

The Fixed Combination of Pioglitazone and Metformin Improves Biomarkers of Platelet Function and Chronic Inflammation in Type 2 Diabetes Patients: Results from the PIOfix Study

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Abstract

Background:

Type 2 diabetes mellitus (T2DM) is characterized by a proinflammatory and procoagulant condition. This study investigates the impact of a pioglitazone plus metformin therapy on biomarkers of inflammation and platelet activation in comparison to a treatment with glimepiride plus metformin.

Methods:

The study was designed as a multicenter, randomized, double-blinded two-arm trial. Patients with T2DM and dyslipidemia under metformin monotherapy with hemoglobin A1c value between 6.5% and 9.0% were eligible for trial participation. Blood was drawn at baseline and after 24 weeks of treatment from patients of five centers. Markers of inflammation and thrombocyte function (soluble CD40 ligand, thromboxane, vWillebrand factor, adhesion molecules, clotting reaction) were evaluated subsequently in a central laboratory.

Results:

A total of 46 patients were included in the final analyses. Mean (\pm standard deviation) age was 58.5 ± 9.0 years (13 women, 33 men; disease duration 6.3 ± 5.0 years; body mass index 32.0 ± 4.8 kg/m²). A total of 25 patients were treated with pioglitazone plus metformin, and 21 patients were in the glimepiride arm. There was a significant decline of E-selectin (-3.7 ± 4.8 ng/ml, $p < .001$ versus baseline), vWillebrand factor ($-19.5 \pm 32.0\%$, $p < .05$), and high-sensitivity C-reactive protein concentrations (-1.08 ± 0.91 mg/liter, $p < .05$) in the metformin + pioglitazone arm only (metformin + glimepiride, -0.5 ± 3.4 ng/ml, $+1.4 \pm 33.2\%$, $+0.08 \pm 0.72$ mg/liter, respectively, all not significant). Also, all other surrogate markers for platelet function and inflammation showed slight improvements in the metformin + pioglitazone arm but not in the metformin + glimepiride arm.

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Abbreviations: (HDL) high-density lipoprotein, (hsCRP) high-sensitivity C-reactive protein, (sCD40L) soluble CD40 ligand, (T2DM) type 2 diabetes mellitus

Keywords: inflammation, oral antidiabetics, pioglitazone plus metformin, platelet aggregation, type 2 diabetes, vascular function

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Abstract cont.

Conclusions:

The fixed metformin + pioglitazone combination treatment showed an overall improvement of laboratory surrogate markers, indicating improvement of platelet function and of chronic systemic inflammation, which was not seen with metformin + glimepiride.

J Diabetes Sci Technol 2011;5(2):426-432