Insulin initiation in primary care

Roger Gadsby

Article points

1. Treatment plans for people with type 2 diabetes are being managed increasingly within the primary care setting.
2. Recent ADA/EASD guidelines recommend that insulin treatment is initiated early.
3. When selecting an insulin regimen, the person's preferences and lifestyle should be taken into consideration.
4. Long-acting insulin analogues have been shown to have a number of advantages over NPH insulin.
5. People who understand their condition and are actively involved in its management are more likely to have better control of their blood glucose levels.

Key words

- Insulin initiation
- Insulin regimens
- Education

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Initiating insulin treatment has often been seen as a last resort for people with poorly controlled type 2 diabetes, where HbA_{1c} levels are >7.5 % and have been so for some considerable time (Brown et al, 2004). However, guidelines published by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD; Nathan et al, 2006) recommend early initiation of insulin treatment as an option for people who do not achieve target HbA_{1c} levels. The aim of this article is to discuss the management of glycaemia in people with type 2 diabetes in primary care and to outline the insulin regimens available. In addition, the mechanics of initiating insulin treatment, approaches to achieve optimal insulin doses, and the importance of structured education programmes for people with diabetes are also discussed.

Type 2 diabetes accounts for more than 85% of diabetes in the general population – the incidence is higher in people of South Asian and Afro-Caribbean origin than in Caucasians. Although more frequently diagnosed in people over the age of 40 (DoH, 2001), there is a worrying increase in incidence in children and young adults (Drake et al, 2002).

To address this increasing burden on the NHS, the DoH published the *National Service Framework for Diabetes: Standards* (DoH, 2001), with the aim of encouraging a 'shared care' approach to the management of diabetes. The nGMS contract, through the quality and outcomes framework, also encourages a more primary-care focused service for the management of diabetes. As a result, treatment for people with type 2 diabetes is being managed increasingly within the primary care setting.

The clinical management of type 2 diabetes

Type 2 diabetes is a progressive condition, initially characterised by insulin resistance. The pancreatic ß-cells attempt to compensate for this tissue resistance by producing more insulin, eventually resulting in ß-cell failure. Although lifestyle changes to improve diet and increase physical activity are key factors in improving glycaemic control, the majority of people with type 2 diabetes will require drug intervention.

Current practice is to prescribe metformin when lifestyle changes fail to control blood glucose levels adequately. In fact, the ADA/EASD guidelines recommend that metformin should be prescribed on diagnosis since lifestyle changes alone are ineffective in the long-term (Nathan et al, 2006). This is a controversial recommendation as many people fear that introducing metformin at the same time as lifestyle change may result in people relying on the tablet rather than concentrating on the challenging but more powerful treatment of lifestyle change. It should be emphasised to people on metformin that lifestyle changes could result in them coming off the drug, however, a reason for starting and continuing metformin is for its cardioprotective qualities.

Current practice states that when oral hypoglycaemic agent (OHA) monotherapy fails to control blood glucose adequately, dual and even triple OHA therapy may be considered. Initiating insulin therapy has, to date, been the final step in the process. The ADA/EASD consensus statement recommends that insulin be considered as an add-on to metformin in people whose HbA_{1c} levels are >8.5 % or for those with symptoms secondary to hyperglycaemia (Nathan et al, 2006).

Managing type 2 diabetes in primary care

With the shift in focus to primary care for the diagnosis and management of people with type 2 diabetes, it is important that primary health care teams develop appropriate guidelines. These guidelines should outline processes for the following.

- Early identification and assessment of people with undiagnosed diabetes.
- Regular patient review and maintenance of wider metabolic control.
- Early detection and management of long-term complications.
- Management of acute diabetic complications.
- Prevention of diabetes in at-risk groups.

A report by Diabetes UK (2006) outlined the key elements for the effective management of diabetes in primary care, which includes the following.

- A planned programme of care for all people with diabetes.
- Clear management plans agreed with the person with diabetes, tailored to meet the needs of individuals and their carers.
- Practice-based diabetes registers to facilitate regular call and recall of patients.

Intensive glycaemic control and the impact on long-term complications of diabetes

Diabetes can lead to significant vascular damage. Microvascular damage can result in retinopathy, nephropathy and neuropathy, while macrovascular damage results in cardiovascular disease, stroke and peripheral vascular disease. In people with diabetes, mortality rates from CVD are up to five times higher and the risk of stroke up to three times higher compared with people without the condition (DoH, 2001).

In 1998 the UKPDS Group published its findings, which demonstrated that intensive glycaemic control, leading to a reduction in HbA_{1c} levels, is associated with a reduced risk of long-term complications (UKPDS, 1998).

NICE recommend target HbA_{1c} levels of 6.5–7.5 % (NICE, 2002). The NSF for diabetes defines poor glycaemic control as HbA_{1c} ≥7.5 % (DoH, 2003). The joint ADA/EASD consensus statement states that an HbA_{1c} >7 % should be considered as a prompt to commence or change treatment (Nathan et al, 2006).

Currently available insulin regimens

When selecting an appropriate insulin regimen, the person's preference and lifestyle should be taken into consideration. It is also important to measure HbA_{1c} levels at regular 3-monthly intervals to ensure optimal treatment (HbA_{1c}<7 %), then every 6 months (Nathan et al, 2006). There are three main options:

1. Continue OHA and add a basal insulin.
2. Continue metformin therapy and add a twice-daily pre-mixed insulin.
3. Change from oral treatment to a basal–bolus insulin regimen.

1. OHA plus basal insulin

This relatively simple treatment regimen is appropriate for the majority of individuals, many of whom may initially be reluctant to commence insulin treatment. In addition, because of the reduced risk of weight gain and hypoglycaemia, it is particularly appropriate for overweight individuals; and also for older symptomatic individuals where intensifying treatment would risk hypoglycaemia.

The most frequently used basal insulins in type 2 diabetes were NPH insulins until April–June 2004 (Information Centre, 2007). However, there are limitations associated with NPH insulin formulations, which include the following.

- Variable absorption.
- Unwanted peaks of action during the night.
- Insufficient duration of action.
- The need to mix thoroughly before injection.

In clinical trials, the more recently available

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1. Currently, NICE recommends the use of insulin glargine with an OHA in people who need help to administer their insulin, who have recurrent hypoglycaemic episodes or who would otherwise require two daily injections of insulin in combination with oral therapy.
2. Insulin detemir, a long-acting insuilin analogue, has recently been licensed for use with OHAs in people with type 2 diabetes.
3. The twice-daily regimen was the most commonly prescribed in the UK for people who were converting from OHA treatment to insulin treatment.
4. A basal–bolus insulin regimen may be an appropriate next step for individuals whose HbA1c level is consistently higher than the target.
5. It has been shown that people who understand their condition and are actively involved in the management of their diabetes are much more likely to have good control of their blood glucose levels.

insulin analogues, insulins glargine and detemir have been shown to have a number of advantages over NPH insulin (Lepore et al, 2000; Plank et al, 2005). Because of their pharmacokinetic profiles, these insulin analogues provide a constant delivery of insulin over a 24-hour period and, hence, a reduced risk of hypoglycaemia (Lepore et al, 2000; Plank et al, 2005). They can also be administered at any time of day, as long as it is the same time each day.

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Insulin detemir, a long-acting insulin analogue, has recently been licensed for use with OHAs in people with type 2 diabetes. It has not yet been subject to a NICE review.

2. Metformin plus twice-daily pre-mixed insulin

The twice-daily regimen was the most commonly prescribed in the UK for people who were converting from OHA treatment to insulin treatment (Gadsby, 2003). However, the nature of the regimen means that the individual ideally must have regular eating habits, eating three meals a day at similar times.

Long-acting insulins complexed with protamines (NPH insulins) and short-acting human insulin pre-mix preparations are commonly used. There are also the more recently available pre-mixes containing the rapid-acting insulins; insulins aspart, lispro and glulisine.

3. Basal–bolus insulin

A basal–bolus insulin regimen may be an appropriate next step for individuals whose HbA_{1c} level is consistently higher than the target with OHA plus basal insulin or metformin plus twice-daily pre-mixed insulin regimens. It provides more flexibility for the individual since it involves one basal insulin injection and two or three pre-meal injections. The advantage of this regimen is that it results in an insulin profile that is closer to that of a healthy individual, provided that the person with diabetes is well-motivated and educated, and able and willing to self-adjust their insulin.

For people who are reluctant to start a full basal–bolus regimen, the 'basal–plus' approach may be considered, where one mealtime short-acting insulin dose is added at the main meal and further doses added to the other meals if glucose control deteriorates further while continuing on basal insulin and OHAs.

Bolus insulin

Until recently, regular human insulin (RHI) was used as the bolus or mealtime insulin. However, the rapid-acting insulin analogues, insulins lispro, aspart and glulisine, demonstrate a number of benefits over RHI. These analogues have been designed to be shorter acting than RHI and more closely match the endogenous secretion of insulin in healthy people at mealtimes. They can be taken directly before a meal, unlike RHI which should be taken 15–30 minutes before a meal, although they can be taken shortly after a meal if forgotten beforehand.

Initiating insulin treatment in primary care

The decision to commence insulin treatment, and the choice of insulin regimen in people with uncomplicated type 2 diabetes can be done by the primary care team following discussion with the person with diabetes. It has been shown that people who understand their condition and are actively involved in the management of their diabetes are much more likely to have good control of their blood glucose levels (Heisler et al, 2002). In fact, it is one of the standards in the NSF for diabetes (DoH, 2001) that people with diabetes are empowered through, for example, educational programmes to maximise control over their diabetes.

Individuals with co-existing conditions (such as renal impairment, thyroid disease or coeliac disease) should be referred to specialist care. This is also the case for pregnant women and for women who plan to become pregnant, where specialist antenatal care is necessary.

Appointments

The first appointment should be arranged at a time convenient to the person with diabetes and then appointments can be made for the following 4–5 days as necessary, to ensure that the individual is comfortable and confident with the regimen and injection technique. Driving restrictions should be discussed until control is settled. The duration of these appointments should be guided by the extent of assistance and reassurance required. Some of these can be telephone appointments rather than face-to-face. Further appointments should be organised for the following week, month, and then in 2–3 months time.

Insulin starting dose and dose titration

When deciding on a starting dose, it is preferable to start on a low dose and titrate up to a higher level. Target blood-glucose levels should be agreed with the individual and the dose adjusted according to the pattern of results, recorded by the individual.

OHA plus basal insulin

A starting dose of 10 units (depending on the weight of the individual) is usual for both NPH insulin and the long-acting insulin analogues. The dose can then be titrated up by 2 units every 3–7 days, provided there is no apparent hypoglycaemia, until the fasting blood glucose target level has been achieved. *Table 1* shows an insulin titrating schedule for an OHA plus basal insulin regimen.

Twice-daily insulin

Depending on the weight of the individual, a starting dose of 6–10 units insulin is usual. The dose can be adjusted according to the individual's planned level of activity. *Table 2* shows an insulin titrating schedule for twice-daily insulin regimens.

Basal–bolus insulin

For individuals who commence a basal–bolus insulin regimen without experience of a previous insulin regimen, the recommended approach based on the common practice of GPs and DSNs is to take one-third of the total daily insulin dose as the long-acting insulin and to divide the remaining two-thirds between the three main meals.

For those who add a mealtime insulin dose to their once-daily basal insulin regimen, the current dose of basal insulin can be continued and the rapid-acting insulin injected before each meal.

Blood glucose levels should be measured regularly and the insulin dose adjusted by 2–4 units, according to the pattern of the results.

Overcoming barriers to successful insulin initiation: Education and support

The progression to insulin treatment poses a number of concerns for many people with type 2 diabetes, and their healthcare professionals which may, in some cases, delay treatment. These include the following.

- Anxiety over the perceived complexity of insulin treatment.
- Fear of needles and injecting.
- Concern over treatment side-effects, such as weight-gain and hypoglycaemia.
- A fear that starting insulin treatment means that their diabetes is out of control.

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2. When deciding on a starting dose, it is preferable to start on a low dose and titrate up to a higher level.
3. The progression to insulin treatment poses a number of concerns for many people with type 2 diabetes.

Table 1. Example of dose adjustment for long-acting insulin analogues in combination with OHAs (adapted from: Barnett et al, 2003).

Fasting plasma glucose (mmol/l)	Adjustment to insulin dose (IU)
5.5–6.7	Increase by 2
6.8–7.8	Increase by 4
7.9–10.0	Increase by 6
>10.1	Increase by 8

If hypoglycaemia occurs, then insulin should be reduced and diet and timing of meals assessed.

Table 2. Example of dose adjustment for insulin with twice-daily mixtures (adapted from: Royal College of Nursing, 2006).

Blood glucose level before evening meal (mmol/l)	Adjustment to breakfast insulin dose (IU)
4–7	No change
7.1–9	Increase by 2
>9	Increase by 4
Blood glucose level before breakfast (mmol/l)	**Adjustment to evening meal insulin dose (IU)**
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>9	Increase by 4

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1. Highlighting the benefits of good blood glucose control and the natural progression of diabetes treatment to insulin may help to improve treatment adherence and therefore glycaemic control.
2. People with diabetes should be offered structured education programmes, starting from diagnosis and continuing through their long-term care.
3. The future of type 2 diabetes management depends largely on primary care teams taking control of treatment plans and providing structured education programmes and support for people with type 2 diabetes.

- Concern over potential loss of job.

The majority of concerns can be addressed by providing information and support. Highlighting the benefits of good blood glucose control and the natural progression of diabetes treatment to insulin may help to improve treatment adherence and therefore glycaemic control.

Following the NSF for diabetes, NICE recommend that people with diabetes should be offered structured education programmes, starting from diagnosis and continuing through their long-term care (NICE, 2003). Indeed, all PCTs are obliged to provide structured education programmes for people with diabetes. A report produced jointly by the DoH and the Diabetes UK Patient Education Working Group outlined the components of a long-term structured education programme (DoH, 2005). These include the following.

- The nature of diabetes.
- The importance of good glycaemic control.
- Interpreting the results of blood glucose monitoring.
- The treatment options.
- Injection technique and dose titration.
- Recognising a hypoglycaemic event and how to counter it.
- Foot care and hygiene.
- 'Sick day' rules.

Conclusion

The future of type 2 diabetes management depends largely on primary care teams taking control of treatment plans and providing structured education programmes and support for people with type 2 diabetes. The need for intensive glycaemic control, alongside other metabolic factors, to reduce the incidence of long-term complications is clear. Initiating insulin treatment earlier and selecting the most appropriate regimen may be a key factor in reducing the impact of the complications of diabetes, not only on the individual but also on the NHS. ■

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