Pravastatin reduced major CHD events in patients with abnormal fasting glucose and a history of CHD

Keech A, Colquhoun D, Best J, et al. **Secondary prevention of cardiovascular events with long-term pravastatin in patients with diabetes or impaired fasting glucose: results from the LIPID trial.** Diabetes Care. 2003;26:2713-21.

QUESTION

In patients with abnormal fasting glucose (AFG) (diabetes and impaired fasting glucose [IFG]) and a history of myocardial infarction (MI) or unstable angina, is pravastatin better than placebo for reducing major coronary heart disease (CHD) events?

DESIGN

Randomized {(allocation concealed*),blinded (clinicians and patients),* placebo-controlled trial}† with median 6-year follow-up (diabetes was a prespecified subgroup analysis of the Long-Term Intervention with Pravastatin in Ischemic Disease [LIPID] trial; the IFG group was added post hoc).

SETTING

87 centers in Australia and New Zealand.

PATIENTS

9014 patients who were 31 to 75 years of age {(median age 62 y, 83% men)}†, who had an MI or hospital admission for unstable angina 3 to 36 months before enrollment, plasma total cholesterol level 4 to 7 mmol/L, and fasting triglyceride level < 5.0 mmol/L. 1077 patients (12%) had diabetes, and 940 patients (10%) had IFG. Follow-up was 99.9%.

INTERVENTION

After an 8-week placebo run-in period, patients were allocated to daily pravastatin, 40 mg (n = 4512 [n = 542 for diabetes, and n = 474 for IFG]) or placebo (n = 4502 [n = 535 for diabetes, and n = 466 for IFG]).

MAIN OUTCOME MEASURES

Major CHD events (CHD death or nonfatal MI); cardiovascular [CV] death; death from any cause; CHD death; stroke; hospitalization for unstable angina; and revascularization by coronary artery bypass graft (CABG) surgery or percutaneous transluminal coronary angioplasty (PTCA).

MAIN RESULTS

Analysis was by intention to treat. Pravastatin, compared with placebo, decreased the risk for CHD death or nonfatal MI, stroke, any CV event, and CABG or PCTA to a similar extent both in patients with AFG and in the complete trial cohort (Table).

CONCLUSION

In patients with abnormal fasting glucose (diabetes and impaired fasting glucose) and a history of myocardial infarction or unstable angina, pravastatin reduced major coronary heart disease events.

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For correspondence: Professor A. Keech, National Health Medical Research Council Clinical Trials Centre, Sydney, New South Wales, Australia. E-mail enquiry@ctc.usyd.edu.au. ■

*See Glossary.

†**The LIPID Study Group.** N Engl J Med. 1998; 339:1349-57.

Pravastatin vs placebo for major coronary heart disease (CHD) events in patients with abnormal fasting glucose (AFG) (diabetes and impaired fasting glucose) and the complete cohort (All) at median 6 years‡

Outcomes	Patient group	Pravastatin	Placebo	RRR (95% CI)	NNT (CI)
CHD death or nonfatal MI	AFG	15.9%	20.8%	26% (9 to 40)	20 (12 to 62)
	All	12.3%	15.9%	24% (15 to 32)§	26 (19 to 42)
Stroke	AFG	4.9%	7.8%	40% (15 to 58)	35 (20 to 135)‖
	All	3.7%	4.5%	19% (0 to 34)§	117 (50 to 2364)
CABG or PTCA	AFG	13.4%	17.4%	27% (9 to 42)	29 (19 to 58)
	All	13.0%	15.7%	20% (10 to 28)§	32 (22 to 71)
Any CV event	AFG	41.4%	49.5%	23% (12 to 32)	13 (9 to 23)
	All	36.0%	40.9%	15% (11 to 18)§	16 (12 to 30)

‡CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty; CV = cardiovascular. Other abbreviations defined in Glossary. Except for stroke in the AFG group, NNT was calculated using the absolute risk reduction and the Cox proportional-hazards ratio from all patients as reported in the article, and CI was calculated using the Wald approach.
§Stratified for qualifying event, as per protocol.
‖Actual risk estimates were used.

COMMENTARY

HMG CoA-reductase inhibitors (statins) decrease CV morbidity and mortality in patients with CHD. This substudy by Keech and colleagues of the LIPID trial adds to the evidence that this remains true for patients who also have diabetes or IFG. The magnitude of treatment effect was consistent with that of diabetes subgroups in other secondary prevention statin trials (1, 2). It is important to note that the results were also similar (17% relative risk reduction [RRR] for CHD death or MI) to those of the 1981 diabetic patients with CHD in the Heart Protection Study, the only trial that stratified the statin and placebo groups by diabetes status (3).

The prespecified analysis of patients with diabetes in the study by Keech and colleagues was underpowered to show a benefit of statin therapy. However, the post hoc addition of patients with IFG to this group showed an RRR that did not differ from the entire study population. The analysis confirms that patients with diabetes or IFG are at higher risk for CHD events and have a greater absolute risk reduction with statin therapy than patients with normal glucose levels. From a practical standpoint, however, patients with established CHD with or without abnormal glucose metabolism should receive the most aggressive treatment regardless of other risk factors.

Apoor S. Gami, MD
Mayo Clinic College of Medicine
Rochester, Minnesota, USA

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