Review: Improved glycaemic control reduces microvascular complications in type 2 diabetes mellitus


Question
In patients with type 2 diabetes mellitus, does intensive glycaemic control reduce complications?

Data sources
MEDLINE (from 1970) was searched using the terms diabetes, retinopathy, neuropathy, nephropathy, cardiovascular disease, atherosclerosis, weight gain, hypoglycaemia, glycaemic control, hyperglycaemia, glycosylated haemoglobin, and blood glucose. The reference lists of relevant studies were reviewed.

Study selection
Studies were selected if they were cohort studies or randomised controlled trials (RCTs) with ≥3-month follow-up that assessed diabetic complication rates. Exclusion criteria were failure to differentiate between type 1 and type 2 diabetes, inadequate measures of glycaemic control, or lack of analyses of statistical significance.

Data extraction
Data were extracted on study design, patient characteristics, details of glycaemic control, fasting blood glucose levels, glycosylated haemoglobin (HbA1c) levels, microvascular complications, myocardial infarction (MI), and mortality.

Main results
3 RCTs examined microvascular complications in type 2 diabetes. 1 trial involved 619 patients and had a mean 13-year follow-up; it showed no difference in proteinuria or retinopathy rates when variable or fixed-dose insulin was compared with placebo. The second RCT involved 110 patients and had a 6-year follow-up. It showed that intensive insulin therapy (HbA1c level 7.1%) was better than conventional insulin therapy (HbA1c level 9.4%) for reducing complications: retinopathy (13% vs 38%, P=0.007), nephropathy (10% vs 30%, P=0.005), and neuropathy (13% vs 65% increase in lower extremity vibration threshold, P<0.05). A third RCT involved 153 men and had a 27-month follow-up. It showed that patients who received intensive therapy (HbA1c level 7.3%) did not have an increased 24-hour albumin excretion rate; patients who received standard therapy (HbA1c level 9.4%) had an increase in 24-hour urinary albumin excretion rate of 144 mg (from 14 to 158 mg, P=0.008). Of the 3 RCTs providing cardiovascular data, 1 trial found that intensive and conventional therapy groups did not differ for rate of MI (20.6% vs 20.2%, P=1.00). The second trial of 620 type 2 diabetic patients with MI showed lower 1-year mortality rates in those who received an acute insulin infusion followed by intensive therapy than in those who received conventional therapy (18.6% vs 26.1%, P=0.03). The third RCT showed a statistically non-significant trend toward a more major coronary heart disease event with intensive therapy than with conventional therapy (21.3% vs 11.5%, P=0.10). 2 trials showed that hypoglycaemia did not differ between intensive and conventional therapy groups.

Conclusions
Improved glycaemic control reduces microvascular complications in patients with type 2 diabetes mellitus. Evidence supporting the benefit of glycaemic control for macrovascular complications is inconclusive.

Sources of funding: Not stated.

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Commentary
Gaster and Hirsch conclude that improvement in glycaemic control reduces microvascular and neuropathic complications in patients with type 2 diabetes, similar to the proven value of glycemic control in patients with type 1 diabetes. However, the benefits of glycemic control in preventing macrovascular disease, a major cause of increased morbidity and mortality in type 2 diabetes, remain inconclusive. Although some epidemiological data support a relation between poor glycemic control and adverse cardiovascular events, and 1 trial showed lower mortality with intensive insulin therapy after MI, no clinical trial found decreased coronary heart disease, stroke, or peripheral vascular disease with improved glycaemic control (1). The results of the United Kingdom Prospective Diabetes Study (UKPDS) that includes >4000 participants will be announced in September 1998.

Macrovascular disease is a multifactorial process. Efforts are being made to understand the increased susceptibility of the vascular wall in diabetic patients to risk factors other than hyperglycaemia, such as dyslipidaemia, hypertension, and smoking. Clinical trials of lipid lowering have shown that aggressive control of low-density lipoprotein cholesterol is at least as effective in improving cardiovascular outcomes in patients with type 2 diabetes as in nondiabetic persons (2, 3). Further, the metabolic risk factors for macrovascular disease already existed in the years before the clinical diagnosis of diabetes (4). Therefore, a multifactorial intervention, in addition to control of hyperglycaemia, is the most logical approach to reducing the burden of macrovascular disease in the increasing number of patients with type 2 diabetes. For optimal control of hyperglycaemia, treatment with insulin should not be withheld if other methods of therapy, including combinations of oral agents, do not result in the desired goals.

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References