Pioglitazone Attenuates Inflammatory Atrial Fibrosis and Vulnerability to Atrial Fibrillation Induced by Pressure Overload in Rats

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Background: Inflammatory processes are involved in the pathogenesis of atrial fibrillation (AF).

Objective: The purpose of this study was to test the hypothesis that atrial fibrosis and enhanced vulnerability to AF evoked by pressure overload can be attenuated by pioglitazone, a peroxisome proliferator-activated receptor-γ agonist, via suppression of inflammatory profibrotic signals.

Methods: Male Sprague-Dawley rats were subjected to abdominal aortic constriction (AAC). Pioglitazone 3 mg/kg/day or vehicle was orally administered for 4 weeks.

Results: Western blot analysis revealed that AAC enhanced expression of monocyte chemoattractant protein (MCP)-1, transforming growth factor-β1 and α-smooth muscle actin in the left atrium (LA), which was suppressed by pioglitazone. Messenger RNA expression of collagen type 1 and atrial natriuretic peptide in the LA was increased by AAC, which was suppressed by pioglitazone. Gelatin zymography demonstrated that activity of matrix metalloproteinase-9 was increased by AAC, which was suppressed by pioglitazone. Pioglitazone attenuated AAC-induced LA fibrosis. In isolated-perfused heart experiments, AAC did not alter the refractory period of the LA or the right atrium (RA), but it did prolong the interatrial conduction time. Programmed extrastimuli from the RA induced AF in all of the AAC-treated rats (8/8 [100%]). This was suppressed by pioglitazone (2/8 [25%], P<.05) with normalization to interatrial conduction time.

Conclusion: The results of this study suggest that inflammatory profibrotic mechanisms are involved in this pressure-overloaded AF model. The results also suggest that pioglitazone is effective at attenuating atrial fibrosis, possibly via suppression of MCP-1-mediated inflammatory profibrotic processes.

Keyword: AF