

NZSSD EXPERT OPINION

Long-Acting Insulin Analogues

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Guidelines for the management of diabetes promote tight glycaemic control with target HbA1c levels of 6.5-7.0%. For patients with type 1 diabetes and those with type 2 diabetes requiring insulin for control, efforts to achieve these glycaemic targets are often compromised by increasing hypoglycaemia. Long-acting insulin analogues have a physiological profile which is superior to NPH insulin in terms of intra-individual reproducibility and in the temporal pattern as a basal insulin. The introduction of long-acting insulin analogues has provided additional options for which the prime benefit is reduced frequency and severity of hypoglycaemia with associated similar or slightly improved glycaemic control.

Currently in New Zealand access to funded long-acting insulin analogues is restricted through special authority to those with type 1 diabetes meeting criteria for hypoglycaemia, with a requirement for annual renewal of this. Furthermore access is restricted to one agent, insulin glargine, with no second-line funded long-acting insulin.

International guidelines, particularly from countries with a similar health budget to New Zealand such as the United Kingdom and Australia, support a wider use of long-acting analogues than is currently funded in New Zealand.

Randomised clinical trials comparing different insulin regimens whilst providing methodological rigor, do not allow for individualisation of regimens which is so much a part of insulin therapy. Furthermore, outcomes are often focused on HbA1c and not on patient-orientated outcomes such as quality of life. For this reason it is difficult to provide trial evidence for benefit of long-acting insulin analogues in patients in whom we intuitively expect it, such as the elderly, those requiring assistance for administering insulin, shift workers, etc.

Type 1 Diabetes: The 2002 NICE (National Institute for Clinical Excellence) guidelines from the United Kingdom recommend insulin glargine as a treatment option for people with type 1 diabetes. Insulin detemir was not considered in that assessment.

In Australia, glargine is a funded option for patients with type 1 diabetes, with no restrictions placed on its use.

The American Association of Clinical Endocrinologists guideline in 2007 recommends intensive insulin therapy with the use of a basal bolus regimen including a long-acting analogue for patients with type 1 diabetes.

Type 2 Diabetes: The 2002 NICE guideline does not recommend routine use in type 2 diabetes, advising commencing NPH insulin in a once or twice daily regimen, for those who do not achieve adequate glycaemic control on oral agents. However, glargine should be considered in:

- those who require assistance from a carer to administer their insulin
- those whose lifestyle is significantly restricted by recurrent symptomatic hypoglycaemia
- those who would otherwise need twice-daily insulin injections in combination with oral antidiabetic drugs.

In May 2008, NICE updated the recommendation for the management of type 2 diabetes. It considered additional trial data and meta-analysis, commenting on the lack of studies comparing long-acting analogues with twice daily NPH regimens. The additional data supports the finding of reduced nocturnal hypoglycaemia, but does not find convincing evidence of improvements in HbA1c. The only addition to the above recommendation is for a trial of glargine in those on NPH insulin who are getting significant nocturnal hypoglycaemia.

The guideline specifically excludes advice on the role of insulin detemir which is currently under review. However studies comparing detemir with NPH insulin were included in the Cochrane meta-analysis by Horvath, with conclusions no different to that for glargine. There is some evidence that detemir may have a more favourable impact on weight.

In Australia, glargine is a funded option for patients with type 2 diabetes, with no restrictions placed on its use.

Recommendation.

Therefore, there appears to be little strong evidence from clinical trials to justify a widespread policy of using long-acting insulin analogues as first-line basal insulin in patients with type 1 or type 2 diabetes.

For those with type 1 diabetes, the strongest evidence is for reduction in the frequency of hypoglycaemia. Whilst the process is frustrating, the criteria for funding appear to be appropriate for this indication. However, the ability to use detemir, even as a second line agent, would be of benefit. Furthermore, the option of using a once daily long-acting analogue in certain patients where compliance with other regimens is questionable, where injections are given by carers, or similar situations would be a welcome addition.

The recommendations from NICE 2008 above for type 2 diabetes would seem reasonable for the consideration of glargine (or detemir though not included in that guideline) in certain circumstances. However, there is not adequate evidence for the recommendation in those who would otherwise need twice-daily insulin injections in combination with oral antidiabetic drugs. At present those patients meeting the other NICE criteria who elect to have a trial of long-acting analogue insulin would need to fund this themselves unless the present PHARMAC criteria are changed. The balance of current evidence does not justify the recommendation for use in those who would otherwise need twice daily injections.

However, long-acting analogues are not a treatment panacea for all patients with problematic hypoglycaemia, and if introduced without adequate education and follow up have the potential to cause more problems than they correct.

References:

NICE guidelines. www.nice.org.uk

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