

U.K. prospective diabetes study 16. Overview of 6 years' therapy of type II diabetes: a progressive disease. U.K. Prospective Diabetes Study Group

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The objective of the U.K. Prospective Diabetes Study is to determine whether improved blood glucose control in type II diabetes will prevent the complications of diabetes and whether any specific therapy is advantageous or disadvantageous. The study will report in 1998, when the median duration from randomization will be 11 years. This report is on the efficacy of therapy over 6 years of follow-up and the overall incidence of diabetic complications. Subjects comprised 4,209 newly diagnosed type II diabetic patients who after 3 months' diet were asymptomatic and had fasting plasma glucose (FPG) 6.0–15.0 mmol/l. The study consists of a randomized controlled trial with two main comparisons: 1) 3,867 patients with 1,138 allocated to conventional therapy, primarily with diet, and 2,729 allocated to intensive therapy with additional sulfonylurea or insulin, which increase insulin supply, aiming for FPG < 6 mmol/l; and 2) 753 obese patients with 411 allocated to conventional therapy and 342 allocated to intensive therapy with metformin, which enhances insulin sensitivity. In the first comparison, in 2,287 subjects studied for 6 years, intensive therapy with sulfonylurea and insulin similarly improved glucose control compared with conventional therapy, with median FPG at 1 year of 6.8 and 8.2 mmol/l, respectively ( $P < 0.0001$ ). and median HbA1c of 6.1 and 6.8%, respectively ( $P < 0.0001$ ). During the next 5 years, the FPG increased progressively on all therapies ( $P < 0.0001$ ) with medians at 6 years in the conventional and intensive groups, FPG 9.5 and 7.8 mmol/l, and HbA1c 8.0 and 7.1%, respectively. The glycemic deterioration was associated with progressive loss of beta-cell function. In the second comparison, in 548 obese subjects studied for 6 years, metformin improved glucose control similarly to intensive therapy with sulfonylurea or insulin. Metformin did not increase body weight or increase the incidence of hypoglycemia to the same extent as therapy with sulfonylurea or insulin. A high incidence of clinical complications occurred by 6-year follow-up. Of all subjects, 18.0% had suffered one or more diabetes-related clinical endpoints, with 12.1% having a macrovascular and 5.7% a microvascular endpoint. Sulfonylurea, metformin, and insulin therapies were similarly effective in improving glucose control

compared with a policy of diet therapy. The study is examining whether the continued improved glucose control, obtained by intensive therapy compared with conventional therapy (median over 6 years HbA1c 6.6% compared with 7.4%), will be clinically advantageous in maintaining health.