

Rosiglitazone, but not ramipril, prevents onset of type 2 diabetes in high-risk patients

An international team of investigators has evaluated the effects of rosiglitazone, an anti-hyperglycemic drug, and ramipril, an angiotensin-converting-enzyme inhibitor, on the development of diabetes in a double-blind, placebo-controlled, randomized, multicenter trial. Results for each drug were reported separately.

In total, 5,269 participants (mean age 54.7 years) who had impaired fasting plasma glucose levels or impaired glucose tolerance were randomly assigned to receive placebo, rosiglitazone or ramipril monotherapy, or both drugs. Participants were followed up for a median of 3 years.

During the trial, diabetes development or death occurred in markedly fewer patients in the rosiglitazone-treated group (11.6%) than in the placebo-treated group (26%). Rosiglitazone treatment reduced both the median fasting plasma glucose level and the 2 h postchallenge plasma glucose concentration, and increased the likelihood of returning to normoglycemia by about 70–80% as compared with placebo treatment. A possible adverse effect of rosiglitazone might be the increased occurrence of nonfatal congestive heart failure (0.5% in rosiglitazone-treated patients versus 0.1% placebo-treated patients), but there were no major differences between the two groups in the incidence of other cardiovascular events.

Compared with placebo, ramipril did not substantially reduce the incidence of diabetes development or death, but it did increase the rate of regression to normoglycemia (by 16%). In ramipril-treated patients, 2 h postchallenge plasma glucose levels were slightly lower than in placebo-treated patients.

The authors suggest that rosiglitazone could be used to treat dysglycemia and might prevent the onset of diabetes in high-risk individuals. Ramipril apparently has favorable effects on glucose metabolism, but extended follow-up might be required to detect any effect on diabetes development. The authors conclude that, at present, ramipril cannot be recommended for diabetes prevention.

Original articles The DREAM (Diabetes Reduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators (2006) Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or

impaired fasting glucose: a randomised controlled trial. *Lancet* 368: 1096–1105

The DREAM Trial Investigators (2006) Effect of ramipril on the incidence of diabetes. *N Engl J Med* 355: 1551–1562

Insulin-independence is rarely sustained after pancreatic islet transplantation

In diabetic patients whose condition is refractory to conventional insulin treatment, a possible therapeutic approach is the transplantation of islets obtained from the pancreata of deceased donors. From nine centers, Shapiro and colleagues report results achieved by islet transplantation combined with glucocorticoid-free immunosuppressive therapy, which is known as the Edmonton protocol.

A total of 77 ABO-compatible islet transplantations were performed on 36 patients with treatment-refractory type 1 diabetes mellitus. Identical procedures were used. By 1 year after the final transplantation, insulin-independence with adequate glycemic control was observed in 16 patients, partial graft function in 10 patients, and complete graft loss in 10 patients. In total, 21 patients attained insulin-independence during the trial. By the end of the second post-transplant year, however, insulin-independence persisted in only 5 patients. Attainment of insulin independence was considerably more likely in patients with no detectable antibodies against islet antigens, but loss of insulin-independence was unrelated to such antibody levels. Previous experience with islet transplantation clearly affected the outcome of the procedure. The main adverse effects of the procedure were immunosuppression-related complications (e.g. mouth ulceration, anemia and leucopenia) and declines in renal function.

These findings imply that although insulin production can be transiently restored by the Edmonton protocol, whole-pancreas transplantation is more likely to result in long-term insulin-independence. Advances in islet transplantation await improved techniques for isolating islets and the development of immunosuppressive agents with reduced toxicity. In view of the limited availability of donors, there is a great need for other sources of insulin-producing cells that can be used for islet transplantation.

Original article Shapiro AMJ *et al.* (2006) International trial of the Edmonton protocol for islet transplantation. *N Engl J Med* 355: 1318–1330