

Gemfibrozil reduced the risk for stroke in men with coronary heart disease and low levels of HDL cholesterol

Rubins HB, Davenport J, Babikian V, et al., for the VA-HIT Study Group. Reduction in stroke with gemfibrozil in men with coronary heart disease and low HDL cholesterol. The Veterans Affairs HDL Intervention Trial (VA-HIT). *Circulation*. 2001 Jun 12;103:2828-33.

QUESTION

In men with coronary artery disease and low levels of high-density lipoprotein (HDL) cholesterol, is gemfibrozil effective for preventing stroke?

DESIGN

Randomized {allocation concealed*}†, blinded {patients, outcome assessors, and study personnel}†, * placebo-controlled trial with mean follow-up of 5.1 years (Veterans Affairs HDL Cholesterol Intervention Trial [VA-HIT]).

SETTING

20 Veterans Affairs medical centers in the United States.

PATIENTS

2531 men who were <74 years of age (mean age 64 y) and had a confirmed diagnosis of coronary artery disease, an HDL cholesterol level < 1.03 mmol/L, a low-density lipoprotein cholesterol level < 3.6 mmol/L, and a triglyceride level < 3.39 mmol/L. Follow-up was complete.

INTERVENTION

{1264 men were allocated to gemfibrozil, 1200 mg/d, and 1267 were allocated to placebo}†. The patients were seen every 3 months by the study coordinator.

MAIN OUTCOME MEASURES

Incidence of first strokes and fatal strokes.

MAIN RESULTS

{Analysis was by intention to treat}†. Fewer patients who received gemfibrozil had a stroke than did patients who received placebo ($P = 0.036$) (Table). The groups did not differ for fatal strokes (3 [0.2%] vs 9 [0.7%], { $P = 0.15$ }‡). 90% of all strokes were ischemic, and the greatest benefit of gemfibrozil was seen in reduction of

atherothrombotic strokes (3 [5%] vs 16 [21%], {unadjusted $P = 0.0028$ }§).

CONCLUSION

In men with coronary artery disease and low levels of high-density lipoprotein cholesterol, gemfibrozil reduced the risk for stroke.

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*See Glossary.

†Rubins HB, Robins SJ, Collins D, et al. *N Engl J Med*. 1999;342:410-8.

‡ P value provided by author.

§ P value calculated from data in article.

Gemfibrozil vs placebo for preventing strokes in men with coronary artery disease and low high-density lipoprotein cholesterol at mean 5.1 years||

Outcome	Gemfibrozil	Placebo	Adjusted RRR (95% CI)¶	NNT (CI)
All strokes	4.6%	6.0%	31% (2 to 52)	55 (33 to 688)

||Abbreviations defined in Glossary; NNT and CI provided by author.

¶Adjusted for baseline variables.

COMMENTARY

The study by Rubins and colleagues is important because it is the first to show that in patients with coronary artery disease, the risk for subsequent stroke (mainly nonfatal atherothrombotic stroke) may be reduced with a fibrate (in this case, gemfibrozil). The results of this study need to be put in the context of similar findings in patients with coronary artery disease who were treated with a statin (1).

Although the clinical characteristics of the patients in both studies were reasonably similar, Rubins and colleagues recruited patients in whom the predominant lipid abnormality was a low HDL level; the investigators of the LIPID (Long-Term Intervention with Pravastatin in Ischaemic Disease) study, however, recruited patients with a broad range of cholesterol levels (1).

What does this mean to practicing clinicians? In essence, we now have a choice of agents that may be useful in protecting patients with

coronary artery disease from stroke. One could argue that gemfibrozil may be more helpful in patients with low HDL levels, but a more general effect has not been ruled out. As yet, we have no information about whether protection shown in either trial is a class effect or relates to each agent specifically. Similarly, we do not know the effect of combining these agents. As is often the case, this study represents a promising development, but more questions need to be answered.

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Reference

- White HD, Simes RJ, Anderson NE, et al. Pravastatin therapy and the risk of stroke. *N Engl J Med*. 2000;343:317-26.