

Adding insulin to hypoglycaemics

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The first three medication steps in long-term glycaemic control for people with type 2 diabetes are relatively easy - the use of one, then two and then three hypoglycaemic agents - but doctors and patients are often reluctant to take the next step and may unnecessarily delay starting insulin therapy.

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he Diabetes Australia guidelines for the first line primary care of adults with type 2 diabetes, Diabetes Management in General Practice, suggest an evidence-based hierarchy for the use of hypoglycaemic agents, as shown in Figure 1.1 Most GPs start with metformin, add a sulfonylurea and then consider adding a glitazone or one of the newer glucagon-like peptide-1 (GLP-1) therapies (exenatide and the dipeptidyl peptidase-4 [DPP-4] inhibitors, or gliptins). However, despite taking maximal doses of several hypoglycaemic agents, most patients with type 2 diabetes will need insulin therapy some five to 10 years after diagnosis to achieve good glycaemic control.2

Doctors and patients often persist with trying different hypoglycaemic agents rather than taking the next step in glycaemic control, the starting of insulin therapy. The initiating of insulin therapy is, therefore, a 'game changer' in diabetes management for both patient and doctor. This article is the third in a series reviewing clinical situations that indicate a major change in the level of risk of diabetes-related complications and prompt the need for a major review of diabetes management. It reviews some of the issues confronting the people on both sides of the surgery desk when insulin therapy becomes necessary, and suggests strategies to address them.

HYPOGLYCAEMIC AGENTS AND INSULIN USE IN TYPE 2 DIABETES1* Start with metformin Add a sulfonylurea (gliclazide, glimepiride, glipizide) Add: a glitazone (pioglitazone, rosiglitazone)† or · GLP-1 therapy (exenatide, saxagliptin, sitagliptin, vildagliptin)‡§ Consider additional use of acarbose for postprandial hyperglycaemia Then start insulin, usually in combination with oral hypoglycaemic agents. (Insulin initiated as basal therapy or as premixed insulins)

ABBREVIATIONS: GLP-1 = glucagon-like peptide-1.

- * Only PBS listed medications are listed.
- † Rosiglitazone is not authorised for triple therapy or for use with insulin; it is approved only as dual therapy with metformin or a sulfonylurea where combination therapy with metformin and a sulfonylurea is contraindicated or not tolerated.
- ‡ Exenatide is approved for use as dual or triple therapy with metformin and/or a sulfonylurea.
- § Dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins) are PBS-subsidised only for dual therapy with metformin or a sulfonylurea where combination therapy with metformin and a sulfonylurea is contraindicated or not tolerated.

Figure 1. Hierarchy of use of PBS-listed hypoglycaemic agents and insulin in type 2 diabetes.

(Adapted from: Harris P, Mann L, Phillips P, Webster C. Diabetes management in general practice. 18th ed. 2012/13. Canberra: Diabetes Australia; 2012.1)

ISSUES FOR PATIENTS (AND DOCTORS) WHEN STARTING INSULIN

Failure - They have 'failed' to 'control' blood glucose levels

Blame/shame – They did not try hard enough and did not 'comply' with management recommendations

Inadequacy - They feel unable to deal with the complexity of the required insulin and lifestyle regimens

Fear - They worry that all the scary stories and old wives tales they have heard are true

Lack of support - They feel they are on their own and unable to cope

ISSUES FOR PATIENTS

Patients with type 2 diabetes may be confronted by a sense of failure, blame and/or shame, inadequacy, fear and lack of support when insulin therapy is required to achieve good glycaemic control, as summarised in the box on this page.³ Doctors too may face these issues.

Patient issue 1. Failure: 'I really did trv ...'

The patient is confronted by his or her failure to control their blood glucose levels (BGLs) and/or to comply with their lifestyle and medication regimen.4 (The italicised words here are often used in consultations and may enhance the patient's sense of failure.)

Response

Type 2 diabetes is a progressive disease and hypoglycaemic medication must also progress to keep BGLs on target. Insulin resistance progressively increases and insulin secretion capacity progressively decreases with time (Figure 2).^{5,6} Once insulin resistance has increased beyond the capacity of insulin secretion, BGLs progressively increase and the need for hypoglycaemic medication also progressively increases.

There are a limited number of oral hypoglycaemic agents available, and their doses can only be increased so much. The need for insulin is not the end of the road but another step on the road of treatment, a step that should be expected and not seen as extreme.

Patient issue 2. Blame and shame: 'I should have tried harder ...'

Some people like naming and shaming, and type 2 diabetes is often seen as the person's fault. After all, 'If they weren't so greedy, lazy and fat, they wouldn't have got diabetes in the first place and if they had the gumption to get off their backsides and do what they were told, it would still be under control'.

Patients are told, 'You are in control, you are responsible for your future health', but really they do not have the capacity to control the pathophysiology that progressively increases glycaemia. These patients are not in control and should not be held accountable when things go wrong.

Response

The issue should be identified and discussed. An analogy that can be used is that people become physically and mentally older with time. It is true that a healthy lifestyle can improve a person's health and extend his or her healthy lifespan, but everyone gets old. No one likes it much but most people will accept it, although it may not be easy, and then get on with their lives.

The need for insulin therapy is part of living with type 2 diabetes – the longer a person lives with diabetes, the more likely insulin will be needed. Taking insulin is much better than the alternative of hyperglycaemia impairing quality of life in both the short term by symptoms (e.g. tiredness, fatigue, polyuria and infections) and in the long term by microvascular and macrovascular complications.

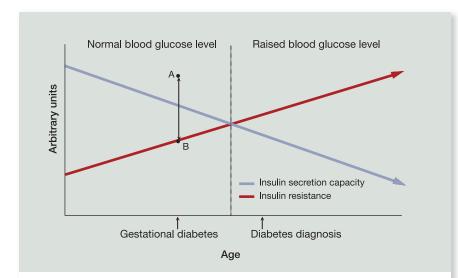


Figure 2. Insulin resistance and secretion capacity. In a person developing type 2 diabetes, insulin resistance progressively increases with time and insulin secretion capacity progressively decreases. Once insulin resistance exceeds insulin secretion (after the point of intersection), the blood glucose level progressively rises. Diagnosis of diabetes usually follows shortly after the point of equivalence. Pregnancy temporarily increases insulin resistance to above the insulin secretion capacity (A), precipitating gestational diabetes, which resolves at delivery as insulin resistance decreases back to below the insulin secretion capacity (B).

Patient issue 3. Inadequacy: 'It's too hard, I couldn't cope and I certainly couldn't give myself an injection'

Using insulin is seen by patients as complicated: needles, syringes, insulin vials, special diets, special tests, many different health professionals to see, much to learn and many ways to make mistakes.

It is true that in the 'old days' (15 to 20 years ago) insulin therapy was quite complicated: two or more injections a day; insulin drawn from a vial after first injecting air into it; using a syringe with a scale that was difficult to read; and blood glucose monitoring with a bulky meter that needed a large drop of blood (sometimes difficult and painful to get) and which took several minutes to complete. Nowadays when starting insulin therapy, only one injection a day is needed; a pre-loaded pen injector is used, dialling the dose and injecting it;

and blood glucose tests are performed using a small meter that only needs a tiny drop of blood and takes seconds to give

Nonetheless, many people find it hard enough to cope with the current demands made on them, such as work, finances, family, friends and other medical problems. Starting insulin was not on their agenda, and it all seems too much.

Patients who are already taking insulin can be valuable resources as believable advisors for people starting insulin therapy, providing reassurance from their own personal experience of starting and living with insulin. Experienced GPs, practice nurses and Credentialled Diabetes Educators can draw on their involvement with many people who have not had problems starting insulin and who have commented how much easier it was than they expected and how much better they felt afterwards.

COMMON CONCERNS ABOUT INSULIN THERAPY AND SUGGESTED RESPONSES

- · Injection will be painful
 - Demonstrate that today's fine needles do not hurt
- Insulin treatment will lead to addiction
 - People with diabetes inject insulin because the gut would destroy it if taken by mouth
 - Millions of people take insulin but they are not addicted to it
- · Weight gain
 - Weight gain (approximately 2 kg in first year for each 1% [11 mmol/mol] decrease in A,) can occur but can be avoided if lifestyle changes are made (eating less/walking more)
- Insulin will worsen glycaemic control
 - Large swings in blood glucose levels are common in people with type 1 diabetes taking insulin but blood glucose levels are more stable in people with type 2 diabetes taking insulin
- Insulin will cause complications
 - Insulin improves diabetes control and thus reduces the risk of complications
- · Insulin is the end of the road
 - Insulin is an expected step on the road of diabetes treatment after lifestyle change and maximum oral hypoglycaemic therapy
- Loss of independence
 - The routines of insulin therapy are easy to learn and perform, and almost anyone can manage insulin therapy
- Employment issues
 - Few occupations bar people using insulin. Diabetes Australia has an advocacy officer who can provide advice if discrimination occurs
- · Loss of driver's licence
 - The rules differ between states and territories in Australia but usually licences may be held by people using insulin subject to medical advice on capability



Patient issue 4. Fear: 'My neighbour's uncle started insulin and he lost his leg six months later'

Common concerns about insulin therapy include pain, addiction, weight gain, risk of hypoglycaemic episodes, loss of independence, employment restriction and loss of driving licence. Suggested responses to these and other concerns are discussed below and summarised in the box on page 53.

Pain

The needles for pen injectors are so fine that most injections are painless, with only a sense of pressure from the needle; rarely will a minor prick be felt. It is recommended that readers who have not experienced this themselves do so: no one is more convincing than someone who knows from personal experience. Insulin is given by injection because if given orally it would be digested before being absorbed.

Addiction

Usually insulin therapy will be continued

indefinitely once started. This, however, is also true in many cases for medications for high blood glucose and lipid levels and for high blood pressure. People do not become addicted to insulin or any other of these medications.

Weight gain

An increase in weight is common with insulin therapy, partly because reducing BGLs also reduces glycosuria and therefore stops the loss of glucose (and its energy). Modest lifestyle changes can, however, counter this.

Hypoglycaemia

The risk of hypoglycaemia is very low for people with type 2 diabetes starting insulin. This is because continuing endogenous insulin secretion can be switched off if too much insulin is given, inadequate carbohydrate is eaten or extra physical activity is taken. With time, however, this endogenous insulin secretion and the protection from hypoglycaemia it offers is lost; this usually occurs many years after starting insulin.⁷

Complications

Clinical trials have shown that for each 1% (11 mmol/mol) decrease in glycosylated haemoglobin (A_{1c}) the risk of microvascular complications decreases by 25 to 30%.⁸ Some people with type 2 diabetes starting insulin have had poor glycaemic control for many years and have already developed complications. These people may blame insulin therapy for the complications when they cause problems, such as neuropathy predisposing to foot problems and amputation.

End of the road

Insulin is an expected step on the road to lifelong glycaemic control.

Independence

People usually find it easy to learn and carry out the routines of insulin therapy and to fit them into their daily lives. Insulin injectors and blood glucose meters are easy to use; people with limited visual acuity or manual dexterity can use the larger Innolet device (Figure 3).

Employment

In the author's experience, the only occupation barred for people using insulin is a commercial airline pilot. In some professions (e.g. the police force), they may be barred from certain sections of the workforce, but employers usually make arrangements for them to continue employment in another section.

Motor vehicles licence

Rules vary between the Australian states and territories but private and commercial vehicle driver's licences are available to people using insulin subject to medical advice on driver capability.⁹

Patient issue 5. Lack of support: 'There's so much to learn and no one can help me'

The patient starting insulin therapy has much more to cope with than does his or her doctor, who only has to decide the injector, insulin type, starting dose and titration schedule and can refer to fellow medical, allied health and nursing professionals for advice. The patient has to cope with the threat to self-esteem and the changes in self-image, and with the daily routines and lifestyle, not to mention the senses of failure, shame and blame, inadequacy and fear discussed earlier. There is a lot to learn about, including insulin, food values, injections, dose adjustment, blood glucose testing and precautions. No wonder the patient wants help.

Response

Apart from any support GPs and practice nurses can provide, the allied health and nursing professionals consulted by patients to help with the practical issues related to insulin therapy can also help them cope with the psychological issues. However, a referral for specific psychological support (e.g. a counsellor or psychologist) may be worthwhile. There is also an online counselling service. Diabetes Counselling Online (www. diabetes counselling.com.au).

ISSUES FOR DOCTORS

In a general practice population of 1000 adults, about 40 will have known type 2 diabetes.¹⁰ Assuming 50% of these require insulin therapy within five to 10 years to maintain A_{1c} below 7%,² only two or three of these patients will start insulin each year. Starting insulin is, therefore, not a familiar or routine process in many general practices. A GP's only personal experience may have been as a student or junior doctor in hospitals where glycaemic control with insulin was difficult, and wide blood glucose swings and hypoglycaemia were common.

Doctors may experience some of the senses of failure, shame and blame experienced by patients when they cannot control a patient's BGL, but the more common barriers to insulin therapy on the doctor's part are dealing with the patient's concerns and with their own lack of experience and expertise in insulin therapy. One response to these issues is to refer the patient to a specialist or GP colleague who has the skills and systems for insulin therapy but this breaks the continuity of care and leaves the doctor without the background to deal confidently with any subsequent problems with insulin. It is much better for the doctor to decide that insulin is needed and to coordinate the process of insulin initiation and titration, liaising with a specialist colleague and a certified diabetes educator if necessary.

Insulin therapy in type 2 diabetes used to be complicated, and a team of specialised hospital-based medical, nursing and allied health professionals were needed. Nowadays, the process is much simpler and, with more support in primary care, GPs can easily manage it. This support includes:

SIX STEPS TO STABLE SUGARS IN PATIENTS WITH TYPE 2 DIABETES¹¹

The KISS - or 'Keep insulin safe and simple' - approach involves the six steps to stable blood glucose levels (BGLs) outlined below.

Before starting a patient with type 2 diabetes on insulin

- Step 1. A_{1c} levels indicating insulin therapy
 - If A_{1c} >7% (53 mmol/mol), which indicates average BGL >8 mmol/L, consider starting insulin
 - If A_{1c} >8% (64 mmol/mol), which indicates average BGL >10 mmol/L, strongly consider starting insulin
- Step 2. Making lifestyle or medication changes, and treating other medical conditions
 - Check whether making lifestyle or medication changes and treating other medical conditions might get the patient's A_{1c} closer to target; insulin may still be necessary

When starting a patient with type 2 diabetes on insulin

- Step 3. Selecting the insulin and the injection device
 - Choose between intermediate-acting human insulin (isophane insulin), long-acting analogue insulin (detemir or glargine) and premixed insulin
 - Choose between syringe, pen and other injector.
- Step 4. Adjusting the basal insulin dose
 - Start with 10 units at bedtime if fasting BGL is high or 10 units in the morning if fasting BGL is on target but evening preprandial BGL is high
 - Increase doses every two to three days using agreed protocol
 - Consider adding a second basal insulin dose if the other preprandial BGL remains high
- Step 5. Stopping oral hypoglycaemic agents and/or adding short- or very short-acting bolus insulin to basal insulin
 - Consider stopping sulfonylurea and glitazone and decreasing metformin dose
 - If preprandial BGLs are on target and A_{1c} is high, check that BGL and A_{1c} measurements are accurate and whether there is postprandial hyperglycaemia
 - Consider starting short-acting bolus insulin if preprandial BGLs are on target but A_{1c} and postprandial BGL are not. Use short-acting human insulin (neutral insulin) or very short-acting analogue insulin (aspart, glulisine or lispro); start with 10% of the total daily basal dose and increase in steps of 10 to 20%, depending on closeness to BGL target (which is usually between 6 and 10 mmol/L)
- Step 6. Coping with potential problems when starting insulin
 - Educate the patient regarding injection technique and blood glucose monitoring and how to cope with hypoglycaemia and weight gain
 - Discuss psychological insulin resistance with the patient

Remember to tell patients: 'Insulin works, insulin is good, insulin is your friend'

- following the KISS or 'Keep insulin safe and simple' – approach to initiating insulin therapy, which involves six steps to stable sugars, as outlined in the box on this page¹¹
- using GP Management Plans (GPMPs) and/or Team Care Arrangements
- (TCAs), which enable GPs to refer patients to specialist nursing and allied health professionals to learn the necessary skills and daily routines
- having practice managers and nurses set up systems to identify those people with type 2 diabetes who need

insulin therapy and to start and titrate such therapy.

The greatest issues for the GP are deciding to recommend insulin therapy and then convincing the patient that it is in their best interest and that insulin therapy is safe and simple. Once the patient has agreed to insulin therapy, the GP needs to:

- decide the type of insulin to use: basal insulin (intermediate-acting human isophane insulin or one of the longacting analogue insulins determined glargine) or a premixed insulin
- decide the type of injection device (syringe or injector) to use
- complete the GPMP and/or TCA process
- refer the patient to a Credentialled Diabetes Educator who can collaborate with the doctor and/or practice nurse to start and titrate insulin therapy according to a prearranged dosage schedule based around the target preprandial BGL (initially 5 to 7 mmol/L, A_{1c} 7.5 to 8% [58 to 64 mmol/mol], and later, if appropriate, closer to the ideal of 4 to 6 mmol/L, A_{1c} below 7% [53 mmol/moL]).¹²
 - Resources that may be useful include:
- Care Plans templates are available through medical software and General Practice networks
- Diabetes Australia guidelines Diabetes Management in General Practice. Guidelines for Type 2 Diabetes. 18th ed. 2012/13¹
- Diabetes Australia patient information sheets, including that on insulin and diabetes (see http://www.diabetes australia.com.au/en/NDSS-Content/Diabetes-Information-Sheets/Insulin--Diabetes).

Once the patient has started and been stabilised on insulin the GP is likely to look back and realise how simple it really was, and the patient is likely to look back, realise how much better they feel and say: 'I wish I had started insulin months ago'.

CONCLUSION

Type 2 diabetes is a progressive disease and hypoglycaemic medication must also progress to keep BGLs on target. The need for insulin is another step in its treatment, to be taken when the use of multiple oral hypoglycaemic agents at maximum doses is no longer achieving good glycaemic control. Many patients with type 2 diabetes need insulin therapy within 10 years of diagnosis to maintain good glycaemic control (A_{1c} below 7% [53 mmol/mol]), and often comment how much better they feel having started insulin.

Starting insulin may not be a routine process for doctors and may be seen as 'too hard'. However, initiation and titration of insulin therapy is well within the competence of all Australian GPs as long as they can refer to nursing and allied health staff and have established systems within their practice.

Patients and doctors may have to deal with associated senses of failure, blame or shame, fear, inadequacy and lack of support when the need to start insulin therapy becomes apparent, and it is a big step for a GP to recommend insulin therapy and for the patient to accept the need for it. Patients are often particularly concerned about the insulin and its injection (pain, perceived addiction, worsening health and signifying the 'end of the road') and perceived associations with weight gain, loss of independence, employment issues and loss of driver's licence. It is important to have strategies and systems in place in general practice to deal with these issues and make insulin therapy acceptable and easy to initiate.

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