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ORIGINAL ARTICLES

Combined Pioglitazone and Metformin Treatment Maintains the Beneficial Effect of Short-Term Insulin Infusion in Patients with Type 2 Diabetes: Results from a Pilot Study

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Abstract

Background:

The aim of our study was to examine the efficacy of short-term intravenous insulin intervention followed by oral pioglitazone/metformin therapy to prevent patients from continuous insulin application.

Methods:

This prospective, open-label, 4-month pilot study comprised of 14 diabetes patients (5 female, 9 male; age 60 ± 2 years; body mass index 29 ± 3.2 kg/m²; hemoglobin A1c [HbA1c] 7.6 ± 1.1%) with (1) insufficient glycemic control under a dose of metformin ≥1700 mg/day and/or metformin plus additional oral antidiabetes drugs (OADs) and (2) appropriate residual β-cell function. Initially, an inpatient 34 h continuous intravenous insulin infusion was performed, and metformin was given (2x 850 mg/day). Insulin was stopped, and pioglitazone 30 mg/day was added at the second inpatient day. Patients were followed for four months. Efficacy parameters [change of HbA1c, fasting blood glucose [FBG], intact proinsulin, adiponectin, and high-sensitivity C-reactive protein (hsCRP)] were assessed after initial normalization of blood glucose values by intravenous insulin and at the study end point.

Results:

During the acute insulin intervention, FBG levels were stabilized in all study subjects. In the following OAD treatment period, five patients showed an improvement of HbA1c > 0.5% [35.7%; seven patients remained stable (50.0%), two patients were nonresponders (14.3%)].

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Abbreviations: (FBG) fasting blood glucose, (HbA1c) hemoglobin A1c, (HOMA-IR) homeostasis model assessment of insulin resistance, (hsCRP) high-sensitivity C-reactive protein, (NS) not significant, (OAD) oral antidiabetes drug, (PPARγ) peroxisome proliferator-activated receptor γ, (T2DM) type 2 diabetes mellitus

Keywords: cardiovascular risk, glycemic control, pioglitazone, type 2 diabetes

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Abstract cont.

Fasting glucose values dropped after insulin infusion (-17.7%; $p < .001$). This effect was maintained during the consecutive OAD treatment period (glucose +0.3%, not significant (NS); HbA1c -6.0%; $p < .05$). The initial decrease in fasting intact proinsulin levels was also maintained during the study (end value -41%, $p < .05$).

Improvements in hsCRP values (postinsulin value, -15%, NS; end value -37%; $p < .05$) and adiponectin values (postinsulin value +15%, NS; end value +128%; $p < .001$) were demonstrated at end point only after continued glitazone intake.

Conclusions:

Our pilot study demonstrated that a beneficial effect of a short-term intravenous insulin application on glycemic control was effectively maintained by pioglitazone/metformin treatment for at least 4 months. In addition, the oral therapy significantly improved cardiovascular risk parameters.

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