Review: α glucosidase inhibitors improve glycaemic control but have uncertain effects on patient-important outcomes in type 2 diabetes

Van de Laar FA, Lucassen PL, Akkermans RP, *et al.* Alpha-glucosidase inhibitors for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2005;(2):CD003639.

Clinical impact ratings GP/FP/Primary care ★★★★★★☆ IM/Ambulatory care ★★★★★☆☆ Endocrine ★★★★★☆☆

Q In patients with type 2 diabetes mellitus, are α glucosidase inhibitors effective for improving glycaemic control?

METHODS

Data sources: Medline (to April 2003), EMBASE/Excerpta Medica (to April 2003), the Cochrane Central Register of Controlled Trials (Issue 3, 2003), LILACS (to April 2003), databases of ongoing trials (all to April 2003), *Current Contents* (to December 2003), contacting experts and manufacturers, and bibliographies of relevant studies.

Study selection and assessment: randomised controlled trials (RCTs) in any language with ⩾12 weeks' duration that compared α glucosidase inhibitor monotherapy with any other intervention in patients with type 2 diabetes and included ⩾1 predefined clinical outcome. Study quality assessment included randomisation, allocation concealment, blinding, and attrition.

Outcomes: glycaemic control, lipid concentrations, body weight, adverse effects, mortality, diabetes related morbidity, and quality of life.

MAIN RESULTS

41 RCTs (n = 8130) were included. Most studies were 24 weeks in duration. α-glucosidase inhibitors improved glycated haemoglobin and fasting blood glucose concentrations (table). Lipid concentrations and body weight were not affected. Acarbose was associated with a greater risk of gastrointestinal adverse effects than placebo (table). Acarbose and sulphonylureas did not differ for glycated haemoglobin or fasting blood glucose concentrations. Data were lacking on the effects of α glucosidase inhibitors on mortality, diabetes related morbidity, and quality of life.

CONCLUSIONS

In patients with type 2 diabetes, α glucosidase inhibitors improve glycaemic control in studies of mainly 24 weeks' duration. Data are lacking on the effects of α glucosidase inhibitors on mortality, diabetes related morbidity, and quality of life.

Abstract and commentary also appear in ACP Journal Club.

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Commentary

α Glucosidase inhibitors are sparsely used in the US compared with some other countries because of their modest efficacy and untoward gastrointestinal side effects, particularly "hyperflatulence." α Glucosidase inhibitors produce very modest improvements in glycaemic control, primarily affecting postprandial glucose excursions. The 0.2% lowering of glycated haemoglobin over 3 years seen in the UKPDS[1] is probably closer to real world experience.

The publication of the STOP-NIDDM trial,[1] showing greater reductions in cardiovascular events and hypertension in patients with impaired glucose tolerance treated with acarbose than with placebo, has caused physicians to rethink the utility of these drugs. A 2004 meta-analysis[3] of studies with 52 weeks' follow up showed a 64% reduction in myocardial infarction with acarbose compared with placebo. Whither the difference with the meta-analysis by Van de Laar *et al*? 5 of the 7 studies included in the 2004 review did not meet the stringent criteria for inclusion in this meta-analysis. 2 were unpublished studies with data available only from the manufacturer. Hence the analyses and conclusions between the 2 reviews are hardly comparable. At best, data indicating that α glucosidase inhibitors are cardioprotective are not compelling.

The problematic side effects and limited efficacy of α glucosidase inhibitors make them unlikely to be a mainstay of diabetic therapy. This view has been voiced in official public pronouncements in Europe.[4 5] I see no reason to differ.

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1 Holman RR, Cull CA, Turner RC. A randomized double-blind trial of acarbose in type 2 diabetes shows improved glycemic control over 3 years (UK Prospective Diabetes Study 44). *Diabetes Care* 1999;**22**:960–4.
2 Chiasson JL, Josse RG, Gomis R, *et al.* Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. *JAMA* 2003;**290**:486–94.
3 Hanefeld M, Cagatay M, Petrowitsch T, *et al.* Acarbose reduces the risk for myocardial infarction in type 2 diabetic patients: meta-analysis of seven long-term studies. *Eur Heart J* 2004;**25**:10–6.
4 McIntosh A, Hutchinson A, Home PD, *et al. Clinical guidelines and evidence review for type 2 diabetes: management of blood glucose.* Sheffield, UK: School of Health and Related Research, University of Sheffield, 2001. www.nelh.nhs.uk/guidelinesdb/html/fulltext-appendix/Bloodglucose2.html (accessed 14 Oct 2005).
5 Rutten GE, Verhoeven S, Heine RJ, *et al.* Guidelines on type 2 diabetes. *Huisarts Wet* 2000;**42**:67–84.

α Glucosidase inhibitors *v* placebo in type 2 diabetes*

Comparisons	Number of comparisons (n)	Outcomes	Weighted mean difference (95% CI)		
Acarbose *v* placebo	28 (2831)	Change in glycated haemoglobin (%)	−0.8 (−0.9 to −0.6)		
Miglitol *v* placebo	7 (1088)		−0.7 (−0.9 to −0.4)		
Voglibose *v* placebo	1 (238)		−0.5 (−0.6 to −0.3)		
Acarbose *v* placebo	28 (2838)	Change in fasting blood glucose (mmol/l [mg/dl])	−1.1 (−1.4 to −0.8) [−19.8 (−14.4 to −25.2)]		
Miglitol *v* placebo	2 (398)		−0.5 (−0.9 to −0.2) [−9.0 (−3.6 to −16.2)]		
Voglibose *v* placebo	1 (234)		−0.6 (−1.0 to −0.2) [−10.8 (−3.6 to −18)]		
			Event rates	**RRI (CI)**	**NNH (CI)**
Acarbose *v* placebo	4 (1442)	Gastrointestinal adverse effects	59% *v* 34%	86% (60 to 110)	4 (3 to 5)

*Abbreviations defined in glossary; RRI, NNH, and CI calculated from data in article using a random effects model. Most studies were 24 weeks in duration.