Effects of Pioglitazone on Brachial Artery Flow-Mediated Dilation and Circulating Levels of microRNA-21 in Hypertensive Type 2 Diabetic Patients

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Background:
Endothelial dysfunction has been documented in patients with type 2 diabetes or in patients with hypertension. We prospectively investigated the effects of pioglitazone in improving endothelial function in hypertensive type 2 diabetic patients during the 6-month follow-up.

Methods:
Hypertensive type 2 diabetic patients were randomly assigned to pioglitazone(n=25) or placebo(n=25). Primary endpoint was to compare changes in brachial artery flow-mediated dilation(baFMD) during the 6-month follow-up. Secondary endpoints were to compare changes in the circulating levels of microRNA-17,-21,-92a,-126 and -145 which have been known as indicators of endothelial cell migration and atherosclerosis progression during the 6-month follow-up. Inflammatory markers such as IL-6, TNF-alpha, high-sensitive C-reactive protein, adiponectin, ICAM-1, and VCAM-1 were compared during the follow-up.

Results:
The rates of risk factors such as hyperlipidemia, smoking, stroke, and family history of coronary artery disease did not show significant differences between the 2 groups. Increases in baFMD(3.3±3.4mm vs. 0.2±2.5mm, p0.05, respectively) and in the level of circulating microRNA-21(0.23±0.05 vs. -0.06±0.04, p0.05, respectively) were significantly greater in the pioglitazone group when compared to the placebo group during the 6-month follow-up. No occurrence of new onset heart failure, fracture, and bladder cancer was noted during the follow-up in both groups. Decreases in the levels of inflammatory marker such as IL-6 (-2.54±2.32pg/mL vs. -1.34±2.12pg/mL, p0.05, respectively), TNF-alpha (-1.54±1.51pg/mL vs. 0.14±1.12pg/mL, p0.05, respectively), ICAM-1 and VCAM-1 were significantly greater in the pioglitazone group compared to the placebo group during the follow-up.

Conclusion:
Pioglitazone significantly increased baFMD with increases in endothelial cell microRNA-21 and decreases in inflammatory markers such as IL-6, TNF-alpha, ICAM-1 and VCAM-1 during the 6-month follow-up.