Taking diabetes care to another level: the UKPDS

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In 1988 I was one of many thousands of people who sat in a conference hall in Barcelona to hear the first results of the United Kingdom Prospective Diabetes Study (UKPDS). The data were subsequently published in a series of papers; the two that stand out were those proving that tight glycaemic and blood pressure control significantly reduce the risk of vascular morbidity and mortality in patients with type 2 diabetes (UKPDS, 1998a; 1998b).

The news had a profound effect on the diabetes community and majorly influenced our approach to the management of type 2 diabetes. The results have been quoted worldwide and support many recommendations for diabetes care (the NSFs for Diabetes and Coronary Heart Disease, NICE guidance in the UK and other national and international bodies).

The UKPDS was the largest and longest study ever conducted in type 2 diabetes. It randomised over 5 000 patients with newly diagnosed type 2 diabetes to conventional or intensive glycaemic treatment regimens. It lasted for 20 years. During the study a separation in HbA_{1c} of only 0.9% in favour of tight control was associated with profound risk reductions, particularly for microvascular endpoints. Overall, there was a significant 25% risk reduction for microvascular disease and 12% for any diabetes-related endpoint. A 16% reduction in risk of myocardial infarction just failed to reach significance.

A large subgroup of patients had hypertension and were randomised to a tight blood pressure versus conventional control. The mean blood pressure achieved was 144/82 vs 154/87 mmHg in favour of tight control. This was associated with profound and significant risk reductions for microvascular endpoints over the 9 years of the study, predominantly retinopathy and nephropathy (around 37%), diabetes related endpoints (25%), deaths related to diabetes (32%) and stroke (44%).

At last health professionals and patients had evidence-based targets to aim for. These studies were the first in a series of work published over the next 5–6 years, testifying to the importance of good glycaemic control and aggressive screening and management of hypertension and dyslipidaemia. Given that diabetes is a cardiovascular disease and this accounts for around 80% of deaths (many prematurely), having such an evidence base for management is vital. Multiple vascular risk intervention should include lifestyle advice with aggressive management (usually requiring pharmacotherapy) of hypertension, dyslipidaemia and glycaemia to reduce morbidity and mortality. Virtually none of this evidence was available pre-UKPDS.

Other messages that arose from the UKPDS included the fact that type 2 diabetes is progressive and no matter what treatment is used as a monotherapy, deterioration in glycaemic control usually appears inevitable. This emphasises the importance of early and aggressive glycaemic management and the necessity in most patients to use multiple drug therapies in combination from different drug classes (including insulin) to reach target. The same is true for managing hypertension; most patients will require two or more antihypertensives from different drug classes to reach blood pressure target.

The cardioprotective properties of metformin were demonstrated by the UKPDS (for reasons that may relate to improvement in insulin sensitivity). Metformin should be the firstline treatment for the management of type 2 diabetes and certainly in those with BMI > 25 kg/m^2 and probably in virtually all people with type 2 diabetes, unless there are tolerability problems or contraindications to its use. Further benefits of combination therapy with sulphonylureas in improving glycaemia was stressed, as well as early treatment with insulin for those not achieving glycaemic targets. A critical message from the blood pressure sub-study was that it does not matter which blood pressure agents are used to lower blood pressure – the most important aspect is to get blood pressure down and keep it down!

Since the publication of the UKPDS, other trials have testified to the importance of multiple cardiovascular risk intervention to reduce morbidity and mortality. However, the UKPDS remains in my mind as the study that changed my approach to the management of type 2 diabetes and in that sense changed my life... and most importantly benefited my patients.

United Kingdom Prospective Diabetes Study (UKPDS) Group. (1998a) Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* **352**: 837–53.

United Kingdom Prospective Diabetes Study Group. (1998b) Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *British Medical Journal* **317**: 703–13

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