Low-dose rosiglitazone plus sulfonylurea was effective and safe for treating hyperglycemia in type 2 diabetes mellitus

Wolffenbuttel BHR, Gomis R, Squatrito S, Jones NP, Patwardhan RN. **Addition of low-dose rosiglitazone to sulphonylurea therapy improves glycaemic control in type 2 diabetic patients.** Diabet Med. 2000 Jan;17:40-7.

QUESTION

How effective and safe is low-dose rosiglitazone combined with sulfonylurea for treating hyperglycemia in patients with type 2 diabetes mellitus?

DESIGN

Randomized (allocation concealed*), blinded (clinician and patient),* placebo-controlled trial with 26-week follow-up.

SETTING

60 centers in 6 European countries (Italy, the United Kingdom, France, Spain, The Netherlands, and Switzerland).

PATIENTS

593 patients between 30 and 80 years of age who had type 2 diabetes, a fasting plasma glucose level ≤ 15.0 mmol/L, a hemoglobin (Hb) A_{1c} level ≥ 7.5%, a fasting C-peptide level ≥ 0.27 nmol/L, and a body mass index between 22 and 38 kg/m^2 and who had been treated with sulfonylurea for ≥ 6 months. Exclusion criteria were renal or hepatic disease, symptomatic diabetic neuropathy requiring treatment, abnormal electrocardiographic or laboratory test results, or need for insulin therapy or medications other than sulfonylureas that lower blood glucose levels. 574 (97%) patients (mean age 61 y, 59% men, 97% white) were included in the intention-to-treat analysis.

INTERVENTION

After a 2- to 4-week run-in period with placebo and sulfonylurea therapy, patients were allocated to receive oral rosiglitazone, 1 mg twice daily {*n* = 205}† or 2 mg twice daily {*n* = 190}†, or twice-daily placebo {*n* = 198}† for 26 weeks. Patients continued to receive their existing sulfonylurea therapy.

MAIN OUTCOME MEASURES

Changes in HbA_{1c} and fasting plasma glucose levels, and adverse events.

MAIN RESULTS

Analysis was by intention to treat. At 26 weeks, both groups receiving rosiglitazone plus sulfonylurea had lower HbA_{1c} levels (mean reductions 0.59% and 1.03%, respectively, $P < 0.001$) and lower fasting plasma glucose levels (mean reductions 0.95 and 2.09 mmol/L, respectively, $P < 0.001$) than did the group receiving placebo plus sulfonylurea. No differences existed between groups for rates of adverse events.

CONCLUSION

Combination therapy with low-dose rosiglitazone and sulfonylurea was associated with lower hemoglobin A_{1c} and fasting plasma glucose levels than was sulfonylurea monotherapy and was safe in patients with type 2 diabetes mellitus.

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*See Glossary.

†Information provided by the author.

COMMENTARY

The study by Wolffenbuttel and colleagues is 1 of a growing number of studies that show the efficacy of combining various doses of oral hypoglycemic agents of different drug classes to achieve improved glycemic control in persons with type 2 diabetes mellitus. We know that many patients at first respond inadequately to sulfonylureas and that an even greater number gradually lose their responsiveness over time. About 25% of patients with a fasting plasma glucose level of 12.2 to 13.3 mmol/L who are treated with either sulfonylurea or metformin monotherapy achieve acceptable glycemic control (fasting plasma glucose level < 7.8 mmol/L or HbA_{1c} level < 8.0%)(1). Because 4 major classes of oral hypoglycemic agents are now available, combining agents from ≥ 2 classes is becoming commonplace. Metformin and sulfonylurea have been combined most often (2–4), but other combinations are being studied and used, such as acarbose plus sulfonylurea and metformin and thiazolidinedione plus sulfonylurea. In addition, oral agents can be combined with insulin therapy.

Thus, treatment of type 2 diabetes is becoming similar to treatment of such other chronic diseases as hypertension, chronic obstructive lung disease, and congestive heart failure. Multiple treatments that work through complementary mechanisms achieve better control of the condition.

Combination drug therapy for diabetes should be used if regular exercise, modest weight loss, and monotherapy are inadequate to achieve euglycemia.

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