis.[4] PPAR-γ has been implicated in the pathology of numerous diseases including atherosclerosis, obesity, diabetes, and cancer because of its role in modifying adipocyte differentiation, decreasing insulin resistance, and inhibiting vascular endothelial growth factor-induced angiogenesis.[5]

PPARs have three isotypes: PPAR-α, PPAR-γ, and PPAR-ß/δ. There are four isoforms of PPAR-γ in the human. PPAR-γ 1 is found in almost all tissues and PPAR-γ 2 found in adipose tissue.[3,6] PPAR-γ 3 is found in adipose tissue, colon, macrophages, and T-lymphocytes.[6] There are currently no information regarding the distribution of PPAR-γ 4.[6]

The effect of PPAR-γ agonists on inflammatory markers is complex. Although, several in vivo and in vitro studies reported the anti-inflammatory effect of these drugs, however, the complexity of the pro- and anti-inflammatory PPAR-γ functions have also been observed. Several mechanisms for anti-inflammatory action of PPAR-γ are proposed: (1) inhibition of metalloproteinases expression and activity for example metalloproteinase-9 expression in atherosclerotic plaques.[6] (2) Repression the expression of several inflammatory response genes (iNOS, TNF-α,…) in activated macrophages,[7] TNF-α, plasminogen activator inhibitor-1, and IL-6 expression in adipose tissue[8] or TNF-α, IL-6, and IL-1 in human monocytes.[7] (3) Reduction of transcriptional activities (nuclear factor-κB, AP-1, and STAT) or inability of these factors to bind to the iNOS promoter in monocytes.[6] (5) Suppression the lipopolysaccharide (LPS)-induced TNF-α in human alveolar macrophages.[9]

However, other studies demonstrated that PPAR-γ ligands induce certain pro-inflammatory responses. They induce macrophage differentiation and upregulate the macrophage pro-inflammatory surface receptors (such as CD14, CD11/CD18, and scavenger receptor B1).[6] 15-Deoxy-Delta-12,14-prostaglandin J2 (15d-PGJ2), a PPAR-γ agonist, induces expression of IL-8 and at the same time suppresses the expression of monocyte chemoattractant protein-1.[10] In another study, rosiglitazone did not have effect on LPS-induced IL-8, but it suppressed matrix metalloproteinase-9.[11] Therefore, it seems that the effect of PPAR-γ ligands on the inflammatory response is complex and depend upon the mediators that are measured, PPAR-γ ligand used and its concentration and the activation state of the target cell.[6,12]

Conflict of Interests

Authors have no conflict of interests.

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