Prevention of Complications in Non-Insulin-Dependent Diabetes Mellitus (NIDDM)

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Summary

It is expected that the number of patients with diabetes mellitus will increase in the near future. The high rate of microvascular and macrovascular complications developing in these patients will place an even higher burden on our healthcare systems. Several pathophysiological factors are involved in the development of complications, among which are hyperglycaemia per se, the consequent formation of advanced glycation end-products (AGEs) and the intracellular accumulation of sorbitol. In addition, hypertension and dyslipidaemia also play an important role, especially in the development of coronary heart disease and stroke.

The major therapeutic goals in patients with non-insulin-dependent diabetes mellitus (NIDDM) are to reduce obesity and normalise lipid disturbances and increased blood pressure, in order to improve the well-being of the patient and reduce the risk of the development of late diabetic complications. Often, pharmacological treatment of the hyperglycaemia is necessary, in which case sulphonylureas, metformin, α-glucosidase inhibitors such as acarbose, or insulin may be employed. It is believed that medical interventions, by their effect on improving metabolic control, reduce the incidence and severity of diabetic complications, especially when considering the toxic effects of glucose and the accumulation of AGEs as a consequence of raised tissue glucose levels. This concept is also based on extrapolation of the finding of the Diabetes Control and Complications Trial that intensive glycaemic control in IDDM will prevent the progression of at least the microvascular complications like retinopathy and nephropathy.

There are, however, no long term studies in NIDDM patients to show that treatment with oral antihyperglycaemic agents helps to postpone or prevent complications. It is expected that the UK Prospective Diabetes Study will show whether better metabolic control, either with oral antihyperglycaemics or with insulin, will indeed improve outcome. Several other studies aiming at specific risk factor intervention (hypertension, hyperlipidaemia, lipid oxidation) in NIDDM patients are currently ongoing.

In this review, we discuss the pathophysiology of complications and the current management of non–insulin-dependent (or type 2) diabetes mellitus (NIDDM), and whether current management of NIDDM may retard the development of diabetic complications. Since various excellent reviews have dealt with the pathogenesis of NIDDM and its current management,[1-5] and with its complications,[6-8] the interested reader is referred to these reviews. The results of the recently published Diabetes Control and Complications Trial (DCCT), which shows retardation of the development of complications in patients with IDDM, may be of relevance for the treatment of NIDDM patients as well.[9]

1. Pathophysiology of Non–Insulin-Dependent Diabetes Mellitus (NIDDM)

1.1 Disturbances in Insulin Release and Insulin Sensitivity

NIDDM is a heterogeneous disorder, characterised by defects in insulin secretion as well as reduced insulin action.[1,10,11] In nondiabetic individ-