Glycaemia Control in Diabetes Mellitus
Towards The Normal Profile?

Bruce R. Zimmerman
Mayo Clinic, Rochester, Minnesota, USA

Summary

The Diabetes Control and Complications Trial and the Stockholm Study have conclusively demonstrated that improving the blood glucose control in patients with insulin-dependent diabetes mellitus (IDDM) reduces the risk of developing retinopathy, nephropathy and neuropathy. Each patient with IDDM should be carefully evaluated for the appropriateness of institution of an intensive insulin treatment programme. In particular, the risk of severe hypoglycaemia must be considered and the goals modified if necessary to reduce the risk.

Successful implementation of an intensive treatment programme requires an experienced healthcare team and a knowledgeable and well motivated cooperative patient. Several variations of intensive treatment programmes can be used, with no definite superiority of one treatment method over the others. Individualisation is the key to success. Each programme has the same general principles. Regular insulin is used to control the postprandial glucose excursion and a slow infusion of regular insulin by a pump or injected intermediate or long-acting insulin is used to balance fasting glucose utilisation and production.

The treatment will not be successful without self-monitoring of blood glucose by the patient and frequent adjustment of the insulin doses to compensate for variations in blood glucose levels, diet and activity. The treatment should be followed with quarterly glycated haemoglobin determinations and a regular follow-up plan. During follow-up the main challenge for the healthcare team will be to maintain motivation in the patient and to assist with behaviour modification. A detailed understanding of intensive treatment programmes may be beyond the skill of the average primary care physician, but any physician caring for patients with diabetes will benefit from an understanding of the general treatment principles outlined in this article.
In early 1922 the first successful use of pancreatic extracts to treat diabetes mellitus in humans became widely known. Since then, the problems of insulin production have been overcome and insulin treatment has recently been considered to be 'one of the most dramatic events in the history of the treatment of human disease' (Bliss 1982). Although the problem of treatment-induced hypoglycaemia quickly became evident, it was not until the 1930s that the long term complications of diabetes were recognised and not until 1954 that Lundbaek (1954) proposed a common microangiopathy interrelating the complications. Clearly, insulin injection treatment did not solve all the problems of diabetes.

In the 1920s blood glucose measurements were slow, imprecise, and not widely available. Little was known of insulin composition, structure or physiology. In 1959, Berson and Yalow (1960) developed the immunoassay for insulin allowing measurement of its complex secretory pattern. Even now the pulsatile nature of insulin secretion and its importance is still being explored. Insulin measurements also demonstrated that most patients with diabetes mellitus were not completely deficient in endogenous insulin. In fact, some had normal insulin levels. Gradually, the different types of diabetes were defined.

In the 1960s, studies during which blood glucose levels were continuously measured demonstrated how far insulin treatment methods at the time were from normal physiological patterns (Service et al. 1970). With clinical use of glycated haemoglobin (HbA1c) measurements in the late 1970s, it quickly became obvious that treatment was ineffective in returning the blood glucose to near normal in most patients. Crude methods allowing patients to measure their own blood glucose introduced in the late 1970s were quickly refined into the accurate, rapid methods almost universally available today. Better understanding of glucose/insulin dynamics and self monitoring of blood glucose (SMBG) allowed the use of complex, multiple daily insulin injection (MDI) programmes and insulin infusion pumps (continuous subcutaneous insulin infusion, CSII).

From the time of their recognition, the cause of the long term complications of diabetes was debated (Zimmerman 1992). Gradually, evidence accumulated suggesting that hyperglycaemia was the major determinant of the complications. It was impossible to answer this hypothesis in humans with insulin-dependent diabetes mellitus (IDDM, type I diabetes) until the use of complex insulin programmes coupled with SMBG allowed the patient to adjust each insulin dose, and glycated haemoglobin measurements monitored the success of the treatment. These 3 factors (complex insulin programmes, SMBG and glycated haemoglobin determinations) combined to permit studies which by 1993 had finally shown that returning the blood glucose to near normal reduces the complications of diabetes.

Overall, the Diabetes Control and Complications Trial (DCCT) demonstrated 39 to 74% reductions in retinopathy, nephropathy and neuropathy in patients with IDDM, whether they had clinical evidence of complications at the onset of the trial or exhibited early complications (Diabetes Control and Complications Trial Research Group 1993). The smaller Stockholm Study demonstrated similar findings (Reichard et al. 1993). Together, these studies should have a major impact on the treatment of all patients with diabetes.

Careful review of these 2 studies and numerous other trials attempting glucose control discloses that even the best motivated patients failed to completely normalise their blood glucose over any period of more than a few days. Indeed, in the DCCT trial, less than 5% of patients achieved the intensive treatment goal of HbA1c <6.05% over the entire period of study. Except for pancreas transplantation, no available treatment method can achieve sustained normalisation of blood glucose in patients with IDDM. This article reviews some of the so-called intensive treatment methods available and discusses their application to individual patients.