Hyperglycaemia in diabetes: what next?

PAT J. PHILLIPS MB BS, MA, FRACP

This new series is aimed at helping the busy GP diagnose and manage patients with diabetes and its complications. How would you manage the following case?

Case history

Leo is 67 years old and has had type 2 diabetes for 12 years. He was a council worker and now lives frugally on the pension with his wife, Betty, aged 62. He takes gliclazide (Diamicron, Glyade, Nidem), two 80 mg tablets twice daily, and metformin, two 500 mg tablets three times daily. He also takes medication daily for his:

- high blood pressure – lisinopril 20 mg, hydrochlorothiazide 12.5 mg
- high cholesterol – atorvastatin (Lipitor) 20 mg
- gastro-oesophageal reflux – omeprazole (Losec, Acimax, Maxor, Probitor) 20 mg
- cardiovascular protection – enteric coated, low dose aspirin 100 mg.

Leo has had panretinal laser therapy for preproliferative diabetic retinopathy and has had microalbuminuria for the past five years. He is troubled by 'pins and needles' in his feet, particularly at night. He has lost a few kilograms in weight since his last visit six months ago (from 87 to 84 kg) and 'feels fine'.

Leo's blood glucose profile is as follows:

- breakfast-time 9 to 11 mmol/L
- lunchtime 7 to 9 mmol/L
- teatime 6 to 8 mmol/L
- bedtime 8 to 10 mmol/L.

Leo's HbA_{1c} has increased from 8.1 to 9.3% over the past six months.

What's your next step?

Check for correctable causes of hyperglycaemia.

- Could Leo's lifestyle be healthier? Could he 'eat less, walk more'? Leo is 1.78 m tall. His BMI is his weight (kg) divided by his height $(m)^2$, that is 84 divided by 1.78^2, which is 26.5 kg/m^2. A healthy BMI is 20 to 25 kg/m^2, overweight 25 to 30 kg/m^2 and obese more than 30 kg/m^2. As a rough rule, healthy weight is approximately height (cm) minus 100, which is 78 kg in Leo's case. Leo's weight has decreased over the past six months, but this probably reflects hyperglycaemia and glycosuria (or underlying illness) rather than a healthy lifestyle.
- Is Leo taking his medication? After all, tablets only work if you take them. In the rule of thirds, one third of patients take medication as directed, one third take it but incorrectly and one third don't take it at all.
- Has Leo developed a further medical problem, such as an infection (e.g. urinary tract infection), cancer (e.g. intra-abdominal cancer) or other endocrine condition (e.g. apathetic hyperthyroidism)?

How will you convince Leo to start insulin?

Theoretically Leo could try adding a glitazone to his medications and this might control his blood glucose. However, at the time of writing, the glitazones were not on the Pharmaceutical Benefits Scheme and Leo probably would not be able to afford about $150 per month for a private script. Leo should, therefore, be given insulin to control his hyperglycaemia.

Patients (and their doctors) often have justified and unjustified fears of insulin. It may be helpful to do the following:

- Show Leo an insulin syringe and explain to him that the injections do not hurt. Often the injections are painless and certainly they are much less hassle than the blood glucose testing he is doing at present.
- Explain that the wide blood glucose swings that occur in type 1 diabetes (that people associate with the insulin injections) do not occur to the same extent in type 2 diabetes. In type 2 diabetes, insulin secretion continues and can increase or decrease to compensate to some degree if too little or too much insulin is given.
- Explain that as diabetes progresses, so must the treatment progress. Insulin use is an expected, not extreme, measure.
- Stress that insulin will control Leo's diabetes and make complications less likely. Some people associate insulin treatment with deteriorating diabetes, losing vision or limbs, or having heart attacks or strokes. Leo already has significant microvascular disease affecting his eyes, kidneys and nerves. This will progress unless he controls his blood glucose.
- Point out that the insulin preparations used today are identical to human insulin, extremely pure, and very unlikely to cause problems at injection sites. He will not become 'addicted'. Insulin is just another medication, like the tablets he is taking, but it is

Dr Phillips is Senior Director, Endocrinology Unit, North Western Adelaide Health Service, The Queen Elizabeth Hospital, Woodville, SA.

injected rather than swallowed.
- Appeal to Leo's pocket. He will save money by taking insulin. His medication schedule will cost less.

What should you start with?

The KISS principle applies: keep it safe and simple. Night-time insulin and daytime metformin have been shown to be the best starting schedule, resulting in less hypoglycaemia, less weight gain and better blood glucose control.[1,2] Bedtime insulin controls blood glucose through the night and gets the next day off to a good start. Daytime metformin (e.g. one 850 mg or 1 g tablet at breakfast and at teatime) will help control daytime blood glucose and also help Leo to control his weight. Start low and go slow (e.g. 10 units of intermediate insulin at bedtime): you don't want to give Leo a 'hypo' on his first night of insulin treatment.

Injections are convenient and easy with the new devices that can be used for preparations of short acting and isophane insulin (e.g. the pen injectors and other similar devices).[3]

A diabetes nurse and dietitian will help simplify the process and can review Leo's lifestyle habits and diabetes routines. Leo will need to 'eat less and walk more' if he is not to regain the 3 kg he has lost (and probably put on more). He has previously had glycosuria, losing energy sources from the body. As his blood glucose comes under control this energy source will be restored. Eating less and walking more will help to maintain energy balance and, ideally, will achieve a net energy deficit that will be associated with gradual weight loss towards his healthy weight.

Case continued

Leo follows your recommendations on medication and lifestyle changes. His blood glucose profile is now:
- breakfast-time 8 to 10 mmol/L
- lunchtime 6 to 8 mmol/L
- teatime 5 to 7 mmol/L
- bedtime 7 to 9 mmol/L.

What should you do now?

The goal is for the night-time insulin to control Leo's fasting blood glucose. Increase the night-time dose of insulin at intervals of several days in, for example, 2 to 4 unit increments, depending on the response. In Leo's case, his fasting blood glucose is still fairly high (ideal level is 4 to 6 mmol/L),[4] so increase by 4 units (from 10 to 14 units) and review the situation in two to three days' time.

Case continued

All went well for the next two years. Leo's night-time insulin dose is currently 28 units and his fasting blood glucose is on target. However, his HbA_{1c} is now 8.4% (ideal value is less than 7%) and his blood glucose profile is:
- breakfast-time 4 to 7 mmol/L
- lunchtime 7 to 9 mmol/L
- teatime 7 to 9 mmol/L
- bedtime 8 to 10 mmol/L.

What should you change?

You cannot increase the night-time insulin dose for fear of causing night-time or morning hypoglycaemia. Leo needs more hypoglycaemic medication through the day. Increasing the metformin dose might help (as long as his renal function is normal and he is not having gastrointestinal side effects), but he is likely to need a second dose of insulin to control daytime glycaemia.

A short acting insulin at breakfast-time could control the lunchtime blood glucose level but not the evening level and might cause hypoglycaemia in mid-morning with associated extra food intake and weight gain.

Try giving Leo a second dose of his intermediate insulin at breakfast-time and titrate the dose to control his evening blood glucose. Generally, as the evening blood glucose level comes under control the lunchtime level follows. If this does not happen, short acting insulin before breakfast can be added to the schedule (ideally using a second differently coloured pen injector to minimise the risk of mixing up the two insulin types).[1,2]

With short acting insulin (neutral) injections, administration 30 to 40 minutes before meals is recommended to allow the action of insulin to better match the mealtime glucose input. With intermediate insulins, injections can be given before, at, or even after meals since these preparations have a very slow onset of action. The newer, very short-acting insulin analogues (lispro [Humalog], aspart [NovoRapid]) start working very quickly and administration is more convenient since they can be given immediately before meals.

Summary

The main points that are highlighted by this case are:
- remember that insulin will be needed by many patients with type 2 diabetes
- start insulin sooner rather than later
- start with night-time intermediate (isophane) insulin and daytime metformin
- titrate doses of each insulin according to the blood glucose that insulin controls
- aim to achieve an HbA_{1c} under 7%. MT

References

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