Effect of Different Antilipidemic Agents and Diets on Mortality

A Systematic Review

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[Statins, interrupt the formation of cholesterol in blood: Lipitor, Lescol, Mevacor, Pravachol, Crestor, Zocor]

[Fibrates, cholesterol-lowering drugs that primarily lower triglycerides: Lopid, Tricor]

[Resins, increase the disposal of cholesterol in intestines: Questran, Prevalite, Lo-Cholest, Colestid, Wel Chol]

FROM ABSTRACT:

Background:

We aimed to assess efficacy and safety of different lipid-lowering interventions based on mortality data.

Methods:

We conducted a systematic search of randomized controlled trials published up to June 2003, comparing any lipid-lowering intervention with placebo or usual diet with respect to mortality.

Outcome measures were mortality from all, cardiac, and noncardiovascular causes.

Results:

A total of 97 studies met eligibility criteria, with 137,140 individuals in intervention and 138,976 individuals in control groups.

Compared with control groups, risk ratios for overall mortality were:

0.87 for statins [means a 13% reduced death rate, with a range between 6% - 19% reduced death rate]

1.00 for fibrates [means no reduced death rate, with a range

between 9% reduced death rate to an 11% increased death rate]

0.84 for resins [means a 16% reduced death rate, with a range

between 34% reduced death rate to an 8% increased death rate]

0.77 for n-3 fatty acids [means a 23% reduced death rate with a range between 3% - 37% reduced death rate]

0.97 for diet [means a 3% reduced death rate, with a range between 9% reduced death rate to a 4% increased death rate]

Compared with control groups, risk ratios for cardiac mortality were:

0.78 from statins [means a 22% reduced death from heart problems with a range between 16% - 28%]

0.70 from resins [means 30% reduced death from heart problems with a range between 1% - 50% reduced risk]

0.68 from n-3 fatty acids [means 32% reduced death from heart problems with a range between 10% - 58% reduced risk]

Risk ratios for noncardiovascular mortality was increased from fibrates by 13% with a range between 1% - 27%.

Conclusions:

Statins and n-3 fatty acids are the most favorable lipid-lowering interventions with reduced risks of overall and cardiac mortality.

Any potential reduction in cardiac mortality from fibrates is offset by an increased risk of death from noncardiovascular causes.

THESE AUTHORS ALSO NOTE:

Lipid-lowering drugs for the prevention of cardiovascular diseases have been in use for more than 4 decades.

"Large-scale metaanalyses of randomized controlled trials are important tools to document the overall benefit of interventions and to explore effect sizes of clinically relevant outcomes in important subgroups. The goal of the present meta-analysis is to investigate the efficacy and safety of different lipid lowering interventions in the primary and secondary prevention of CHD based on mortality

data."

These authors classified trials according to the following groups:

statins	35 trials
fibrates	17 trials
resins	8 trials
niacin	2 trials
n-3 fatty acids	14 trials
dietary interventions	17 trials

The analysis was limited to trials with at least 1000 individuals per group.

In total, there were 137,140 individuals in the intervention and 138,976 individuals in the control groups.

The average relative reduction in levels of total cholesterol was:

Statins	20%	range, 7%-36%
fibrates	8%	range, 0%-14%
resins	15%	range, 8%-24%
niacin	11%	range, 8%-14%

n-3 fatty acids	2%	range, –2% to 9%
diet	10%	range, 1%-24%

This study "confirms the benefit of statins in reducing the risk of overall and cardiac mortality in patients with or without CHD and additionally shows that n-3 fatty acids reduce overall and cardiac mortality in patients with CHD."

These authors "found no reduction in overall mortality and an increased risk of death from noncardiovascular causes in individuals taking fibrates compared with individuals in placebo or control groups."

"If used in appropriate doses, n-3 fatty acids are as effective as fibrates to reduce triglyceride levels but are associated with a reduction in overall mortality."

"However, n-3 fatty acids lower total cholesterol level to a very small extent, which indicates that beneficial effects must be mediated by other means. Studies suggest that n-3 fatty acids may have antiarrhythmic properties with membrane stabilizing effects in addition to antithrombotic and anti-inflammatory properties on the endothelial level."

"In conclusion, this systematic review suggests that statins and n-3 fatty acids offer the most favorable benefits by reducing the risk of cardiac and overall mortality. Use of fibrates may be associated with an increased risk of noncardiovascular mortality."

"Future trials should explore whether n-3 fatty acids in combination with statins lead to additional reduction in CHD mortality, especially in patients with metabolic syndrome."

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KEY POINTS:

1) This article found all randomized controlled trials through June 2003 that evaluated the effect on mortality by lowering blood lipids by various methods. A total of 97 studies were used with 137,140 individuals in intervention and 138,976 individuals in control groups. Consequently, this study has harvested the best available evidence on the topic and should be taken seriously.

2) **Ironically, omega-3 essential fatty acids did the worse job at reducing blood cholesterol (mean of only 2% reduction), yet they did the best job at reducing death from all causes (mean of 23% reduction) and death from heart problems (mean of 32% reduction).**

3) Statin drugs did the best job at lowering cholesterol levels (mean of 20% reduction). Statin drugs were 10 times more effective in lowering blood cholesterol than were omega-3 fatty acids (20% v. 2% reduction).

- **Yet, omega-3 fatty acids were 44% more effective than statin drugs in reducing death from cardiac events**

- **32% more effective than statin drugs in reducing death from all reasons.**

4) **Statin drugs reduced cardiac deaths by a mean of 22%.**

Omega-3 fatty acids reduced cardiac deaths by a mean of 32%.

5) **Statin drugs reduced all deaths by a mean of 13%.**

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Omega-3 fatty acids reduced cardiac deaths by a mean of 23%.

6) Omega-3 fatty acids lower cholesterol levels to a very small extent, which indicates that their beneficial effects are mediated by other means, such as their antiarrhythmic properties, their membrane stabilizing effects, as well as their antithrombotic and anti-inflammatory properties.

COMMENTS

This study offers the best proof in history that the problem is not cholesterol. Omega-3 fatty acids proved to be significantly more effective at reducing all deaths and in particular cardiac deaths, yet they reduced cholesterol very little.

- Statin drugs
  - make tens of billions of dollars for drug companies yearly,
  - are very expensive for the consumer and for the government (taxpayers) beginning in 2006
  - are associated with numerous serious side effects.
  - Omega-3 fatty acids work significantly better than statin drugs (proved by this article), are significantly less expensive, and have no side effects.
  - Plus, we have seen numerous articles that prove that omega-3s benefit the brain, the immune system, and the joints.

According to Ray Moynihan, in Selling Sickness, How the World's Biggest Pharmaceutical Companies are Turning us all into Patients, Nation Books, 2005, page 1, cholesterol-lowering drugs "generate revenues of more than $25 billion a year for their manufacturers."

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