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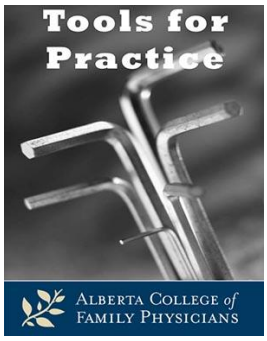
Reviewed: January 29, 2018
Evidence Updated: New systematic reviews
Bottom Line: Unchanged
First Published: October 26, 2010



The Long and Short of Long Acting Insulin Analogues (versus NPH)

Clinical Question: In patients with diabetes, how do the long-acting insulin analogues (LAIA) (e.g. glargine and detemir) compare to NPH?

Bottom Line: Compared to NPH insulin, long-acting insulin analogues have no advantage in A1c, no evidence for hard outcomes, and no difference in severe hypoglycemia. The small reductions in other hypoglycemic symptoms have a high risk of bias. Patients with significant hypoglycemia from NPH should consider using lower NPH doses first. If NPH dosage reduction doesn't resolve hypoglycemic episodes, patients and clinicians may consider LAIAs.

Evidence:
Systematic review of 49 randomized controlled trials of insulin analogues found[1,2]:

- A1c: Glargine or determir versus NPH.
  - No difference in attaining A1c <7%.
  - Mean A1c: Most comparisons not statistically different, and none were clinically significant (e.g. A1c on NPH was 0.28% lower than glargine in patients not on oral medications).
- Hypoglycemia: Glargine (with oral meds).
  - Severe hypoglycemia: No statistical difference.
  - Overall hypoglycemia (patients with ≥1 episodes):
    - Glargine (47.2%) statistically significantly lower than NPH (55.9%), Number Needed to Treat (NNT)=12.
  - Nocturnal hypoglycemia (patients with ≥1 episodes):
    - Glargine (18.8%) statistically significantly lower than NPH (33.1%), NNT=7
- Hypoglycemia: Detemir (with oral meds).
  - Similar to glargine versus NPH (except overall hypoglycemia not different).

Limitations of this evidence:

1. Definitions of hypoglycemia varied considerably.
2. Unblinded: Everyone knew who was on which insulin.

3. Hypoglycemic symptoms are:
   - Non-specific and heterogeneous.[3]
   - Poorly correlated with biochemical hypoglycemia.[4,5]
4. All trials counted unconfirmed (untested) hypoglycemia (including severe).
5. Trials were primarily industry-funded with poor quality (e.g. >90% were unclear in explaining how randomizations was assured).

Context:

- Cochrane review[6] and other reviews[7,8,9] of LAIA reported very similar results:
  - Cochrane conclusion: LAIA offer "if at all only a minor clinical benefit" and recommend "until long-term efficacy and safety data are available, we suggest a cautious approach to therapy with insulin glargine or detemir."
- Other issues:
  - Weight gain (seven studies): +0.18 kg more with NPH.[1]
  - Cancer risk: Some concern about insulin glargine but the data is observational and not conclusive.[10]
  - Quality of life: Rarely measured but not statistically significant when measured.[11,12]
- LAIA are not cost-effective.[13]

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