Effect of fibrates on lipid profiles and cardiovascular outcomes: a systematic review

CRD summary
This review concluded that fibrates improved lipid profiles and were associated with an important decrease in non-fatal myocardial infarction, but did not substantially affect all-cause mortality. The conclusions followed from the evidence presented, but potential omission of relevant evidence may make them less reliable.

Authors' objectives
To review the literature examining the effect of fibrates on lipid profiles and cardiovascular outcomes.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched for relevant English-language studies published up to June 2007. Search terms were reported.

Study selection
Double-blind placebo controlled trials that randomised at least 100 patients and had at least eight weeks follow-up were eligible for inclusion in the review. Trials had to investigate the effects of fibrates on lipid profiles and cardiovascular outcomes. Inclusion was restricted to trials that evaluated three specific fibrates: bezafibrate, fenofibrate and gemfibrozil. Mean age of participants in included trials ranged from 47 to 68 years. The proportion of males ranged from 42% to 100%. Study duration ranged from eight to 322 weeks.

The authors did not state how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Rates of non-fatal myocardial infarction and all-cause mortality were extracted to allow calculation of odds ratios (ORs) and related 95% confidence intervals (CIs).

Two reviewers extracted data. Disagreements were resolved by consensus or a third reviewer.

Methods of synthesis
Odds ratios were pooled using a random-effects model. Statistical heterogeneity was investigated using $X^2$ and $I^2$ statistics.

Results of the review
A total of 20 randomised trials (RCTs) (n=25,655) were included in the review: four evaluated bezafibrate (n=4,984); nine evaluated fenofibrate (n=12,398); and seven evaluated gemfibrozil (n=8,273).

Compared with placebo, fibrate therapy was associated with a statistically significant decrease in non-fatal myocardial infarction (OR 0.78, 95% CI 0.69 to 0.89, p=0.0001; five RCTs), but had no significant effect on all-cause mortality (OR 1.05, 95% CI 0.95, 1.15, p=0.34; six RCTs).

Relative to placebo, fibrates were associated with greater reductions in total cholesterol and triglycerides (range -321.3mg/dL to -20.8mg/dL) and an increase in high-density lipoprotein (range 1.1mg/dL to 17.9mg/dL). Fibrates tended to be associated with a reduction in low-density lipoprotein, although results were not entirely consistent.

Adverse event rates were similar between groups.
Authors’ conclusions
Fibrates improved lipid profiles and were associated with an important decrease in non-fatal myocardial infarction, but did not substantially affect all-cause mortality.

CRD commentary
This review was based on a question that was clearly defined in terms of interventions, comparator, outcomes and study designs of interest. Attempts were made to minimise bias during extraction of data from included studies and it appeared that appropriate methods were used to combine these data. Validity of individual studies was not assessed, but relatively strict inclusion criteria meant that poorer quality studies were likely to be excluded from the review. However, no attempts to minimise bias and error in study selection were reported and (as the authors acknowledged) limiting inclusion to English language publications potentially introduced language and publication biases. Consequently, the authors’ conclusions appeared to follow from the evidence presented, but the conclusions may not be reliable if relevant evidence was omitted.

Implications of the review for practice and research
Practice: The authors stated that physicians should consider use of fibrates as monotherapy in patients who were intolerant or resistant to statin, in patients with hypertriglyceridaemia or as an adjunct to statin therapy.

The authors did not state any implications for research.

Funding
Supported by the Canadian Institutes of Health Research (MOP: 82918). Individual authors received funding from McGill University, Fonds dela Recherche en Sante du Quebec (FRSQ), Canadian Institutes of Health Research, and Novartis.

Bibliographic details

PubMedID
19698935

DOI
10.1016/j.amjmed.2009.03.030

Original Paper URL
http://dx.doi.org/10.1016/j.amjmed.2009.03.030

Indexing Status
Subject indexing assigned by NLM

MeSH
Anticholesteremic Agents /administration & dosage; Bezafibrate /administration & dosage & adverse effects; Cardiovascular Diseases /etiology /mortality /prevention & control; Cholesterol, LDL /drug effects; Clofibric Acid /administration & dosage /adverse effects; Female; Fenofibrate /administration & dosage /adverse effects; Gemfibrozil /administration & dosage /adverse effects; Humans; Hyperlipidemias /blood /complications /drug therapy; Prognosis; Randomized Controlled Trials as Topic; Risk Assessment; Survival Analysis; Treatment Outcome

AccessionNumber
12009109302

Date bibliographic record published
03/02/2010
Date abstract record published
25/08/2010

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.