Intensive blood glucose control reduced type 2 diabetes mellitus--related end points

UK Prospective Diabetes Study Group.


Question
In patients with newly diagnosed type 2 diabetes mellitus, what is the effect of intensive plasma glucose control on the risk for macrovascular and microvascular complications?

Design
Randomized controlled trial with median follow-up of 10 years.

Setting
23 hospital-based diabetes clinics in the United Kingdom.

Patients
3867 patients (mean age 53 y, 61% men, mean body mass index 27.5 kg/m²) with newly diagnosed type 2 diabetes and fasting plasma glucose (FPG) levels between 6.1 mmol/L and 15.0 mmol/L after 3 months of dietary therapy without symptoms of hyperglycemia. Exclusion criteria were ketonuria > 3 mmol/L, serum creatinine level > 175 μmol/L, myocardial infarction (MI) in the previous year, heart failure or angina, major vascular events, retinopathy requiring laser therapy, malignant hypertension, an uncorrected endocrine disorder, an occupation precluding insulin therapy, or severe concurrent illness. Follow-up was 96%.

Intervention
After stratification for obesity (body weight > 120% of ideal), 2729 patients were allocated to intensive treatment aiming for FPG levels of < 6 mmol/L (by dietary treatment and use of oral medication [chlorpropamide, glibenclamide, glipizide, or metformin] or insulin); and 1138 patients were allocated to conventional dietary treatment aiming for FPG levels < 15 mmol/L without hyperglycemic symptoms.

Main outcome measures
A first diabetes-related predefined clinical end point, death related to diabetes, all-cause mortality, MI, stroke, amputation or death from peripheral vascular disease, and microvascular disease.

Main results
Analysis was by intention to treat. Patients allocated to intensive treatment had lower median hemoglobin A₁c level (7.0% vs 7.9%, P = 0.001), reduced diabetes-related clinical end points (46.0 events/1000 patient-y, P = 0.001), and less microvascular disease (P = 0.01). Increased major hypoglycemic episodes (0.7%/y for conventional treatment, 1.0%/y for chlorpropamide, 1.4%/y for glibenclamide, and 1.8%/y for insulin, P < 0.001), and a mean 3.1-kg greater weight gain (P < 0.001) than those allocated to conventional treatment.

Conclusion
In patients with type 2 diabetes, intensive blood glucose control reduced diabetes-related end points and microvascular disease, increased major hypoglycemic episodes, and had no effect on macrovascular end points.

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