

CLINICAL CHALLENGE

Diabetes

Question:

I read in the *British Medical Journal* that the UK Prospective Diabetes Study Group recently announced the results of their extensive long term studies on type 2 diabetics. What were their main findings? Are there implications for primary care doctors?

Comments:

The United Kingdom Prospective Diabetes Study (UKPDS) was a randomised controlled trial which compared the effects of intensive glucose control with conventional treatment on the risk of micro- and macrovascular complications of type 2 diabetes. As hypertension was recognized to be an equally important risk factor, the effects of tight blood pressure control was also examined in the study. The UKPDS started in 1977 and went on for 20 years and the main findings were published in four papers in September 1998.¹⁻⁴

The participants of the UKPDS were 3867 newly diagnosed patients with type 2 diabetes who, after three months of dietary treatment, had fasting glucose of 6.1-15 mmol/l. They were randomly assigned to an intensive policy with either a sulphonylurea or insulin, or to a conventional policy with diet. During the trial, a stepwise addition of hypoglycaemic agents was required in many patients in the intensive treatment group in order to maintain fasting glucose <6.0mmol/l. The dietary policy also allowed patients to be given hypoglycaemic agents when their glycaemic goal (fasting plasma glucose <15 mmol/l) was not met. The failure of diet and the gradual failures of the hypoglycaemic agents to maintain glycaemic goals resulted in substantial therapeutic overlap between comparison groups which made subsequent comparisons of the different types of therapy more difficult. In the blood pressure study, 1148 hypertensive patients with type 2 diabetes were randomised to either tight blood pressure control (target

BP<150/85 mmHg with the use of an angiotensin converting enzyme inhibitor or a beta blocker) or to less tight control (BP<180/105 mmHg). For both the diabetes and hypertension management protocols, the primary outcomes were "hard" clinical end points, including severe cardiovascular events, vision loss and renal failure.

During the trial, HbA_{1c} was reduced by 11% (from 7.9 to 7.0) in the intensive treatment group compared to conventional treatment. The reduction was smaller than that in DCCT where a reduction of 20% was achieved.⁵ An increased incidence of hypoglycaemia and more weight gain were observed in the intensive treatment group but intensive treatment was associated with a significant reduction of 12% in the risk for any diabetes related end points. The observed decrease, however, was in fact mainly due to the 25% reduction in the risk of microvascular events. There was no effect on diabetes-related mortality or all cause mortality. The blood glucose study therefore shows that tightly controlling blood glucose concentration in type 2 diabetes reduces the risks of microvascular complications but the evidence on macrovascular complications is inconclusive. As for the beneficial effects of the different types of treatment, sulphonylureas and insulin seem to produce equally good results. The data on metformin is controversial. For reasons that remain unclear, metformin was effective in reducing important end points in obese patients but appeared to work less well in combination with other drugs.

The blood pressure study showed that tight blood pressure control in hypertensive patients with type 2 diabetes resulted in a significant reduction in both diabetes related end points and diabetes related deaths. Not only was there a significant reduction in the risk of microvascular end points, there was also a 44% decrease in the risk of stroke. Both angiotensin converting enzyme inhibitor and beta blocker appeared to be similarly effective in reducing the incidence of diabetic complications. The study also highlighted the fact that additional antihypertensive agents were often required and

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about one-third of the patients in the tight blood pressure control group required three or more antihypertensive agents to maintain blood pressure below the target levels.

In summary, tight glucose and blood pressure control in patients with type 2 diabetes is important as it can significantly reduce the risk of the long term complications of diabetes. Based on the findings of the UKPDS, it has been suggested that glycaemic goal should be aimed at HbA_{1c} 7% or lower, taking into account the condition of the patients, and any reduction of HbA_{1c} from a high value is important. In patients with hypertension, the suggested goal of blood pressure is around 140/85 mmHg or lower. ■

References

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