The use of **insulin** in **Type 2 Diabetes**

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Key points:

- Insulin is under used in people with type 2 diabetes
- There is evidence that early initiation of insulin is beneficial
- Initiation of insulin requires a team approach and close follow up
- Start with low doses of insulin and then slowly but steadily titrate until target HbA_{1c} is reached
- Combined therapy with insulin and oral metformin can result in improved glycaemic control, less weight gain and fewer hypoglycaemic episodes

Insulin often required for best management of type 2 diabetes

The challenge of achieving optimal blood glucose control in people with type 2 diabetes is something faced on a daily basis by many GPs. The progressive effects of diabetes on beta cell function and insulin resistance mean that oral anti-diabetic medications become less effective with time.[1] Best management of type 2 diabetes therefore inevitably results in consideration of the use of insulin.

The task of initiation of insulin therapy has traditionally been undertaken in a secondary care setting. Factors such as the increasing prevalence of diabetes, an aging population, financial constraints, the push for tighter control and the earlier need for insulin to achieve this mean that this role will increasingly fall to primary health care teams.[2,3]

Insulin is under used in people with type 2 diabetes

There is evidence that insulin is under used in people with type 2 diabetes.[4,5] Studies show that for most people with type 2 diabetes, a target HbA_{1c} level of 7% is not achieved, HbA_{1c} levels are higher than recommended by most guidelines for extended periods of time (at least 12 months) and changes to treatment may not occur until mean HbA_{1c} is 9% or more.[1, 5] Even after intensification of treatment, there is evidence that the HbA_{1c} remains above the target level for at least another six months, because insulin doses are not titrated as frequently as required.[1]

The benefits of adding insulin

Insulin can be the most effective drug for controlling hyperglycaemia in people with diabetes. It has more potential to lower blood glucose than oral medication and its use is limited only by hypoglycaemia.[10,11] There is increasing evidence that if insulin is initiated early then beta-cell damage and hence disease progression may be slowed.[12, 13] It is also now known that sulfonylureas, which stimulate the beta-cells to secrete insulin, may actually accelerate beta-cell failure.[14]

What is an acceptable HbA_{1c}?

A target HbA_{1c} of 7% remains the ideal for all diabetic patients. This may not be a realistic target for everyone but generally the lower the HbA_{1c} the better and any reduction in level is beneficial.[6] A higher HbA_{1c} may need to be negotiated in people who have frequent hypoglycaemic episodes or hypoglycaemic unawareness, in elderly people who are frail or have significant comorbidities and in people at risk of hypoglycaemia who may live alone.[6]

The current New Zealand guideline recommends that an individual target HbA_{1c} is negotiated with each patient taking into account the following factors:[6]

- Risk factors (e.g. age, BMI, blood pressure, lipid status). The type and number of risk factors may influence treatment decisions particularly about insulin
- Presence of complications or comorbidities
- Adverse effects of therapy, particularly hypoglycaemia
- Patient choice
- Psychosocial circumstances e.g. frailty, age, living alone, mental illness, chaotic lifestyle

New evidence shows that reducing HbA_{1c} below 7% is unlikely to be beneficial for older patients with long standing disease.[7] These patients with predominantly macrovascular complications, may not benefit from lowering HbA_{1c} below 7%, if other vascular risk factors are controlled.[8, 9]

Barriers to the use of insulin.[10, 11, 12, 15]

Patient

- The thought of injections
- Adverse effects including weight gain and hypoglycaemia
- The feeling they have failed
- Misconceptions about treatment with insulin – pre-existing ideas are often based on negative experiences from others
- Practical considerations (including the "hassle" factor)
- Technical skills and equipment required for self monitoring blood glucose (SMBG) and injections
- The possible impact on driving – this may impact on their job (e.g. taxi, passenger service vehicle, see page 36)
- Thoughts of discrimination or employment restrictions at work
- "Live for today" people – some people prefer to live with an increased risk of complications, particularly in situations where they currently have no symptoms that impact on day to day life

Doctor

- The complexity of the initiation process and of educating patients
- "Clinical inertia" [11]
- The need to change the view of insulin as a threat, punishment or last resort that is used only after patients have "failed"
- Adverse effects (e.g. weight gain, hypoglycaemia) including countering any patient anxiety about these
- Lack of resources, primarily time and personnel

Most people with type 2 diabetes will eventually require insulin

Endogenous insulin production will decrease over time for all people with type 2 diabetes. Most people with type 2 diabetes will eventually require insulin. Understanding this right from the time of diagnosis, is likely to reduce the shock, when it is decided that insulin is required. Starting insulin is likely to be a significant event for any patient – for many it will be overwhelming.[11] However if discussed early, it is less likely to be seen by patients as a failure or punishment.

Best practice tip: Tell patients they are not failing, only their beta cells are!

When should insulin be initiated?

Insulin is part of the normal progression in the management of people with type 2 diabetes

Insulin should be considered in all people with type 2 diabetes who have unsatisfactory glycaemic control, despite lifestyle support and maximal oral hypoglycaemic agents. For a patient with significant hyperglycaemia who is already on maximal oral agents, the move to insulin should be immediate. The presence of diabetic complications and personal patient preference may also influence the decision to initiate insulin.

It is difficult to set an HbA_{1c} level where insulin should always be initiated, as it will vary from patient to patient. One problem that GPs have, is knowing when to escalate treatment, and there is a tendency to leave people with type 2 diabetes with high HbA_{1c} levels for long periods of time. This occurs both with initiation and titration of oral therapy and with initiation of insulin. Insulin should be viewed as just another step in the treatment ladder, and the most important thing is that action is taken, if the HbA_{1c} level is unacceptable for a particular patient.

Occasionally insulin will need to be started in a person newly diagnosed with type 2 diabetes. Often these patients will be unwell with weight loss, hyperglycaemic symptoms

and significant ketonuria and require referral for hospital treatment.

Are there patients who may not benefit from insulin?

Early initiation of insulin is beneficial for younger patients who have a high lifetime risk of complications.[16] However in some older patients with no complications, the risks of insulin treatment may outweigh the benefits particularly if there is a short history of diabetes, no symptoms and less likelihood of complications developing in the patient's lifetime.

Initiation of insulin may not be a suitable option for the following groups of people:

- Some patients who are morbidly obese – treatment with insulin alone can increase weight which may make control of their diabetes more difficult
- Asymptomatic elderly people – if there is only a short history of diabetes then long term complications may not be a concern within their lifetime
- People with mental health problems or other comorbidites that may mean they are unable to cope with insulin treatment
- People in whom the potential risks outweigh the potential benefits

The simplest insulin regimen is the addition of an intermediate acting insulin to existing oral medication.

A recent review has shown no consensus in the choice of insulin regimen.[17] In general practice the simpler insulin regimens are easier to initiate and manage, however they will not suit everyone. Specialist advice may be required.

The simplest insulin regimen to initiate in general practice is the addition of an intermediate acting insulin to existing oral medication. Evidence supports the ongoing use of oral metformin,[17] however sulfonylureas should usually be stopped. The easiest approach is to stop the sulfonylurea when insulin is initiated, although some clinicians wean the dose over three months. Always reinforce the importance of continuing a good diet and maintaining exercise levels.

The advantages of combining oral therapy and insulin include:

- A simpler treatment regimen with minimum injections (at least initially)
- Less risk of hypoglycaemia because the starting dose can be lower and increases made gradually
- Better glycaemic control in the initial introduction and adjustment stage.
- Lower risk of weight gain

Autoimmune diabetes in adults

In people with type 2 diabetes who have a BMI <25, a history of thyroid disease or who are younger it is worth checking GAD (glutamic acid decarboxylase) antibodies, as some will have an adult form of type 1 diabetes and may do better with early initiation of insulin alone.

An example of a once daily insulin regimen

1. Start with 8–10 units of protophane or Humulin NPH usually before bed e.g. 9 to 11pm
2. Continue oral metformin at current dose e.g. 1 g twice daily
3. Minimum SMBG for this regimen is:
   - Pre-breakfast to titrate the dose and check for morning hypoglycaemia
   - Pre-evening meal to check for hypo or hyperglycaemia and give information for varying the regimen if control is not achieved
   - Two hours post-evening meal to check for surging glucose level as this may require a different insulin regimen

   Once stable, SMBG should be done as often as required to allow freedom from hypoglycaemia and to give information to keep HbA_{1c} at the target level e.g. three to four times a day, two to three days per week.
4. Dose should be titrated aiming to achieve a pre-breakfast glucose of 6 mmol/L.

For the majority of patients, starting insulin as an evening dose is recommended. This is because high morning fasting glucose levels, due to excessive glucose production overnight, are characteristic of poorly controlled type 2 diabetes. Some elderly patients who have higher levels in the afternoon however may respond better to insulin given in the morning.

Once initiated, adjust the insulin dose slowly

Once initiated, slow increases in insulin dose are recommended.[16] This is likely to reduce the risk of hypoglycaemia and increase both patient and doctor confidence. Depending on fasting SMBG results, the dose of insulin should be increased every one to two weeks as necessary.

One suggested method of titration is to increase the insulin dose by: [16]

- 2 units if pre-breakfast glucose readings are consistently above 6 mmol/L
- 4 units if pre-breakfast glucose readings are consistently above 8 mmol/L

These gradual increases can continue for the first two to three months and then the HbA_{1c} should be rechecked. Ideally there should be a reduction in HbA_{1c} of about 1%. If this is not the case then check the patient is still using the insulin and also continuing to take their oral metformin.

Over the next six to twelve months, further gradual increases in insulin dose may be required depending on HbA_{1c} levels. The majority of people with type 2 diabetes are insulin resistant so the insulin doses required may be higher than expected.[18] People who are obese and those who had high initial HbA_{1c} levels are likely to need the highest doses.

If HbA_{1c} remains above target level once fasting glucose levels are normalised, information from SMBG (pre-evening meal and two hours after meals) will help guide a change of insulin regimen. This may require a move to a twice daily premixed insulin regimen (e.g. Penmix 30:70 or Humalog Mix 25) or the addition of rapid acting insulin pre-meals. At this stage advice from a specialist diabetes team is often useful.

Normalising blood sugar

Slow is best. Sudden normalisation of long standing high blood glucose levels can in some cases cause temporary progression of complications e.g. diabetic retinopathy, insulin neuritis (acute symptomatic neuropathy) or pseudo hypos (hypo symptoms at normal glucose levels). These usually settle with time.

Getting started with insulin

A team approach is required

Successful initiation of insulin in a primary care setting requires education, resources and time and is likely to require input from GP, practice nurse, pharmacist and diabetic educators. Realistically in most general practices the education and support that the patient requires will be undertaken by the practice nurse.

There is a lot of information that needs to be given to the patient. Check that they fully understand what treatment with insulin involves. It may be useful to encourage them to talk to someone who is already doing well on insulin. If the patient is still uncertain or reluctant it may be helpful to suggest a three month trial.

Before starting insulin the patient needs to develop the technical skills to self monitor blood glucose (SMBG) and self inject. Generally once they have overcome the psychological barrier of the injections they will persist with treatment.

What needs to happen once the decision to start insulin is made?

Initiating insulin is likely to require a longer consultation and multiple visits. How much and just what information is conveyed at each contact will depend on the individual patient and the complexity of the regimen to be started.[15]

The key information required should initially cover;

- SMBG techniques and frequency
- Injection technique including injection sites
- Reinforcement of the need for a good diet and maintaining exercise levels
- Hypoglycaemic awareness and treatment
- Storage of insulin, disposal of needles

The choice of delivery device

For the simple regimen discussed on page 34 there is a choice of two insulin's (protophane or Humulin NPH) and therefore two pen devices available. Protophane is manufactured by Novo Nordisk and requires a NovoPen. Humulin NPH is manufactured by Eli Lilly and requires a Humapen. An insulin pen from one manufacturer will not fit insulin cartridges from another manufacturer.

Individual patient preference for a particular pen may determine the brand of insulin although in more complicated regimens the choice of a specific type of insulin will determine the type of pen (e.g. switching to Humalog Mix 25 requires a Humapen Luxura). Factors which may guide choice include the patient's manual dexterity, any visual impairment and the size of the dose likely to be required.

The reusable pen devices are usually preferred by patients as they are convenient and discrete and may improve compliance. Injections with pens are thought to be easier, faster and more accurate.

How to help patients overcome their fear of injections

A good tool to help get over the fear of self injection is to give a "dummy injection". This can help with fears accompanying the thought of the actual injection – how easy is it, how do you do it, where does it go, does it hurt, what are the likely problems with injections. Once a patient has given a supervised injection they are often relieved how easy and relatively painless it is. A pen with placebo

may be given to the patient to practice at home prior to the next consultation. For patients who may have a needle phobia, the NovoPen 3 PenMate could be considered. It is an additional device that is used with a NovoPen 3 to conceal the needle.

Check that the patient knows how to monitor their blood glucose

SMBG is not routinely recommended for patients with type 2 diabetes who are on diet or metformin alone, however once a patient is started on insulin it is necessary. It is important to check that patients have the equipment and skills to do this. How often they will need to perform SMBG will depend on their individual insulin regimen. For example with the simple insulin regimen discussed on page 34, this will initially be at least three times every day, until stable then perhaps three days per week. The key is that testing is done to guide dose changes and to look for trends in high and low glucose levels.

Other practical issues at the time of initiation

1. When? The ideal time to schedule the first injection is earlier in the week so that the patient can be seen again if required. A low dose of intermediate acting insulin at night will seldom cause problems with hypoglycaemia in the day or overnight. Driving restrictions are not usually needed but patients should test before driving.
2. Where? Some patients prefer the surgery setting, for others home may be preferable.
3. Do they require a support person? Having a partner, friend, carer or family member present may help in recall of information, providing support and transport home.
4. Do they know who to contact in an emergency? Make sure they have appropriate contact numbers written down and consider a Medic Alert emblem.
5. Do they know how to store their insulin and what to do with sharps?
6. Do they know what to do if they are unwell, when they exercise, or if the weather is hot? (this may be learnt over time rather than at initiation)
7. Do they know that it is important to contact the practice regularly e.g. weekly to enable titration of doses?

Regular follow up is required

Regular follow up will be required, usually weekly initially, with perhaps more frequent phone contact. This contact provides an ideal opportunity for dose titration, provision of more detailed dietary advice, reinforcement of good injection techniques and time for answering any questions that may have arisen. Written information to back up verbal instructions should be provided. Information pamphlets are widely available.

LTSA requirements

People with type 2 diabetes who use insulin are generally considered fit to drive, however vocational drivers will need to see a diabetes specialist for individual assessment. If in doubt about any patient's driving risk, refer to a local diabetes team.

A person may be deemed unfit to drive if they have severe or recurrent hypoglycaemia or if they have hypoglycaemia unawareness i.e. they are unable to detect developing hypoglycaemia and to respond to it appropriately and in good time.

For further information see the LTSA website: **www.landtransport.govt.nz/licensing/medical-aspects/4.html**

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