Type 2 Diabetes: When to Initiate And Intensify Insulin Therapy

Julie Bate on behalf of:
Dr John Wilson
Endocrinologist
Capital and Coast DHB
Declarations

I have received travel funding and speaker fees from manufacturers of Insulin.

There has been no input from pharmaceutical companies in designing my presentation today.
Synopsis of talk

- NZ trends for Type 2 Diabetes
- Starting basal insulin
- Titrating basal insulin
- Adding in additional insulin
- What to do with those oral hypoglycaemics
The epidemic

Diabetes prevalence in New Zealand
- 243,125 in New Zealand with Diabetes (12/2013)
- 90% T2DM
- 5% of population
Ethnic Differences

- 4% of NZ European
- 10-15% of Maori, Pacific Island, Asian
Early and consistent management of glycaemic control is necessary to avoid micro-vascular and macro-vascular complications.

Good glycaemic control is difficult to maintain over time as the condition progresses.

More intensive treatment is usually required over time to meet treatment targets.
Insulin treatment is part of the normal progression in the management of people with Type 2 diabetes

“hormone replacement therapy”
Priority area-initiation of insulin for glycaemia control

“Shift in diabetes service delivery from secondary care to primary care”

“Recommended primary care be given the skills, capability and permissions to initiate insulin where appropriate”
Mr B

- 51 year old male
- BMI 34
- HbA1c 95 mmol/mol
- Type 2 Diabetes since 2006
- Metformin 1g bd
- Gliclazide 160mg bd

What is next for his diabetes?
Management of glycaemic control

Target HbA1c 50–55 mmol/mol or as individually agreed

**Lifestyle modification**
- Food, physical activity and behavioural strategies

If measured HbA1c does not meet or closely approach agreed target within 3 months, or if patient is symptomatic, drug therapy should be considered

**First line drug therapy**
- Metformin
  - Gastrointestinal tolerance may be improved by gradual introduction
  - Stop if eGFR < 30 ml/min/1.73 m²

If metformin not tolerated or contraindicated

**Sulphonylurea**
- Educate the person on the possibility of hypoglycaemia
  - Note acarbose therapy

Review medication adherence and dose optimisation

If above target > 3 months

**Second line drug therapy**
- Add sulphonylurea

If metformin and sulphonylurea not tolerated or contraindicated or if an alternative to insulin is required

**Third line drug therapy**
- Insulin
  - Note DPP-IV inhibitor and GLP-1 agonist

If no congestive heart failure
- If at significant risk of hypoglycaemia
- Consider the increased risk of fracture in women
  - Note DPP-IV inhibitor
"God, I hate needles!"
Together you and Mr B decide that insulin is the next step
Patient Barriers to insulin use

- The thought of injections
- Adverse effects including weight gain and hypoglycaemia
- The feeling that 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 skill and equipment required for self monitoring blood glucose and injections
Patient Barriers to insulin use

- The possible impact on driving – this may impact on their job (e.g., taxi, passenger service vehicle)
- Thoughts of discrimination or employment restrictions at work
- Embarrassment
- “Live for today” people - some 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 barriers to insulin initiation

- Complexity of the initiation process and of educating patients
- 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 (eg weight gain, hypoglycaemia) including countering any patient anxiety about these
- Lack of resources, primarily time and personnel
### Mr B’s blood sugars

<table>
<thead>
<tr>
<th>Before Breakfast</th>
<th>Before dinner</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.2</td>
<td>13.2</td>
</tr>
<tr>
<td>11.7</td>
<td>12.8</td>
</tr>
<tr>
<td>13.9</td>
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<tr>
<td>9.9</td>
<td></td>
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<tr>
<td>11.0</td>
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</tr>
</tbody>
</table>
**Initiation of insulin in primary care**

**Monitor blood glucose (BG) profile**

Choose one of:

**Once daily isophane insulin – at night**
Choose if the person has predominantly high fasting BG levels that decrease or stay the same during the day.

**Once daily isophane insulin – pre breakfast**
Choose if the person’s fasting BG levels are acceptable but rise during the day.

**Twice daily isophane insulin**
This may be considered if the person has high BG levels during the day and night or is markedly hyperglycaemic.

**Initiate once daily isophane insulin**
Prescribe a starting dose of usually 10 units isophane insulin* at bedtime (if high fasting glucose) or pre breakfast (if predominantly daytime hyperglycaemia). Continue with oral metformin and sulphonylurea.

**Initiate twice daily isophane insulin**
Prescribe a starting dose of usually 6–10 units isophane insulin* twice daily (given pre breakfast and pre evening meal). Discontinue sulphonylurea.

**Titrate the dose**
- Review BG levels and adjust dose until the individually-agreed BG target is reached or hypoglycaemia limits further titration. Patients should be given instructions on how to self-adjust the dose.
- Review every 2–4 days or agreed timeframe depending on response.
- Use of other regimes.

* Currently funded isophane insulin is Protaphane or Humulin NPH.

**Follow-up and specialist advice**
Why start with basal insulin?

Comparison of 24-hour glucose levels in untreated vs treated patients with diabetes

You start 10 units Isophane NPH at night
Dose adjustment-first fix fasting

- Slow titration-Patient lead
- Fast titration-Doctor/nurse lead
Slow titration

- Increase dose of insulin by 2 units every 3-4 days
- Continue increasing until Blood sugar levels below 6
Fast titration

- Doctor/nurse lead
- Increase insulin by 2-8 units every 3-4 days depending on what fasting sugar has been like
<table>
<thead>
<tr>
<th>Mean fasting blood glucose (mmol/L)</th>
<th>Increase in insulin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>* See below</td>
</tr>
<tr>
<td>4–5.9</td>
<td>No change</td>
</tr>
<tr>
<td>6–6.9</td>
<td>2 units</td>
</tr>
<tr>
<td>7–7.9</td>
<td>4 units</td>
</tr>
<tr>
<td>8–10</td>
<td>6 units</td>
</tr>
<tr>
<td>&gt;10</td>
<td>8 units</td>
</tr>
</tbody>
</table>

Starting dose 10 units, adjust dose twice weekly to reach the target FBG of <6mmol/L. Insulin dose may be decreased (small decreases of 2 to 4 units) if there is severe hypoglycaemia (requiring assistance) or if BGL <3.0 mmol/L in preceding week. Do not increase insulin dose if fasting BGL <4 mmol/L at any time in preceding week.

Mr B’s summary so far

- Elevated HbA1c on optimal doses of 2 oral hypoglycaemic agents
- Lifestyle measures
- Insulin therapy appropriate and started
- Insulin doses titrated as appropriate
- To be reviewed with repeat bloods and blood sugars at 3 months
Mr B’s 3 month review

- Isophane NPH 30 units at night
- Metformin 1g bd
- Gliclazide 160mg bd

- Fasting glucose average 5.8 (without hypoglycaemia)
- HbA1c 78 mmol/mol
Next steps

- Corrected the fasting glucose but still elevated HbA1c
- Need to find the hidden hyperglycaemia
- Requires additional blood glucose testing
- Ideally 6x per day for 3-4 days
Adding additional insulin

- Will depend on pattern
You discuss possible options with Mr B

Options

– Additional intermediate or long acting insulin
– Prandial insulin
  – Fast acting insulin
  – Mixes

Best for Mr B will depend on Blood sugar profile and Mr B preference
## NOVO NORDISK - BALANCING INSULIN AND DELIVERY.

<table>
<thead>
<tr>
<th>Brand</th>
<th>Presentation</th>
<th>Schematic Time-Action Profile*</th>
<th>Insulin Profile*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NovoRapid®</td>
<td>3ml Penfill®</td>
<td>orm: 10-20 minutes, Peak: 1-3 hours</td>
<td>Duration: 3-5 hours</td>
</tr>
<tr>
<td>Levemir®</td>
<td>FlexPen®</td>
<td>orn: 3-14 minutes, Peak: Up to 24 hours</td>
<td>Duration: 24 hours</td>
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<tr>
<td>Actrapid®</td>
<td>3ml Penfill®</td>
<td>orn: 30 minutes, Peak: 1-3 hours</td>
<td>Duration: 8 hours</td>
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<tr>
<td>Protaphane®</td>
<td>3ml Penfill®</td>
<td>orn: 1.5 hours, Peak: 2-8 hours</td>
<td>Duration: 24 hours</td>
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<tr>
<td>PenMix® 30 &amp; Mixtard® 30 (10mL)</td>
<td>3ml Penfill®</td>
<td>orm: 30 minutes, Peak: 2-8 hours</td>
<td>Duration: 24 hours</td>
</tr>
<tr>
<td>PenMix® 10</td>
<td>3ml Penfill®</td>
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<td>Duration: 24 hours</td>
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<td>PenMix® 20</td>
<td>3ml Penfill®</td>
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<td>PenMix® 40</td>
<td>3ml Penfill®</td>
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<tr>
<td>PenMix® 50 &amp; Mixtard® 50 (10mL)</td>
<td>3ml Penfill®</td>
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</table>

Please review Data Sheet before prescribing. Full Data Sheet is available from the Novo Nordisk Customer Care Centre 0800 733 737. In clinical practice, the duration of insulin action may be shorter or longer than the durations specified. Variations between and within patients may occur depending upon injection site and technique, insulin dosage, as well as diet and exercise. © Registered trademark of Novo Nordisk A/S. Novo Nordisk Pharmaceuticals Ltd PO Box 5768 Parnell, Auckland. www.novonordisk.co.nz

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### Lilly Insulin Range

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Type of Insulin (generic name)</th>
<th>Product Description</th>
<th>Presentation</th>
<th>Schematic Action Profile*</th>
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<tbody>
<tr>
<td>Humalog®</td>
<td>Insulin lispro (lispro)</td>
<td>RAPID-ACTING</td>
<td>10mL vials and 3mL cartridges</td>
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HUMALINS® LUXRA CAN ONLY BE USED WITH LILLY 3ML INSULIN CARTRIDGES. BEFORE PRESCRIBING PLEASE REVIEW THE PRODUCT DATA SHEET.
Prandial insulin
Fast acting versus mixes
Rapid acting insulin

**Advantages**
- Able to mimic meals better (CHO counting)
- Able to titrate doses better
- No set dosing

**Disadvantages**
- Requires more injections
- If adjusting doses requires additional knowledge and mathematical ability
Mixes

Advantages
- Less injections
- Less need for calculating doses

Disadvantages
- Set doses of rapid acting and intermediate insulin
- Missing meals increased risk of hypoglycaemia
Mr B’s 3 month review

- Isophane NPH 30 units at night
- Metformin 1g bd
- Gliclazide 160mg bd

- Fasting glucose average 5.8 (without hypoglycaemia)
- HbA1c 78 mmol/mol
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<tbody>
<tr>
<td>5.2</td>
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<td>9.8</td>
<td>11.9</td>
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Options

– BD Isophane NPH
– Daily long acting insulin
### Scenario 2

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<th>Before Breakfast</th>
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<th>Before Lunch</th>
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<tr>
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<td>5.1</td>
<td>6.1</td>
<td>5.8</td>
<td>11.0</td>
</tr>
</tbody>
</table>
Only post dinner is high

Options
- Add in a rapid acting insulin
  - start at 4 units
- Change to a mix
  - Start at same dose of Isophane NPH
## Scenario 3

<table>
<thead>
<tr>
<th>Before Breakfast</th>
<th>After Breakfast</th>
<th>Before Lunch</th>
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<tbody>
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<td>9.3</td>
<td>9.0</td>
<td>14.0</td>
</tr>
<tr>
<td>6.1</td>
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<td>9.9</td>
<td>10.5</td>
<td>12.7</td>
<td>10.2</td>
<td>15.0</td>
</tr>
</tbody>
</table>
Generally increases during day

Increases also post breakfast and post dinner

Options

– BD isophane NPH with BD rapid acting insulin
– Switch to daily long acting insulin and bd rapid acting insulin
– Switch to bd mixed insulin
Stopping oral hypoglycaemics?
Metformin

- Increases insulin sensitivity
- Should continue as may require less insulin
- Only stop if side effects or other contraindications

(Pioglitazone also in this group)
Sulphonylureas

- Work by increasing secretion of insulin by pancreas
- Once on bd isophane or prandial insulin should be stopped
Mr B summary

- Started and titrated up insulin to fix the fasting glucose
- Still elevated HbA1c
  - Looked for hidden hyperglycaemia
- Appropriate additional insulin added
- Ongoing review required
Practice points

- Don’t delay insulin initiation
- Keep it simple for you and patient
- Ensure patient has expectation that basal dose will increase and what the dose may end up at
- Titrate!!! Fix the fasting then look for hidden hyperglycaemia
Practice points

- If unsure of next step--- ASK!
- Trying to establish secondary care nurses at each primary care practice
- How else can we help you?