Fighting the Hydra: Optimizing treatment for type 2 diabetes

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Insulin detemir versus insulin glargine for type 2 diabetes mellitus
Abstract

Background
Chronically elevated blood glucose levels are associated with significant morbidity and mortality. Many diabetes patients will eventually require insulin treatment to maintain good glycaemic control. There are still uncertainties about the optimal insulin treatment regimens for type 2 diabetes, but the long-acting insulin analogues seem beneficial. Several reviews have compared either insulin detemir or insulin glargine to NPH insulin, but research directly comparing both insulin analogues is limited.

Objectives
To assess the effects of insulin detemir and insulin glargine compared with each other in the treatment of type 2 diabetes mellitus.

Search methods
We searched MEDLINE, EMBASE, The Cochrane Library, online registries of ongoing trials and abstract books. Date of last search was January 2011.

Selection criteria
All randomised controlled trials comparing insulin detemir with insulin glargine with a duration of 12 weeks or longer were included.

Data collection and analysis
Two authors independently selected the studies and extracted the data. Pooling of studies by means of random-effects meta-analysis was performed.

Main results
This review examined four trials lasting 24 to 52 weeks involving 2250 people randomised to either insulin detemir or glargine. Overall, risk of bias of the evaluated studies was high. Insulin glargine was dosed once-daily in the evening. Insulin detemir was initiated once-daily in the evening with the option of an additional dose in the morning in three studies and initiated twice-daily in one study. Of randomised patients 13.6% to 57.2% were injecting insulin detemir twice-daily at the end of trial.
Glycaemic control, measured by glycosylated haemoglobin A1c (HbA1c) and HbA1c equal to or less than 7% with or without hypoglycaemia, did not differ statistically significantly between treatment groups.

The results showed no significant differences in overall, nocturnal and severe hypoglycaemia between treatment groups. Insulin detemir was associated with less weight gain. Treatment with insulin glargine resulted in a lower daily basal insulin dose and a lower number of injection site reactions.

There was no significant difference in the variability of FPG or glucose values in 24-hour profiles between treatment groups. It was not possible to draw conclusions on quality of life, costs or mortality. Only one trial reported results on health-related quality of life and showed no significant differences between treatment groups.

**Authors’ conclusions**

Our analyses suggest that there is no clinically relevant difference in efficacy or safety between insulin detemir and insulin glargine for targeting hyperglycaemia. However, to achieve the same glycaemic control insulin detemir was often injected twice-daily in a higher dose but with less weight gain, while insulin glargine was injected once-daily, with somewhat fewer injection site reactions.
Summary of findings: Insulin detemir (intervention) vs. Insulin glargin (control) for type 2 diabetes mellitus

Patient or population: patients with type 2 diabetes mellitus

Intervention: Insulin detemir (intervention) vs. Insulin glargin (control)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed risk Control</td>
<td>Corresponding risk Insulin detemir (intervention) vs. Insulin glargin (control)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mortality - not reported</td>
<td>See comment</td>
<td>Not estimable</td>
<td>-</td>
<td>See comment</td>
<td>Not investigated</td>
</tr>
<tr>
<td>Quality of life and treatment satisfaction – not reported</td>
<td>See comment</td>
<td>Not estimable</td>
<td>-</td>
<td>See comment</td>
<td>Insufficient information as only one included study reported on health-related quality of life.</td>
</tr>
<tr>
<td>Change in HbA1c</td>
<td>The mean change in HbA1c in the intervention groups was <strong>0.07 higher</strong> from -1.25 to -1.68 %</td>
<td><strong>RR 0.82</strong></td>
<td>2250 (4 studies)</td>
<td>⊕⊕⊖⊖ low²²</td>
<td>Change in HbA1c</td>
</tr>
<tr>
<td>Percentage of participants having at least one severe hypoglycaemic event</td>
<td>33 per 1000 (17 to 43)</td>
<td><strong>RR 0.92</strong></td>
<td>2252 (4 studies)</td>
<td>⊕⊕⊕⊕ low³⁴</td>
<td></td>
</tr>
<tr>
<td>Percentage of participants having at least one hypoglycaemic event</td>
<td>544 per 1000 (501 to 571)</td>
<td><strong>RR 0.98</strong></td>
<td>2252 (4 studies)</td>
<td>⊕⊕⊕⊕ low¹</td>
<td></td>
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</tbody>
</table>
### Weight gain

<table>
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<tr>
<th></th>
<th>The mean weight gain ranged across control groups from 1.4 to 3.8 kg</th>
<th>The mean weight gain in the intervention groups was <strong>0.91 lower</strong> (1.21 to 0.61 lower)</th>
<th>2250 (4 studies)</th>
<th>☉☉☉☉ high</th>
</tr>
</thead>
</table>

### Percentage of participants having at least one injection site reaction

|                           | 4 per 1000 (4 to 39) | 13 per 1000 (4 to 39) | RR **3.31** (1.13 to 9.73) | 2252 (4 studies) | ☉☉☉☉ low¹³ |

*The basis for the assumed risk (e.g., the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

**CI:** Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence

- **High quality:** Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low quality:** We are very uncertain about the estimate.

¹ Low number of events

² HbA1c is only a weak surrogate for mortality and diabetes-associated morbidity

³ Due to (i) lack of blinding and (ii) different frequency of injection and different injection devices across treatments

⁴ Wide confidence interval and low number of total events