The use of insulin to improve treatment in type 2 diabetes

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Diabetes is a global problem of increasing proportions and requires adherence to tight treatment targets to prevent complications. This article focuses on the use of insulin to gain good glycaemia control in type 2 diabetes.

The worldwide prevalence of diabetes is projected to increase by 50 per cent in seven years, from 150 million in 2003 to 225 million by 2010 (Zimmet, 2003). This only represents people who have been diagnosed, and due to the insidious, asymptomatic onset of type 2 diabetes many more people may have the condition without being aware of it.

About five per cent of total NHS resources and up to 10 per cent of hospital inpatient resources are devoted to diabetes (Department of Health, 2001). Once perceived as ‘mild’, most patients with type 2 diabetes will die from a cardiovascular event (Haffner et al, 1998). In addition, the condition is now seen in younger patients. In some areas, diagnosis of type II diabetes in children and adolescents now exceeds that of type 1 (Zimmet, 2003).

Treatment targets

The National Service Framework for Diabetes (DoH, 2001) has made reducing complications a priority. There is now conclusive evidence (UKPDS Group, 1998a; UKPDS Group, 1998b) that tight blood pressure and glycaemic control can reduce the incidence of macrovascular and microvascular complications.

Tight blood pressure control among hypertensive patients with type 2 diabetes has also been shown to significantly reduce diabetes-related death and complications (UKPDS Group, 1998a).

Long-term blood glucose control in diabetes is measured with an HbA1c (haemoglobin A1c) blood test. Patients with newly diagnosed type 2 diabetes who are intensively treated to a mean HbA1c of seven per cent experience a significant reduction in complications (UKPDS Group, 1998b).

The management of both hypertension and hyperglycaemia is therefore a high priority in the care of patients with type 2 diabetes.

The treatment pathway

Unless a patient’s symptoms warrant immediate pharmacological intervention, diet and lifestyle changes are usually the first means of controlling hyperglycaemia in newly diagnosed type 2 diabetes. However, because of the progressive β-cell dysfunction associated with type 2 diabetes, patients will eventually need an oral hypoglycaemic agent (OHA) when glycaemic control can no longer be maintained through diet and exercise alone (Turner et al, 1999).

Metformin is the usual first-line monotherapy for patients with a body mass index (BMI) greater than 25kg/m² because it is associated with less weight gain than insulin and sulphonylureas. It is also unlikely to cause hyperglycaemia, and has cardioprotective properties (UKPDS Group, 1998a). When adequate control is not maintained on monotherapy, treatment is most commonly supplemented with a sulphonylurea or a glitazone.

When maximum oral combination therapy fails, insulin should be initiated. In the UKPDS patient population, who were all carefully monitored, half failed to achieve a target HbA1c of less than seven per cent. This suggests that at least 50 per cent of patients with type 2 diabetes will eventually need insulin therapy if they are to maintain tight glycaemic control (Winocour, 2002).

Initially, a single night-time injection of long-acting basal insulin combined with metformin or a sulphonylurea may be sufficient to achieve and maintain glycaemic control. This option also provides the patient with a gentle introduction to insulin.
both insulin and injections, and is often more acceptable than a full basal-bolus regimen requiring four injections a day.

When combination basal insulin and OHAs fail to maintain glycaemic control patients can be offered a step-wise approach to a basal-bolus regimen in which one pre-meal injection of rapid-acting insulin is introduced before the main meal, in addition to the night-time basal insulin. As the condition progresses, pre-meal injections of rapid-acting insulin may be administered before two and, if required, three meals a day to achieve or maintain optimal glycaemic control (Barnett et al, 2003). The use of twice-daily pre-mixed insulin is an alternative to a basal bolus regimen for patients who have regular lifestyles and eating patterns.

Psychological support
Caring for patients with type 2 diabetes is not just about treatment regimens. Patients can be traumatised by their diagnosis and some feel they are to blame, which can create or reinforce low self-esteem and lead to depression. Health care professionals can help by providing psychological support, reassurance and information to enable patients to make informed choices about treatment strategies (DoH, 2001).

There is no doubt that diabetes has a negative effect on quality of life. People with diabetes report lower psychological well-being than those without the disease and, not surprisingly, those who experience complications report a significantly greater negative impact of diabetes on quality of life than those who do not (Bradley and Speight, 2002).

The two most commonly used tools for evaluating treatment satisfaction and quality of life are the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and the Audit of Diabetes-Dependent Quality of Life (ADDQol). DTSQ is valuable for measuring patients’ satisfaction with new treatment strategies. It has shown that although patients view the switch from oral to insulin therapy as a major concern, their satisfaction usually improves after the switch takes place.

The questionnaire does not measure quality of life, although it may be argued that treatment satisfaction is an important influence on this. ADDQol showed the greatest negative impact was on ‘freedom to eat as I wish’. This was true for both insulin and non-insulin treated patients. This suggests that treatments permitting greater dietary freedom, without compromising metabolic control, will improve quality of life for many patients (Bradley and Speight, 2002).

DAFNE (Dose Adjustment For Normal Eating) is a way of managing diabetes that teaches patients to estimate the carbohydrate in each meal and inject the right dose of insulin. It can empower patients with diabetes by helping them take more control of their condition. Adjusting insulin injections to fit lifestyle, rather than the other way round, gives patients the freedom to eat what they want. DAFNE training for 169 adults with type 1 diabetes and poor glycaemic control resulted in significantly improved HbA1c without a significant increase in severe hypoglycaemia. It also resulted in sustained, positive effects on quality of life, satisfaction with treatment and psychological well-being, despite an increase in the number of insulin injections (DAFNE Study Group, 2002).

Barriers to insulin initiation
Patients with type 1 diabetes know that insulin is a life saver, particularly if they have experienced an episode of diabetic ketoacidosis – an acute medical emergency that can result in a mortality rate of 15–28 per cent if not treated appropriately (Jabbour and Miller, 2001).

However, it can be harder to convince patients with type 2 diabetes of the benefits of insulin therapy, particularly if they have only a mildly raised HbA1c and negligible symptoms.

There is a reluctance to commence insulin therapy by both patients and health care professionals, despite its proven benefits for achieving and maintaining glycaemic control (Korytkowski, 2002). While insulin therapy is generally accepted as appropriate for symptomatic, poorly controlled patients, it is often delayed in patients with less marked hyperglycaemia. As a result, patients may experience periods of poor glycaemic control that increase their risk of complications.

The dangers of tardy insulin initiation were shown in a recent US study of 7,208 failed courses of treatment, including those managed without drugs and oral monotherapy. The last HbA1c measurement before treatment initiation ranged from 8.8 per cent to 9.6 per cent; similarly, the last value

REFERENCES

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before treatment was supplemented or abandoned was 8.6–9.6 per cent. As the mean number of months that elapsed before the initiation of alternative or additional treatment ranged from 26.5 to 35.1, the average patient accumulated nearly five years of excess glycaemic burden at an HbA1c of more than eight per cent and ten years at more than seven per cent (Brown et al., 2004).

Recent data from three other countries showed that around 60 per cent of patients have HbA1c greater than 7.5 per cent (Snoek, 2002). There are many reasons for suboptimal HbA1c levels, including the progressive decline of β-cell function, inadequacy of treatment regimens and resistance to polypharmacy and insulin by both doctors and patients (Wallace and Matthews, 2000).

Barriers to initiating insulin therapy include patients’ perception that their diabetes is getting worse, needle anxiety and concerns about hypoglycaemia and weight gain (Korytkowski, 2002). Some patients even see insulin therapy as ‘the medical equivalent of the last rites’ (Wallace and Matthews, 2000). Health care professionals can help to allay disease progression fears by emphasizing, from diagnosis, that insulin initiation is neither a failure of treatment nor of the patient, but a positive progression to a more reliable treatment option offering better glycaemic control.

Needle anxiety generally disappears as treatment commences, but concerns about hypoglycaemia and weight gain are justified. UKPDS showed that the downside of tight glycaemic control is an increase in hypoglycaemic events, and some patients err on the side of hyperglycaemia to avoid the more immediate risk of hypoglycaemia, rather than the seemingly distant prospect of complications. However, the long-acting insulin analogue, insulin glargine, is helping to address this problem because patients experience significantly less hypoglycaemia and weight gain with it (Rosenstock et al., 2001).

A second, recently launched, long-acting insulin analogue, insulin detemir, is currently licensed only as part of a basal-bolus insulin regimen and will therefore be used mainly for patients with type 1 diabetes until the results of studies in type 2 diabetes are known. Preliminary data suggests that insulin detemir, normally administered twice-daily, is associated with a reduced risk of nocturnal hypoglycaemia and weight gain in patients with type 1 diabetes (Home et al., 2004).

A study comparing insulin glargine with traditional insulin for S17 patients with type 1 diabetes, found that patients using it enjoyed greater treatment satisfaction, which was statistically significant and increased over time (Witthaus et al., 2001). Insulin glargine has a similar safety profile to traditional insulin, is at least as effective at lowering HbA1c and has a 24-hour ‘peakless’ activity profile that more closely resembles endogenous insulin secretion than traditional insulins, allowing for once-daily dosing (Owens et al., 2001). Once patients have commenced basal bolus insulin therapy they can find it inconvenient having to inject 20–30 minutes before a meal, reducing the flexibility of mealtimes.

A possible solution is to use rapid-acting analogue insulins (insulin lispro and insulin aspart) that can be injected immediately before a meal. Indeed rapid-acting analogues can control post-prandial glucose fluctuations better than soluble insulin (Owens et al., 2001). The launch of a third rapid-acting analogue, insulin glulisine, is anticipated in the UK during 2005.

Implications for practice
Due to the progressive nature of type 2 diabetes, at least half of patients who develop the condition will eventually require insulin therapy. Health workers should discuss the possibility of insulin therapy soon after diagnosis during the development of an agreed management plan. By addressing the issue early, patients can be educated to see insulin as an effective method of maintaining glycaemic control.

Insulin therapy should be initiated sooner rather than later to protect patients from the risk of complications. Indeed, early initiation of insulin can improve clinical outcomes and treatment satisfaction. With more insulin initiation taking place in primary care, patients will have the reassurance of ongoing support from their usual diabetes support team, who are familiar, local and accessible, making it easier to adjust to life on insulin therapy.

Strategies that contribute to the empowerment of patients, such as DAFNE, can help them to take more control of their condition. Similarly, benefits associated with the new rapid and long-acting insulin analogues can help patients to improve glycaemic control while reducing the risk of the unwanted side-effects of hypoglycaemia and weight gain.