

Acarbose reduced the risk for cardiovascular disease and hypertension in impaired glucose tolerance

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.

QUESTION

In patients with impaired glucose tolerance (IGT), does acarbose reduce the risk for cardiovascular disease and hypertension?

DESIGN

Randomized (allocation concealed*), blinded {clinicians, patients, data collectors, and outcome assessors}†, * placebo-controlled trial with mean 3.3-year follow-up (STOP-Noninsulin-Dependent Diabetes Mellitus [STOP-NIDDM]).

SETTING

Hospitals in Canada, Germany, Austria, Norway, Denmark, Sweden, Finland, Israel, and Spain.

PATIENTS

1429 patients who were 40 to 70 years of age (mean age 55 y, 51% women), had a body mass index of 25 to 40 kg/m² (mean 30.9 kg/m²), had IGT according to World Health Organization criteria plus a fasting glucose level of 5.5 to 7.8 mmol/L (mean 6.2 mmol/L), and did not have a cardiovascular event in the previous 6 months. Follow-up was 96%.

INTERVENTION

Patients were allocated to acarbose, 100 mg 3 times daily with meals (*n* = 714), or placebo (*n* = 715).

MAIN OUTCOME MEASURES

Composite endpoint for major cardiovascular event (coronary heart disease [myocardial infarction, new angina, or revascularization procedures], cardiovascular death, congestive heart failure, cerebrovascular events, and peripheral vascular disease). Secondary outcomes were incident hypertension and rates of each type of cardiovascular event.

MAIN RESULTS

Analysis was by intention to treat. Acarbose reduced the risk for a major cardiovascular event and hypertension (Table).

Acarbose vs placebo in impaired glucose tolerance at mean 3.3-year follow-up†

Outcomes	Acarbose	Placebo	Adjusted RRR (95% CI)	NNT (CI)
Any major cardiovascular event§	2.2%	4.7%	48% (4.9 to 72)	44 (30 to 436)
Myocardial infarction	0.15%	1.7%	91% (28 to 99)	65 (60 to 212)
Angina	0.73%	1.7%	55% (-28 to 84)	Not significant
Revascularization procedures	1.6%	2.9%	39% (-26 to 71)	Not significant
Cardiovascular death	0.15%	0.29%	45% (-506 to 95)	Not significant
Cerebrovascular event or stroke	0.29%	0.58%	44% (-205 to 90)	Not significant
Hypertension	11%	17%	32% (10 to 49)	19 (13 to 59)
			RRR (CI)	NNH
Peripheral vascular disease	0.147%	0.146%	14% (-93 to 17)	Not significant

‡Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from hazards ratio, which was adjusted for baseline variables, in article.

§Coronary heart disease (myocardial infarction, new angina, or revascularization procedures), cardiovascular death, congestive heart failure, cerebrovascular events, and peripheral vascular disease.

CONCLUSION

In patients with impaired glucose tolerance, acarbose reduced the risk for cardiovascular disease and hypertension.

Source of funding: Bayer AG.

For correspondence: Dr. J.L. Chiasson, Centre Hospitalier de l'Université de Montréal-Hôtel-Dieu, Montreal, Quebec, Canada. E-mail: jean.louis.chiasson@umontreal.ca. ■

*See Glossary.

†Information provided by author.

COMMENTARY

IGT is a key phase in the development of type 2 diabetes and is a potent risk factor for atherosclerotic cardiovascular disease (1). Randomized trials have shown that diet, exercise, and pharmacologic strategies can prevent diabetes in persons with IGT (2, 3). However, the study by Chiasson and colleagues is the first to show that a therapy that prevents diabetes can also reduce the risk for cardiovascular disease and hypertension. Impressively, the prevention of cardiovascular events occurred despite 30% of the participants stopping acarbose during the trial.

The mechanism by which acarbose prevented cardiovascular events in STOP-NIDDM is unclear. Acarbose inhibits the enzymatic cleavage of dietary carbohydrate into simple sugar and is therefore fundamentally akin to dietary modification (raising the glycemic index of food). The improvements in metabolic measures in participants receiving acarbose (with substantial reductions in blood pressure, weight, waist circumference, triglycerides, and plasma glucose) suggest improvements in carbohydrate metabolism and insulin action. Perhaps through these effects (i.e., by improving insulin resistance and the so-called metabolic syndrome), acarbose prevents both diabetes and cardiovascular events.

While trials that will shed light on this issue are ongoing, clinicians should continue to offer effective interventions that prevent diabetes in patients at risk. Such strategies may reduce the risk for cardiovascular events at the same time.

Daniel G. Hackam, MD
University of Toronto
Toronto, Ontario, Canada

References

- Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care*. 1999;22:233-40.
- Chiasson JL, Josse RG, Gomis R, et al. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet*. 2002;359:2072-7.
- Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393-403.