Niacin added to statins for cardiovascular disease (CVD)? 1 + 1 = 1

Clinical Question: In patients with CVD and low HDL levels, does adding niacin to statin therapy decrease future cardiovascular events?

Bottom-line: In patients with CVD on conventional therapy, adding niacin does not reduce cardiovascular events. Among lipid treatments, only statin monotherapy has strong evidence for CVD prevention (regardless of lipid levels).

Evidence:
- HPS2-THRIVE: Randomized Controlled Trial (RCT) of 25,673 patients (mean age 65, 83% male) with previous CVD taking simvastatin 40 mg +/- ezetimibe 10 mg.
  - Randomized to niacin extended-release 2,000 mg plus laropiprant 40 mg or placebo for ~4 years.
  - No difference in primary outcome (combined CVD): 13.2% versus 13.7%.
  - Niacin increased risk of:
    - Serious adverse events: 55.6% versus 52.7%, Number Needed to Harm (NNH)=35.
    - Discontinuation due to adverse events: 25.4% versus 16.5%, NNH=12.
  - Niacin improved lipids versus placebo.
    - LDL -0.25 mmol/L, HDL +0.16 mmol/L, Triglycerides -0.37 mmol/L.
- Meta-analysis of 11 RCTs (including HPS2-THRIVE) of 35,301 patients:
  - No difference between niacin versus placebo on death, non-fatal myocardial infarction or stroke.
- The Coronary Drug Project RCT: Only trial to demonstrate cardiovascular benefit of niacin over placebo.
  - Enrolled men 30-64 years-old with prior myocardial infarction.
  - Limitations: Over 40 years old, before statins and other proven secondary prevention therapies (aspirin, ACE inhibitors, beta-blockers, etc).

Context:
- Surrogate outcomes like lipids can be misleading.
The drug torcetrapib reduced LDL 25% and increased HDL 72%, but increased CVD and mortality.\(^5\)

- Statins improve CVD outcomes irrespective of initial lipid levels\(^6\) or the degree of LDL reduction.\(^7\)
  - Good evidence demonstrates that statins reduce CVD, particularly in secondary CVD prevention.\(^8\)
  - Canadian cardiovascular society guidelines\(^9\) recommend treating to lipid targets (LDL, non-HDL, and ApoB), including adding ezetimibe, bile acid resins, or PCSK9 inhibitors to statins if needed.
  - Niacin recommended only if LDL goal not achieved despite all of the above.
  - American guidelines\(^10\) recommend against niacin due to risk of serious harm with no clinical benefit.
  - Canadian Primary Care Lipid Guidelines do not recommend niacin.\(^11\)

**References:**

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at http://bit.ly/signupfortfp. Archived articles are available on the ACFP website.

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