Review: α-Glucosidase inhibitors improve glycemic 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: GIM/FP/GP ★★★★★☆ Endocrinology ★★★★★☆

QUESTION

In patients with type 2 diabetes mellitus, are α-glucosidase inhibitors effective for improving glycemic 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: Randomized controlled trials (RCTs) in any language ≥ 12 weeks in 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 randomization, allocation concealment, blinding, and attrition.

Outcomes: Glycemic control, lipid levels, body weight, adverse effects, mortality, diabetes-related morbidity, and quality of life.

MAIN RESULTS

41 RCTs (*n* = 8130) were included. 30 RCTs evaluated acarbose, 7 evaluated miglitol, 1 evaluated voglibose, and 3 compared different α-glucosidase inhibitors. Most studies were 24 weeks in duration. α-Glucosidase inhibitors improved glycated hemoglobin and fasting blood glucose levels (Table). Lipid levels and body weight were not affected. Acarbose was associated with a greater risk for gastrointestinal adverse effects than was placebo (Table). Acarbose and sulfonylureas did not differ for glycated hemoglobin or fasting blood glucose levels. 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 glycemic control in studies mainly 24 weeks in duration. Data are lacking on the effects of α-glucosidase inhibitors on mortality, diabetes-related morbidity, and quality of life.

α-Glucosidase inhibitors vs placebo in type 2 diabetes*

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

COMMENTARY

α-Glucosidase inhibitors are sparsely used in the United States 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 glycemic control, primarily affecting postprandial glucose excursions. The 0.2% lowering of glycated hemoglobin over 3 years seen in the UKPDS (1) is probably closer to real-world experience.

The publication of the STOP-NIDDM trial (2), 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-week 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 and colleagues? 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 only available 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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References
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