MedicineToday PEER REVIEWED ARTICLE POINTS: 2 CPD/2 PDP

The insulin KISS in older people with type 2 diabetes ('keep insulin safe and simple')

With increasing frailty, the goal of glycaemic control in patients with type 2 diabetes becomes the maintaining of a balance between hypoglycaemia and hyperglycaemia rather than the preventing of the long-term complications of the disease.

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Type 2 diabetes becomes progressively more common with age, affecting 15 to 20% of Australians over the age of 60 years[1] (Figure 1), and a higher proportion of those in residential care. As people age, generally their comorbidities and use of medications increase and their physical and mental capacities decrease. The pathophysiology and consequences of type 2 diabetes and the priorities for care are different in elderly people than in younger adults. These factors affect targets for glycaemic control, use of oral hypoglycaemic agents and the timing of starting insulin therapy relative to the course of the diabetes.

Insulin therapy is generally started earlier in elderly people with type 2 diabetes than in younger patients with the disease but follows the basic insulin KISS approach ('keep insulin safe and simple' – that is, first control the fasting blood

IN SUMMARY

- **In the 'young old' – people with a chronological age of over 65 years and a biological age of younger than 75 – tight glycaemic control can still reduce the complications of diabetes. In the 'old old' – people with a chronological age of over 65 years and a biological age of 75 or older – tight glycaemic control offers few long-term advantages and increases the burden of care and may reduce quality of life. The goal of glycaemic control in the 'old old' is to maintain a balance between hypoglycaemia and hyperglycaemia.**
- **The range of oral hypoglycaemic agents is more limited in the elderly and insulin therapy is generally started earlier in the course of type 2 diabetes in elderly people than in younger patients with the disease.**
- **Starting insulin in the 'young old' and 'old old' follows the same KISS ('keep insulin safe and simple') approach as applies to younger people, although in the 'old old' preprandial targets are likely to be higher (such as 5 to 7 mmol/L rather than 4 to 6 mmol/L) to reduce the risk of hypoglycaemia and/or reduce the burden of care.**
- **The basic insulin KISS approach is to first control the fasting blood glucose level (BGL), then the evening preprandial BGL and then any mealtime BGL increases.**
- **The choice of the insulin formulation is largely determined by the injection device suitable for the patient and/or carer but analogue insulins have advantages over traditional insulins in some circumstances.**
- **Premixed insulin preparations offer the benefit of convenience but are limited by fixed, and sometimes inappropriate, proportions of basal and bolus insulins.**

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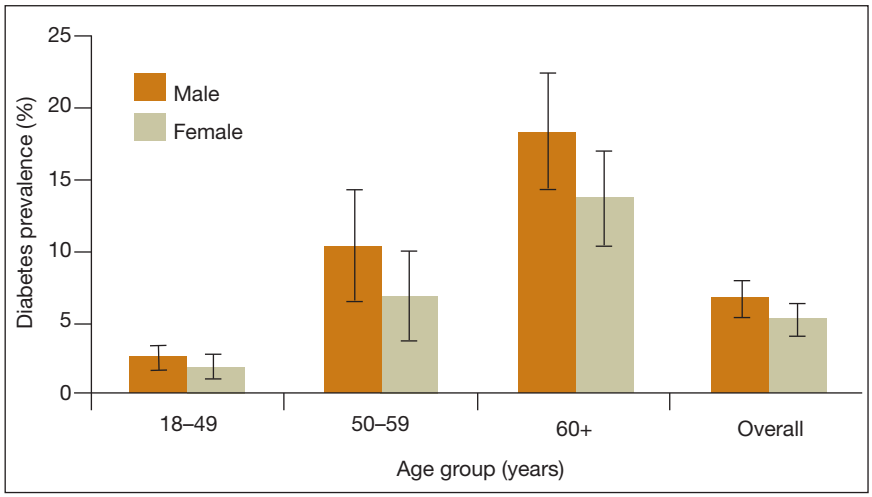

Figure 1. Diabetes prevalence increases with age.[1]

REPRODUCED FROM GRANT J, ET AL. NORTH WEST ADELAIDE HEALTH STUDY. BASELINE BIOMEDICAL AND SELF REPORT DATA. ADELAIDE: POPULATION RESEARCH AND OUTCOMES STUDIES UNIT, SOUTH AUSTRALIAN DEPARTMENT OF HEALTH; MARCH 2005.

glucose level [BGL], then the evening BGL and then any mealtime BGL increases).[2,3]

This article reviews the problems associated with hyperglycaemia in older people with type 2 diabetes and outlines a 'hypoglycaemic hierarchy' to moderate glycaemia and avoid the extremes of hyperglycaemia and hypoglycaemia.

Who is 'old' these days?

As the Australian population ages and the baby boomers move into their 60s, the practical definition of 'old' is becoming biological (or functional) rather than chronological. The default definition of old has generally become the male qualifying age for the age pension, currently 65 years. The elderly have been divided into the 'young old' and 'old old' based on whether they were aged 65 to 75 years or 75 years and older, each group being further subdivided into 'healthy' and 'frail'. This subdivision by chronological age is not particularly useful with regards to assessing care needs as the health and management issues related to many conditions, including diabetes, are generally more dependent on functioning than on age alone.

Taking a biological age of 75 years as the dividing age between 'young old' and 'old old' is likely to be more useful in practice. For example, a biologically young 78-year-old (that is, a person with a chronological age of 78 but a biological age of younger than 75) may still be in full- or part-time work and enjoying a wide range of recreational and social activities whereas a biologically old 78-year-old (that is, a person with a chronological age of 78 but a biological age of 75 or older) may be housebound, or even bedbound, because of previous cardiovascular events, musculoskeletal problems, respiratory disability or other conditions. The medication burden and potential for medication related problems for the biologically 'old' 78-year-old is likely to be much greater than for a biologically younger peer. Similarly, a biologically old 68-year-old (chronological age 68 and biological age over 75) may have many more health issues than a biologically young 68-year-old.

What is known about glycaemic control in older adults?

Not a lot in terms of evidence-based medicine, as there have been no studies specifically in people aged over 75 years. Evidence-based priorities exist for blood pressure control, appropriate use of antiplatelet coagulant agents and foot protection in the elderly,[4] but there are few relevant trials outside these areas. There may be long-term benefits from lipid control for macrovascular disease and from glycaemic control for microvascular disease.

Glycaemic control potentially has considerable short-term and long-term benefits in people with type 2 diabetes.

In the short term, hyperglycaemia can significantly reduce any person's level of energy, alertness and capacity to enjoy life. For older people, fatigue, confusion and daytime sleepiness caused by hyperglycaemia could mistakenly be attributed to the process of getting older or to dementia. In addition to causing annoying polyuria and uncomfortable thrush, glycosuria can cause incontinence and interfere with the activities of daily life and sleep. Hypoglycaemia can change a functional older person into someone who is effectively demented (cognitively impaired) and functionally unable to cope.

In the long term, the macrovascular and microvascular complications of type 2 diabetes may affect quantity and quality of life. Age and type 2 diabetes are two major risk factors for cardiovascular disease and minimising the impact of cardiovascular problems is a high priority in this older population.

For the health care system, congestive heart failure (most commonly due to ischaemic cardiomyopathy) is one of the major reasons for hospital admissions in the western world. For the individual, the effects of myocardial infarction, stroke or lower limb gangrene and need for amputation can be devastating.

The impact of microvascular disease in the short and long term depends on life expectancy, duration of diabetes and the level and progression of existing microvascular disease. Microvascular disease such as severely progressive retinopathy or disabling painful neuropathy can be a major short-term problem. Improving glycaemic control is likely to reduce progression and symptoms. The findings of

the United Kingdom Prospective Diabetes Study (UKPDS) suggested that glycaemic control reduced both macrovascular and microvascular complications, but this study was not carried out in an older population.[5] The UKPDS also showed an epidemiological association of benefit from better control.

Setting glycaemic targets

Glycaemic control in patients with diabetes is assessed by measurement of blood glucose levels (BGLs) and glycosylated haemoglobin (also known as glycated haemoglobin and HbA_{1c} – shortened to A_{1c}). Measurement of levels of blood glucose gives day-to-day information of the glycaemic highs and lows relating to meals. The A_{1c} value reflects the average daily BGL over the preceding several weeks.[6]

As previously noted, the evidence base for the older population is less strong than for younger people and the benefits of long-term glycaemic control are less clear. However, the burdens of the necessary care to produce such glycaemic control are clear, namely insulin dose preparation and administration, extra monitoring of blood glucose, ongoing monitoring of carbohydrate intake, physical activity levels and insulin dosage, and more frequent professional consultations.

It is generally known that:

- the major contributor to overall glycaemia is the fasting blood glucose
- people with type 2 diabetes are not prone to the extreme glycaemic swings that occur in those with type 1 diabetes
- the short-term and long-term problems associated with hyperglycaemia increase progressively with increasing blood glucose and A_{1c} levels.

Worldwide there is a fair consensus about targets for glycaemic control (Table 1). The Australian targets for preprandial BGL of 4 to 6 mmol/L and an overall A_{1c} of below 7% recommended as ideal for people with diabetes are appropriate in some older people.[3] In other older people, however, preprandial BGL targets of 5 to 7 mmol/L and A_{1c} targets of 7 to 9% may be indicated. Such people should aim for preprandial BGLs that are not too low (that is, in the range of 2 to 4 mmol/L) and not too high (that is, in the range of 8 to 10 mmol/L). Glycaemic targets for an individual are a balance between the potential short-term and long-term benefits (symptoms and complications), the burden of this level of care for the person, carer or health care system, and the risks of weight gain and hypoglycaemia associated with tighter glycaemic control.

In the absence of evidence-based medicine, the fairytale *Goldilocks and the Three Bears* may offer a guide to glycaemic control – not too high, not too low, 'just right'.

Table 1. Targets for glycaemic control in type 2 diabetes

	Healthy	RACGP	ADA/EASD	AACE	IDF
A_{1c} (%)	Below 6.0	Below 7	Below 7	6.5 and below	Below 6.5
Fasting blood glucose (mmol/L)	Below 5.5	4 to 6	3.9 to 7.2	6.0 and below	Below 6.0

ABBREVIATIONS: RACGP = Royal Australian College of General Practitioners; ADA/EASD = American Diabetes Association/European Association for the Study of Diabetes; AACE = American Association of Clinical Endocrinologists; IDF = International Diabetes Foundation.

The 'young old'

Case scenario

Alice is 82 years old, lives independently and does all her own housework, shopping and gardening. She enjoys her weekly game of bridge with her friends and regularly goes to the city theatres to see plays (mostly comedies). Her feet swell in summer but she doesn't think she has any other problems with her health. Prediabetes (impaired fasting glucose) was diagnosed three years ago and a recent fasting glucose was 7.6 mmol/L. She has no glycosuria on urinalysis but has had nocturia (one or two voids per night) for the past year or so.

Her weight has been steady at 63 kg, and her height is 1.55 m (BMI, 26 kg/m^2).

Her current medications are simvastatin 40 mg per day, aspirin 150 mg per day and fosinopril/hydrochlorothiazide 10/12.5 mg per day.

- What glycaemic targets would you aim for?
- What special considerations might apply to Alice's glycaemic management now compared with if she was aged 50 years?

Targets

A patient such as Alice who has diabetes and has reached the age of 82 years and remained in good health – a 'young old' person – is likely to have less central obesity and to have avoided the ill effects of cardiovascular disease that were responsible for the earlier mortality of his or her previous peers. He or she will also have less comorbidity than his or her biologically older chronological peers – the 'old old'.

An 82-year-old person with a biological age of, say, a 65-year-old can expect a further 10 to 20 years of living with diabetes, which is plenty of time for diabetic complications to occur and reduce the person's functional independence and quality of life. For such a person, the glycaemic targets may be the same as those of the general population with type 2 diabetes – that is, preprandial BGL below 6 mmol/L and A_{1c} below 7%.

Special considerations

Hypoglycaemic medications

Although the general advantages and disadvantages of hypoglycaemic medications still apply in older patients, there may be

continued

Table 2. Medications and renal impairment in type 2 diabetes[7]

Nephrotoxic medications

Radiocontrast agents – the high osmolality ionic contrast agents cause more adverse effects; use the low osmolality nonionic agents instead and avoid dehydration
NSAIDs, including COX-2 'specifics' – use paracetamol instead
ACE inhibitors – check renal function

Medications needing dose adjustment if GFR is below 60 mL/min

Allopurinol – adjust dose to 100 mg per day per 30 mL/min of GFR
Digoxin – check levels
Sulfonamides – halve the dosage if GFR is below 30 mL/min

Medications not to be used if GFR is below 30 mL/min

Some hypoglycaemics – i.e. acarbose, glibenclamide, glimepiride, metformin
Potassium sparing diuretics – i.e. amiloride, triamterene, spironolactone
Tetracyclines

ABBREVIATION: GFR = glomerular filtration rate.

The Cockroft-Gault equation[8]

A simple form of a Cockroft-Gault equation for calculating GFR is:

For women, GFR (mL/min) =

$$\frac{(140 - \text{age}) \times \text{weight}}{\text{serum creatinine } (\mu\text{mol/L})}$$

where weight is 'healthy' weight in kg, calculated by height in cm minus 100.

For men, use the above equation and multiply the answer by 1.25.

In Alice's case (age 82 years, height 155 cm),

- if her serum creatinine were 100 µmol/L then her GFR would be ([140 – 82] x [155 – 100]) ÷ 100 = 32 mL/min.
- if her serum creatinine were 120 µmol/L then her GFR would be ([140 – 82] x [155 – 100]) ÷ 120 = 27 mL/min.

ABBREVIATION: GFR = glomerular filtration rate.

some special considerations and changes to the usual hypoglycaemic hierarchy. Even the 'young old' are more likely than younger patients to have medical problems that may affect the use of hypoglycaemic medications.

The more limited range of oral hypoglycaemic options in older patients means that insulin is used earlier rather than later in the course of diabetes. Furthermore, when Alice does start insulin there would be a stronger case for stopping oral hypoglycaemic medications than in younger patients.

Renal function

Doses of certain medications may need to be adjusted in a person of any age with impaired renal function. If a patient's glomerular filtration rate (GFR) is less than 60 mL/min (but not less than 30 mL/min), then dosage adjustment of some medications is advised. If the GFR is less than 30 mL/min, certain medications should not be used and the dosage of many others should be adjusted (Table 2).[7]

Renal function declines with age and a person's GFR falls roughly 1 mL/min each year, even if the person is healthy. In older people, therefore, a normal serum creatinine (in the range 50 to 110 µmol/L) may be associated with a low GFR. For example, if Alice's serum creatinine were greater than 100 µmol/L, her GFR would be less than 60 mL/min, and if it were greater than 120 µmol/L, her GFR would be less than 30 mL/min, as calculated using the Cockroft–Gault equation, which takes into account her age (see the box on this page).[8] Although metformin is the appropriate initial oral hypoglycaemic medication for both a patient aged 50 years and a 'young old' patient such as Alice if renal function were normal (with dosage increments up to a total dose of 2 to 3 g per day), it should be used at lower doses (such as up to 1 g per day) if GFR were between 30 mL/min and 60 mL/min and not be used at all if GFR were less than 30 mL/min.

It should be noted that estimated GFR (eGFR), which is now calculated (using a different formula to the Cockroft-Gault equation) and reported by most Australian laboratories with every serum creatinine ordered for adult patients, should not be used to estimate GFR to guide drug dosage. For dosage adjustment, the Cockroft-Gault equation should be used.

The choice of sulfonylurea might also be affected by the patient's GFR because both glimepiride and glibenclamide have renally excreted active metabolites that may accumulate and cause hypoglycaemia.

Also, acarbose is contraindicated in patients with severe renal impairment, further limiting the range of available oral hypoglycaemic agents.

Oedema

Alice's leg oedema may be an ongoing problem and could be contributing to her nocturia as the peripheral fluid moves from the extracellular to the plasma compartment and is excreted. If so, use of a glitazone as the hypoglycaemic agent would be expected to worsen this and potentially precipitate cardiac failure because of the side effect of fluid retention.

When insulin is started, Alice should be warned that her leg swelling might get worse because insulin increases renal sodium retention. She may need to consider wearing a support stocking.

Hypoglycaemia

Many people think all those using insulin are in the same category. However, the pathophysiology of type 1 and type 2 diabetes are very different, as is the likelihood of glycaemic swings. The rate of hypoglycaemia is much lower in type 2 than type 1 diabetes. In the two trials assessing the relation between glycaemia and complications, Diabetic Control and Complications Trial (DDCT) and UKPDS, at the same level of glycaemia (A_{1c}), the risk of severe hypoglycaemia in patients with type 1 diabetes was very much higher than in those with type 2 diabetes.[5,9]

There is, however, still a risk of severe hypoglycaemia in patients with type 2 diabetes, particularly in those who have low A_{1c} values or who are older, have autonomic neuropathy or have had diabetes for many years.

Personal, medical, medication-related and diabetes management factors increase the risk of hypoglycaemia (Table 3). These factors increase the hypoglycaemic effect of insulin, reduce the effectiveness of counter-regulation or delay recognition of hypoglycaemia.

Because of their age, older people are more likely to have social and medical problems and to be taking potentially dangerous medications. As people with diabetes age they develop these problems, as well as microvascular complications (loss of vision, renal impairment and somatic and autonomic nerve damage). Moreover, as noted above, the risk of severe hypoglycaemia increases as diabetes progresses. This increased risk of severe hypoglycaemia with age may also be associated with an increased likelihood of permanent neurological damage if hypoglycaemia occurs.

Hypoglycaemia is therefore more likely to occur in older people because they are more likely to have hypoglycaemic risk factors. It is also more likely to have catastrophic effects, including myocardial infarction, stroke, seizure or trauma caused by falling.

In older patients with hypoglycaemic risk factors or a history of severe hypoglycaemia, the following items should be reviewed:

- hypoglycaemic and other medication (e.g. by a Home Medicines Review)
- self-management techniques (lifestyle, medication and monitoring)
- action plans for sick days, hypoglycaemic episodes and mistakes in medication dosing, and 24-hour access to advice.

Initiating insulin in the 'young old'

Starting insulin in the 'young old' follows the same KISS approach as applies to younger people, although preprandial BGL targets may be slightly higher to reduce the risk of hypoglycaemia and/or the burden of care.[2]

The 'old old'

Case scenario

Allan is 72 years old and a nursing home resident. A myocardial infarction followed by atrial fibrillation and a large embolic stroke two years ago left him with a dense right hemiplegia and he is unable to live independently. He is able to sit out of bed but is not able to communicate well and does not seem interested in reading, watching television or listening to music or the radio.

He has type 2 diabetes and his current hypoglycaemic medication is intermediate-acting basal insulin (isophane) 24 units in the evening and metformin 500 mg twice daily.

The nursing staff are concerned about his blood glucose values: his fasting (morning preprandial) BGL is 8 to 10 mmol/L, and his other random BGLs through the day range widely between 6 and HI (that is, over 25 mmol/L).

- How would you decide whether to intensify insulin treatment?
- Assuming you are going to intensify insulin treatment, what would be your next steps?
- Should you use analogue insulins?
- Should you use a premixed insulin preparation?

Table 3. Type 2 diabetes: hypoglycaemic risk factors

Personal
- Erratic lifestyle
- Lives/sleeps alone
- Older age
- Longer diabetes duration

Medical
- Liver and/or renal dysfunction
- Hypothyroidism and/or adrenalism
- Autonomic neuropathy

Medication
- Affecting sulfonylurea pharmacokinetics:
  - sulfonamides
  - cimetidine
  - azole antifungal agents
  - NSAIDs
  - fluoxetine
  - fluvoxamine
- Causing hypoglycaemia or reducing response:
  - alcohol
  - beta blockers
  - ACE inhibitors
  - high-dose salicylates
  - perhexiline

Management
- Lifestyle
- Medication adherence
- Diabetes techniques (injection, monitoring)

When to intensify insulin therapy

In the 'old old' there may not be any long-term theoretical benefits of tight glycaemic control on diabetic complications. Moreover, ideal glycaemic control (preprandial BGL, below 6 mmol/L; postprandial BGL, below 8 mmol/L) exposes these biologically old people to the risk of hypoglycaemia, which can have severe consequences. The more appropriate preprandial BGL targets for the 'old old' are 5 to 7 mmol/L.

In Allan's case, the goal is to avoid

Basal insulin titration in the elderly

Start with 10 units of basal insulin, either isophane insulin or an analogue insulin, usually at bedtime but for some patients in the morning. Using the guidelines below, adjust the dose twice weekly to reach the target fasting blood glucose level (BGL) of below 6 mmol/L for the 'young old' and below 7 mmol/L for the 'old old'. (The 'young old' are those people with a chronological age of over 65 years and a biological, or functional, age of younger than 75 years; the 'old old' are those with a chronological age of over 65 years and a biological age of 75 years or older.)

Mean fasting glucose over preceding two days (mmol/L)	Insulin increase (U/day)
For a target fasting BGL of below 6 mmol/L:	
Above 10	8
8 to 10.0	6
7 to 7.9	4
6 to 6.9	2
For a target fasting BGL of below 7 mmol/L:	
Above 11	8
9 to 11.0	6
8 to 8.9	4
7 to 7.9	2

- No increase in the insulin dose if the fasting BGL is below 4 mmol/L for the 'young old' or below 5 mmol/L for the 'old old' at any time in the preceding week.
- No increase and small decreases (2 to 4 units) in insulin dose if there is severe hypoglycaemia (requiring assistance) or the BGL is below 3.0 mmol/L in the preceding week.

Adapted from reference 10 (*Diabetes Care* 2003; 26: 3080-3086).

symptoms of hyperglycaemia (confusion and tiredness, which are usually worse after meals) and glycosuria (which can be a special problem in a marginally continent patient, if nocturia becomes frequent or if associated with thrush), without causing hypoglycaemia between meals (with the symptom of confusion).

Allan's fasting BGL of 8 to 10 mmol/L on its own might not prompt action but high preprandial BGLs are likely to be associated with even higher postprandial BGLs, which may cause confusion, tiredness, polyuria or thrush.

Steps in intensifying insulin therapy

Sometimes blood glucose is monitored at times convenient to the nursing staff rather than preprandially. These random blood glucose values are of little use in guiding therapy. The first step in intensifying a patient's insulin therapy would be to check BGLs before the midday and evening meals. If the fasting BGL is above target (for example, above 7 mmol/L) and the other preprandial values are similar to the fasting, increasing the evening intermediate-acting insulin dose is likely to 'fix the fasting' and the other preprandial values are likely to decrease as well. On the other hand, if the fasting BGL is on target (for example, 5 to 7 mmol/L) and the other preprandial BGLs are significantly higher than the fasting (that is, greater than 7 mmol/L) then a second dose of intermediate-acting insulin may be required in the morning. Allan's fasting BGL is 8 to 10 mmol/L, so an increased evening dose of intermediate insulin would be indicated.

As noted, blood glucose target values are likely to be higher in the 'old old'. The usual insulin titration algorithm can be modified accordingly, as shown in the box on this page.[2,10]

Once the preprandial BGL targets are met in an 'old old' patient, it may be appropriate to stop the metformin to reduce the medication burden and check preprandial values two to three times per week at different times of the day.

It should be remembered that intermediate-acting insulin has a peak in its time–action profile about three to five hours after administration that can cause hypoglycaemia in the middle of the day or night, depending on whether it is given in the morning or the evening. If Allan starts becoming confused during the night, it may be due to hypoglycaemia from his evening dose of insulin; checking his BGL in the middle of the night, such as at 2 a.m., would pick this up. Similarly, checking the BGL before lunch will pick up daytime hypoglycaemia after a morning dose of intermediate-acting insulin.

A preprandial BGL of 5 to 7 mmol/L is likely to be associated with a postprandial BGL of around 10 to 15 mmol/L and an A_{1c} of around 7% (see the box on page 33).[11] Once Allan's preprandial values have been on target for several weeks, a measured A_{1c} significantly higher than 8% would suggest postprandial hyperglycaemia and prompt review of the amount and type of carbohydrate being eaten and consideration of adding acarbose (Glucobay) at the preceding meal.

If A_{1c} remains high, it may be necessary to add a bolus insulin, although such use should be minimised because of the risk and danger of hypoglycaemia. The temptation to fix a high preprandial BGL with bolus insulin should be resisted;

BGL and A_{1c} approximations[10]

Average blood glucose level (BGL; in mmol/L) is approximately equivalent to preprandial BGL + 2, and
Average BGL (in mmol/L) is approximately equivalent to (2 A_{1c} – 6)

Therefore, A_{1c} = (average BGL + 6) ÷ 2 and A_{1c} = (preprandial BGL + 8) ÷ 2

In Allan's case, if his average preprandial BGL is 6 mmol/L then his expected A_{1c} would be (6 + 8) ÷ 2 = 7.0%

A website converter of estimated average glucose to/from A_{1c} can be found at: http://professional.diabetes.org/glucosecalculator.aspx

adjust the preceding intermediate-acting basal insulin dose and/or timing instead.

Bolus insulin may be appropriate in two situations:[6]

- if BGLs before lunch are high despite BGLs before breakfast and the evening meal being on target, the food eaten at breakfast and during the morning being appropriate and a breakfast dose of acarbose being contraindicated or not effective. Increasing the morning intermediate-acting insulin dose is likely to cause hypoglycaemia in the afternoon; adding a dose of quick- or very quick-acting insulin before or with breakfast should control values before lunch
- if BGLs before the evening meal are high despite BGLs before breakfast and lunch being on target, the food eaten at lunch and in the afternoon being appropriate, and a lunchtime dose of acarbose being contraindicated or not effective. Increasing the morning intermediate-acting insulin dose is likely to cause hypoglycaemia before lunch; adding a dose of quick- or very quick-acting insulin before or with lunch will control blood glucose before the evening meal.

When bolus insulin is used, 'go low and go slow' – for example, start with 4 units and increase by increments of 2 units.

Once the desired glycaemic control has been achieved, establish a monitoring schedule to avoid hypoglycaemia and hyperglycaemia. Testing preprandial BGLs several times a week will pick up the lows (BGLs of 2, 3 and 4) and the highs (BGLs of 8, 9 and 10) and prompt changes in the basal insulin dose. Measuring the A_{1c} two to three times a year will check the overall long-term glycaemic control and may prompt changes to the glycaemic targets and/or the monitoring schedule.

Choosing the insulin to use

Often the most important factor in choosing the formulation of insulin to use is the injection device available.[12] Most patients now use multidose insulin injectors to deliver insulin, as they are generally more convenient than insulin vials and disposable syringes. Pen injectors can be either disposable devices that are prefilled or reusable devices that can be reloaded using 3 mL cartridges. Older patients and those with limited vision or dexterity may prefer to use the larger prefilled disposable device known as InnoLet, which is easily adjusted, has large numbers that are easy to see, is easy to grasp and has a plunger that is easily depressed (Figure 2).

The delivery devices available for the basal and bolus insulins are listed in Table 4. It should be noted that, with the exceptions of detemir (Levemir) and the vial preparations of glargine (Lantus) and glulisine (Apidra), the insulin preparations in this table are currently PBS-subsidised for use in type 1 and type 2 diabetes. Detemir is currently PBS-subsidised for type 1 diabetes only.

Insulin analogues

Analogue basal insulins are clear solutions and unlike the cloudy isophane insulin preparations do not require mixing before use to ensure a uniform suspension. This can be a considerable advantage because

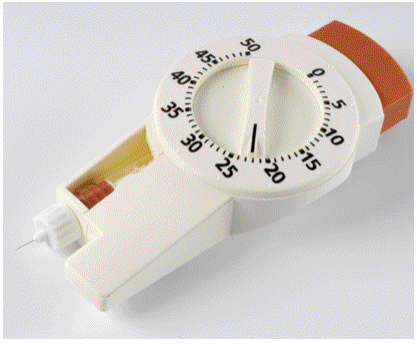

Figure 2. The InnoLet insulin delivery device has a large plunger and a large dial. It is particularly suited to older patients and those with limited vision and dexterity.

although the isophane insulins are cheaper for the health care system they are not always thoroughly mixed by patients or nursing staff. Another advantage of the basal analogues is their long duration and flat profile of activity, which means that the insulin can often be given once daily at any time of the day, as long as that timing is fairly consistent from day to day.

Regular (neutral) and analogue bolus insulins are both clear solutions and do not require mixing. The bolus analogues have the advantage of reaching a peak earlier and controlling postprandial blood glucose better than neutral insulin. Also, they are effective if given immediately before, during or after the meal. Theoretically this could be useful for patients whose food intake is variable, as the dose of bolus analogue could be based on the amount of carbohydrate eaten. However, this complicates the schedule considerably and an alternative strategy might be to stop giving the bolus insulin in this situation. Because of their more rapid onset of action, the bolus analogues also have the potential disadvantage of causing more severe postprandial hypoglycaemia if adequate carbohydrate is not eaten at the meal.

Premixed insulins

Premixed insulin preparations are convenient combinations of basal and bolus

continued

Table 4. Insulins and their delivery devices

Basal insulin

Basal insulin analogues

- Loadable pens – detemir (Levemir), glargine (Lantus)
- Prefilled multidose disposable pens – detemir, glargine
- Vials for syringes – glargine

Isophane insulin

- Loadable pens – Humulin NPH, Protaphane
- Prefilled multidose disposable pens – Protaphane (Novolet and the larger device, InnoLet)
- Vials for syringes – Humulin NPH, Protaphane

Bolus insulin

Neutral insulin, human

- Loadable pens – Actrapid, Humulin R
- Vials for syringes – Actrapid, Humulin R

Bolus insulin analogues

- Loadable pens – aspart (NovoRapid), lispro (Humalog)
- Prefilled multidose disposable pens – aspart, glulisine(Apidra)
- Vials for syringes – aspart, glulisine, lispro

insulins and are commonly used worldwide. Mixes include bolus/basal proportions of 25/75, 30/70 and 50/50. Preparations are either mixes of quick-acting neutral insulin and intermediate-acting isophane insulin (Humulin 30/70, Mixtard 30/70 and 50/50) or mixes of the bolus analogues aspart and lispro with their respective protamine-based longer-acting preparations (Humalog Mix25, Humalog Mix50, NovoMix 30).

Occasionally premixes match the person's need for basal and bolus insulin but often the fixed combination provides too much bolus for the required basal insulin, or vice versa, and results in problems of hypoglycaemia and/or hyperglycaemia and/or weight gain that are not easy to control. If bolus insulin is required and the proportion of bolus to basal insulin is close to that in a premix and is not expected to change in the future, premixed insulins can simplify the insulin schedule. However, insulin requirements usually do change, and a premix appropriate today may no longer be appropriate in a year's time.

If premixes are used, it is important to be aware of the different effects of the basal and bolus insulins on the blood glucose profile. When increasing or decreasing the dose of the premix because of a problem of excess or inadequate basal or bolus insulin, it is easy to also be causing further glycaemic problems, which in turn require further adjustments and may cause further problems.

Conclusion

In the 'young old' – a person with a chronological age of over 65 years and a biological age of younger than 75 – tight glycaemic control can still reduce the complications of diabetes. However, in the 'old old' – a person with a chronological age of over 65 years and a biological age of 75 or older – tight glycaemic control offers few long-term advantages and also increases the burden of care and may reduce quality of life. The goal of glycaemic control in the 'old old' is to maintain a balance between hypoglycaemia and hyperglycaemia.

Starting insulin in the 'young old' and 'old old' follows the same KISS ('keep insulin safe and simple') approach as applies to younger people, although in the 'old old' preprandial targets may be higher (such as 5 to 7 mmol/L rather than 4 to 6 mmol/L) to reduce the risk of hypoglycaemia and/or the burden of care.

The basic KISS principles of insulin therapy – the insulin KISS – are to start basal insulin at 10 units in the evening to control overnight and basal blood glucose, and then add a second basal dose in the morning as needed. Occasionally daytime hyperglycaemia will be the dominant feature, and the first basal dose is then given in the morning, and the second dose is added if needed in the evening. Hyperglycaemia occurring in the middle of the day (before lunch) or after the evening meal requires review of lifestyle, consideration of acarbose and/or addition of bolus insulin.

Although the choice of the insulin formulation is largely determined by the injection device suitable for the patient and/or carer, analogue insulins have advantages over traditional insulins in some circumstances. Premixed insulin preparations offer the benefit of convenience but are limited by fixed, and sometimes inappropriate, proportions of basal and bolus insulins. MT

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A list of references is available on request to the editorial office.

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The insulin KISS in older people with type 2 diabetes ('keep insulin safe and simple')

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