The importance of glycaemic control in preventing complications of diabetes

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Few papers change one's clinical practice, far less one's professional life, and it is a challenge to identify a single paper with such an impact. However, one study did change my professional life, and the lives of most diabetes specialists and people with type 1 diabetes. The seminal paper of the Diabetes Control and Complications Trial (DCCT), in which the key findings are succinctly presented, was published in 1993 (DCCT Research Group, 1993). This trial subsequently generated a multitude of publications of vital importance to the management of type 1 diabetes.

For many years it was not known whether the quality of glycaemic control played a fundamental causal role in the development of the vascular and neuropathic complications of type 1 diabetes, and whether strict glycaemic control would prevent or delay their onset. The rationality of this premise may now seem obvious, but many will be unaware of the heated and often acrimonious debate that once surrounded the 'glucose hypothesis' and the pathogenesis of microangiopathy (Tchobroutsky, 1978). Protagonists debated whether chronic hyperglycaemia could be the principal cause of vascular damage. Advocates of the 'laissez-faire' approach to the management of type 1 diabetes firmly believed that glycaemic control was not important for the development of complications, and that the obsession with achieving near-normoglycaemia not only risked inducing severe hypoglycaemia but diminished a patient's quality of life. However, although by the 1970s many diabetologists intuitively thought that good glycaemic control would protect blood vessels, definitive evidence was lacking – with the exception of the remarkable individual contribution of Jean Pirart in Belgium. Single-handedly, and without the massive resources afforded the DCCT, he prospectively followed a cohort of 4400 of his own patients for nearly 30 years, carefully documenting the prevalence and severity of diabetic complications, and demonstrating that these were more frequent and more severe in people who had 'poor' control (Pirart, 1978). However, this study pre-dated the availability of glycated haemoglobin as an index of glycaemic control and, being European in origin, did not receive unalloyed acceptance in North America.

Several small short-term studies in the 1980s (such as the Kroc, Oslo and Steno studies) indicated that glycaemic control influenced the progression of established microangiopathy (Hanssen et al, 1986), but a longer prospective study was necessary. The DCCT was undertaken to provide a definitive answer to the role of glycaemic control in promoting vascular complications.

Planned with meticulous care, well resourced and executed with clinical skill, stamina and scientific rigour, the outcome of the DCCT was unequivocal. It showed categorically that the better the glycaemic control, the lower the prevalence and severity of the microvascular and neuropathic complications of type 1 diabetes, with no apparent threshold effect. The similar findings of the smaller Stockholm Diabetes Intervention Study (Reichard et al, 1993) provided complementary data. A recent paper examining cardiovascular outcomes has demonstrated that intensive insulin therapy also protects large blood vessels (Nathan et al, 2005). My personal interest in hypoglycaemia was amply addressed by the DCCT, with a plethora of information about its epidemiology and the risk factors for severe hypoglycaemia. Strict glycaemic control is clearly associated with an increased frequency of severe hypoglycaemic events, with intensive therapy promoting a three-fold greater incidence than conventional treatment (DCCT Research Group, 1991; DCCT Research Group, 1997).

The DCCT was a landmark study and a scientific tour de force. The importance of strict glycaemic control to limit vascular damage in type 1 diabetes was proven beyond doubt. The strategic approach to the management of type 1 diabetes was changed radically through the adoption of much stricter therapeutic targets and by embracing the challenge of how these could be attained.

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