

Insulin therapy in the elderly: becoming the norm

By Professor Gregory Peterson

Case study 1

Mrs DL is a 72-year-old diabetic patient (type 2 diabetes for 14 years; last HbA_{1c} was 8.4%), whose blood pressure is generally around 140/95 mmHg. Her latest total cholesterol was 4.4 mmol/L and HDL was 1.1 mmol/L. Her fasting C-peptide level is below 0.1 nmol/L. She is a non-smoker with no evidence of heart failure. Her medications include:

- Aspirin 100 mg daily
- Rosiglitazone 8 mg daily
- Gliclazide MR 90 mg daily
- Metformin 1000 mg twice daily
- Lisinopril 10 mg daily
- Simvastatin 40 mg daily.

She has no known microvascular or macrovascular complications of diabetes and is otherwise reasonably healthy. She is somewhat reluctant to commence insulin treatment.

Case study 2

A pharmacist was performing a Residential Medication Management Review for Mrs SJ, a 74-year-old woman. She had a past medical history of ischaemic heart disease and type 2 diabetes. Her prescribed medications were as follows: aspirin 100 mg each morning, diltiazem SR 240 mg each morning, enalapril 10 mg each morning, glibenclamide 10 mg each morning, metformin 500 mg twice daily, paracetamol 500 mg when necessary, atorvastatin 20 mg daily, isosorbide mononitrate 60 mg each morning, and a glyceryl trinitrate spray for use when required. While her latest HbA_{1c} reading was quite good at 7.3%, it was noted by the doctor that her diabetes control had been erratic over the past 18 months. In particular, Mrs SJ had suffered a number of hypoglycaemic episodes, including one recently that contributed to a fall.

Case study 3

Mr JD is a 75-year-old man with a history of type 2 diabetes diagnosed more than 20 years ago, complicated by non-proliferative diabetic retinopathy and macular oedema, mild diabetic peripheral neuropathy and some proteinuria. His medical history also includes coronary artery disease and dyslipidaemia. Mr JD's management of his diabetes has been acceptable for many years, but control has started to deteriorate over the past 12 months (latest HbA_{1c} was 9.2%). His medications include: metformin 1000 mg twice daily and



Mrs SJ had suffered a number of hypoglycaemic episodes, including one recently that contributed to a fall.

glipizide 5 mg daily. After several discussions with his doctor and pharmacist, Mr JD agrees to commence therapy with 10 Units of isophane insulin (*Protaphane*) at bedtime. Two months later, the insulin dose has increased to 18 Units, the dose of metformin has been decreased to 500 mg twice daily, and Mr JD's HbA_{1c} is 7.9%.

Diabetes is the most common chronic disease in the elderly. In fact, type 2 diabetes affects 20% of the Australian population aged over 65 years and they constitute more than 40% of the total diabetic population.¹⁻³ Approximately one in five nursing home residents have diabetes.⁴ The number of elderly people with type 2 diabetes worldwide is projected to increase exponentially in coming decades.

*'We are approaching an epidemic of diabetes in the elderly. This epidemic and its associated complications will have a significant impact on quality of life in this age group.'*⁵

Older people who have diabetes have twice the mortality of age-matched controls who do not have diabetes, with ischaemic heart disease and stroke being the leading causes of diabetes-related deaths,³⁻⁶ yet elderly people often receive less intensive management of diabetes and other cardiovascular risk factors than younger people. Rectifying this situation could prolong the lives of many elderly people with diabetes.⁹

Diabetes is one of the strongest predictors of functional decline in the elderly. Older patients who have diabetes have a much poorer self-rated quality of life. They also use hospital days and outpatient services at twice the rate of

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Table 1: Issues for discussion with patients about to start insulin¹⁸

Fear	Advice
Insulin means I have failed	Type 2 diabetes is a progressive disease. It is the other treatment options that have failed, not the patient
Fear of injections	Insulin is injected into the fat layer under the skin, not into a vein. The fine, short needles available today do not hurt
Starting insulin is too difficult or complex	Insulin may be as simple as one injection at bedtime in addition to existing oral agents
Fear of hypoglycaemia	Severe hypoglycaemia is rare and occurs much less frequently in type 2 diabetes than in type 1 diabetes
I will gain weight	The long-term benefits of insulin outweigh the risks of modest weight gain. Explore ways of improving diet and increasing activity to counter any weight gain

older people who do not have diabetes.⁵ Patients over 65 years of age who have diabetes are hospitalised more than twice as frequently as those who don't.⁴ Older adults with diabetes are also at greater risk than other older people for several common geriatric conditions, such as depression, cognitive impairment, urinary incontinence, and persistent neuropathic pain.⁶ Interestingly, it has been shown that diabetes mellitus is an independent risk factor for falls among elderly nursing home residents, like Mrs SJ. Maurer *et al.*¹⁰ demonstrated that nursing home residents with diabetes are four times more likely to fall than those who are not diabetic.

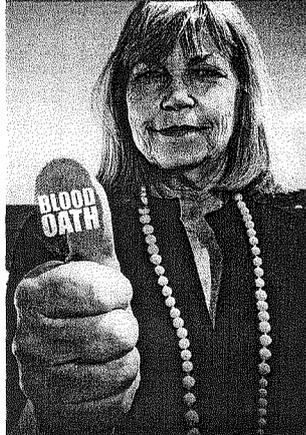
Elderly people often have limited access to mainstream diabetes services due to decreased mobility or factors associated with multiple chronic conditions.³ Partly as a result, diabetic control is often poor in the elderly.¹¹ Multiple oral anti-diabetic agents may serve as a marker for more severe, uncontrolled diabetes in the elderly, as in the case of Mrs DL. The vast majority of patients treated with multiple oral anti-diabetic agents have suboptimal glycaemic control, suggesting a need for intensified efforts to treat this particular group of patients to recommended goal levels.¹² To an extent, target HbA_{1c} levels should be individualised in the elderly. A reasonable goal in relatively healthy adults with good functional status is 7% or lower.³⁻⁷ For frail older adults, persons with life expectancy of less than five years, and others in whom the risks of intensive glycaemic control appear to outweigh the benefits, a less stringent target such as 8% is appropriate.^{5,6}

Often, poor control in long standing type 2 diabetes is a reflection of the change in the condition to become effectively type 1 diabetes with minimal insulin secretion by the pancreas, as evidenced by a low C-peptide level. Over time, many patients with type 2 diabetes will require insulin therapy since pancreatic beta cell secretory dysfunction is progressive and currently no therapies reverse this.¹³ The term secondary failure refers to the 'failure' of oral hypoglycaemic drugs to maintain glycaemic control. The United Kingdom Prospective Diabetes Study (UKPDS)^{14,15} clearly showed that most people with type 2 diabetes will experience progressive pancreatic beta cell dysfunction. The secondary failure rate in this study was 44% after six years of diabetes.

The decision to initiate insulin therapy in elderly patients inadequately controlled with oral anti-diabetic medications is often delayed, as with Mrs DL, for a number of reasons, including doctor reluctance to prescribe insulin, patient reluctance to start insulin because of fear of the injections (as is the case with Mrs DL), concern about hypoglycaemia, or because there is a perception that insulin therapy implies severe disease.¹³ Rural location may also be an issue. Adults with type 2 diabetes who live farther from their source of primary care are significantly less likely to use insulin.¹⁶ This association does not appear to be due to confounding by variables such as age, education, income, health insurance, duration of diabetes, use of oral agents, glycaemic control, or frequency of care, and may be responsible for the poorer physiologic control noted among patients with greater travel burdens.¹⁶ Perhaps patients and doctors are concerned about the risks of insulin and are reluctant to use it if they feel the patient lives too far away from care for rescue in the event of hypoglycaemia.

It is important to discuss the likelihood of insulin with patients early (when they begin oral drug treatment) to help them overcome their fears and increase their acceptance of it (Table 1).^{17,18} Despite patient reluctance to use insulin, when oral agents fail to control glucose

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levels adequately, insulin therapy should be initiated in most circumstances.⁷ The key to when to start insulin is in identifying the appropriate HbA_{1c} target for an individual patient.¹⁷ As indicated above, a target of 7% or lower is reasonable in relatively healthy adults with good functional status. On the other hand, older patients who are not symptomatic and have no microvascular complications such as retinopathy can be allowed to remain in secondary failure at an HbA_{1c} of 8–9%. In these patients, prognosis is governed mainly by macrovascular disease, which is not so greatly influenced by glycaemic control.¹⁷ Clearly, there is also the possibility that age-related changes in functional ability and the senses may affect a patient's ability to administer insulin, monitor blood glucose and manage hypoglycaemia.¹⁹

*'Many patients and practitioners procrastinate as insulin treatment is erroneously considered to be risky and difficult.'*¹⁷

There is no uniform approach on how to make the transition from oral agents to insulin therapy in type 2 diabetes. The simplest approach to initiate insulin therapy is to add 10 Units (or 0.1–0.2 Units/kg) of intermediate-acting isophane insulin at bedtime while continuing treatment with metformin, a sulfonylurea or both.^{7,13,17,18} Smaller doses might be started in underweight and malnourished patients. Administering the insulin as late as possible (e.g. 10 pm–midnight) times the maximum effect to just before dawn when insulin resistance is high, and reduces the risk of nocturnal hypoglycaemia.¹⁸ To reach the glucose target, the dose should be cautiously adjusted every few weeks on the basis of glucose monitoring results for fasting blood glucose levels (generally aim for < 7 mmol/L, or < 10 mmol/L in frail patients). The patient would normally remain on all the oral hypoglycaemic drugs that they are currently taking, with dosage reductions wherever possible. Although the oral drugs have 'failed' in the situation of secondary failure, they are still exerting considerable hypoglycaemic effects.¹⁷

*'It is easier to persuade patients to undertake combined oral drugs and insulin treatment. They are often comforted by the knowledge that they only need to take insulin once daily, in the privacy of their own home and without a great deal of disturbance to their daytime routine. The regimen of giving an insulin injection before bed, to complement the use of maximum oral hypoglycaemic drugs for patients with diabetes in secondary failure, is easy and safe to implement in general practice as the first step of introducing insulin treatment. When they are familiar with insulin injections they become accepting of a more intensive insulin regimen, should this be required.'*¹⁷

If necessary, the next step would be to increase the isophane insulin injections to twice-daily, followed by adding neutral (regular) short acting insulin before meals (see Table 2).¹⁸

Table 2: Approach to insulin initiation in patients with type 2 diabetes¹⁸

Step 1	ADD 10 Units isophane insulin at bedtime. CONTINUE metformin, a sulfonylurea or both (at the same dosage, but no greater than the maximum recommended dose)	
	<ul style="list-style-type: none"> • If evening blood glucose level is high then use 10 units morning isophane insulin. • If both morning and pre evening meal blood glucose levels are high then consider using twice daily isophane. 	
Step 2	ADJUST insulin therapy gradually every 3–4 days according to fasting blood glucose (FBG) level until target FBG is reached (usually 4.0–6.0 mmol/L) ^a	
	Mean FBG (mmol/L)	Insulin dose
	> 10	Increase by 8 units
	8–10	Increase by 6 units
	6–8	Increase by 2 units
	4–6	No change
	< 4	Decrease by 2–4 units
Step 3	CHECK overall blood glucose control with HbA _{1c}	
Step 4	If FBG and evening blood glucose are on target but HbA _{1c} is not, look for hidden 'hypers' – blood glucose peaks that occur during the day, often before lunch or after dinner.	
	Options to correct hidden 'hypers' include:	
	<ul style="list-style-type: none"> • changing preceding meal size or composition • increasing activity after meals • adding acarbose • adding a meal time rapid acting insulin^b 	

a A GP, trained practice nurse, credentialled diabetes educator or the educated patient can adjust insulin dose according to this titration schedule. Adjusting the insulin dose gradually can gain patient confidence and reduce the risk of hypoglycaemia.

b Biphasic or pre-mixed insulin are convenient but require a more strict adherence to the size and timing of meals and dosing can be inflexible leading to blood glucose fluctuation.

The above guide to initiating insulin suggests adjusting insulin by 6 to 8 units for patients with mean FBG levels ≥ 8 mmol/L. We have received feedback that this varies from other local guidelines. This guidance is just one way to initiate and titrate insulin. Prescribers concerned about the risk of hypoglycaemia can adjust insulin in increments up to 4 units (every 3–4 days, according to mean FBG), rather than 6 or 8 units. Alternatively, they can follow RACGP (adjust by increments of 10% to 20%) or local guidelines.

(Table used by the kind permission of the National Prescribing Service.)



The long acting insulin analogue glargine (*Lantus*) and isophane insulin are equally effective, but the former causes significantly less hypoglycaemia.^{5,13} Thus, glargine might be the preferred basal insulin among the elderly because more patients can reach recommended goals more safely.^{7,20,21} The newer long-acting insulin analogue, insulin detemir (*Levemir*), would also be an attractive choice for the elderly in whom hypoglycaemia should be minimised,²⁰ but is currently restricted to use in type 1 diabetes under the Pharmaceutical Benefits Scheme.

The availability of pre-filled disposable injection devices and once-daily dosing should make it relatively easy to introduce insulin in the elderly. However, patients with failing eyesight or limited dexterity who are unable to use an insulin pen may require an *InnoLet* injecting device, which is only available for Protaphane or the pre-mixed insulin, *Mixtard 30/70*.²⁰

The most serious adverse effect of insulin therapy is hypoglycaemia, but the frequency and severity of this effect is less in type 2 diabetes than in type 1 diabetes. The risk that severe or fatal hypoglycaemia will occur with either oral agents or insulin increases exponentially with age.⁵ The risk of hypoglycaemia can be minimised with use of analogue insulin; careful timing of injections, meals and exercise; frequent self-monitoring of blood glucose levels; and patient/carer education about warning symptoms of hypoglycaemia and self-adjustment of the insulin dose and management.²²

*'It is reassuring that in patients with type 2 diabetes, hypoglycaemia due to insulin is usually not severe.'*¹⁷

Patients with hypoglycaemia may have autonomic symptoms (e.g. sweating, hunger, paresthesia, tremor, palpitation, anxiety) or neuroglycopenic symptoms (e.g. dizziness, weakness, confusion and drowsiness). However, diagnosing hypoglycaemia is not always straightforward, particularly in the elderly, as a significant proportion of such patients may be asymptomatic or present with non-specific symptoms, such as altered mental status.²³

It should be borne in mind that although glycaemic control is important, in older persons with diabetes a greater reduction in morbidity and mortality may result from control of cardiovascular risk factors than from tight glycaemic control.^{6,17} Hence, cessation of smoking and control of blood pressure and lipids are also critical.

Pharmacists, either within or independent of the new Diabetes Medication Assistance Service (DMAS), can play an extremely important role in educating and encouraging older patients with regard to the use of insulin therapy. Excellent support materials, including a patient information leaflet,^{18,24-26} are available from the National Prescribing Service and Diabetes Australia.

(See page 585 for Characteristics of insulin preparations.)

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