Niacin added to statins for cardiovascular disease

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Clinical question

In patients with cardiovascular disease (CVD) and low levels of high-density lipoprotein (HDL), does adding niacin to statin therapy decrease future cardiovascular (CV) events?

Evidence

The AIM-HIGH trial[1] was a 3-year RCT of 3414 participants (mean age 65 years, 85% men) with previous CVD taking simvastatin (mean dose 40 mg).

- Participants were randomized to receive 1500 to 2000 mg of extended-release niacin or placebo (with up to 200 mg of niacin to maintain blinding).
  -Combined CVD (primary outcome) was not statistically different between groups (niacin 16.4% vs placebo 16.2%).
  -There was a non-significant trend to harm in ischemic stroke: niacin 1.7% versus placebo 1.1% (P=.11).
  -Niacin improved lipid profiles more than placebo did: 6%, 13%, and 21% improvement in low-density lipoprotein (LDL), HDL, and triglyceride levels, respectively.
- The trial was stopped early owing to lack of efficacy.

The Coronary Drug Project, an RCT[2] of patients with previous CVD, compared niacin and placebo and found

- a relative reduction of 11% in mortality and 27% in CVD over 15 years, but
- the trial is 40 years old (with a moderately high dropout rate of 27%) and was undertaken before most proven therapies (like statins) were used.

An RCT comparing niacin and ezetimibe (both with statin)[3] found significantly less CVD (including myocardial infarction and acute coronary syndrome) with niacin (1% vs 5% for ezetimibe, P=.04), but

- it was a small trial (decreased reliability) with a high dropout rate (38% ezetimibe, 48% niacin) and
- no placebo arm: niacin might be better than ezetimibe but not placebo.

Context

- Surrogate outcomes like lipid levels can be misleading.[4]
  -Torcetrapib reduced LDL by 25% and increased HDL by 72%, but also increased CVD and mortality.[5]
  -Improved CV outcomes occur with statins irrespective of initial lipid levels[6] or the degree of LDL reduction.[7]
- There is good evidence that statins reduce CVD, particularly for secondary prevention.[8]
- Current guidelines still recommend treating to lipid targets (primarily LDL), including adding niacin, fibrates, or ezetimibe to statins to meet LDL targets.[9]
  -Guidelines recommend this despite acknowledging the lack of evidence for adding therapies![9]
- A comprehensive evidence review does not support lipid targets.[7]

Bottom line

In patients with CVD already taking statin therapy, niacin does not improve CV events. Among lipid treatments, only statin monotherapy has strong evidence for CVD prevention (regardless of lipid levels).

Implementation

Rather than adding secondary lipid treatment to achieve targets, clinicians should emphasize adherence to statins. Adherence to statins declines gradually over time and discontinuation of statins is associated with increased morbidity and mortality.[10,11] Fortunately, adherence to statins can be improved through simplification of drug regimens and through patient education and reminders.[12]

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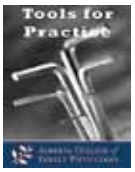

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