Clinical Practice Assessment

Niacin as secondary prevention of coronary heart disease?

Clinical question:
Does niacin alone or in combination with statins benefit patients with cardiovascular disease?

Bottom Line:
The only study comparing niacin to placebo in the secondary prevention of coronary heart disease found no evidence of benefit for the primary endpoints (total and disease-specific mortality). Recent randomized controlled trials of adding Niacin to effective statin based therapy do not show any benefit in cardiovascular endpoints.

Synopsis:
In the only Level 1 study (Coronary Drug Project Research Group, CDP, 1975) niacin reduced the incidence of definite nonfatal myocardial infarction (MI) (Number Needed to Treat, NNT = 28 over 5 years) and increased the incidence of atrial fibrillation and other arrhythmias (Number Needed to Harm, NNH = 76), acute gouty arthritis (NNH = 47), skin problems excluding flushing and itching (NNH = 9) and various abnormal chemistry findings including hyperuricemia (NNH = 4) and hyperglycemia (NNH = 12).

Between March 1966 and October 1969 the CDP enrolled men ages 34-61 with previous MI to receive either 3.0 grams short acting niacin daily (n=1119) or placebo (n=2789) for an average of 5 years follow up (range 4.5 to >6). CDP also enrolled additional subjects to blinded treatment with conjugated estrogens, dextrothyroxine and clofibrate. Due to excess mortality, the estrogen and thyroxine arms were terminated early; clofibrate results showed no mortality benefit and statistically significant excess incidence of thromboembolism, angina pectoris, intermittent claudication, cardiac arrhythmia, any definite or suspected fatal or nonfatal cardiovascular event, and gallstones.

Niacin had no effect on total or disease-specific mortality (21.2% of the niacin group died compared to 20.9% of the placebo group during the 5 year average follow up period). Diagnosis of definite, nonfatal MI was statistically significantly lower in the niacin group (8.9% v 12.2%). Negative effects of niacin included increased incidence of atrial fibrillation (2.6% v 1.3%), acute gouty arthritis (6.4% v 4.3%), ichthyosis (3.1% v 0.8%), acanthosis nigricans (3.6% v 0.7%), hyperpigmentation (5.1% v 2.0%), and any dermal abnormality (26.3% v 15.8%) excluding flushing and itching that occurred in 92% and 48.9%, respectively, v 4.3% and 6.2% of the placebo group. At some time during the study, niacin caused elevations in SGOT (50.2% v 34.6%), alkaline phosphatase (32.8% v 18.2%), CPK (18.4% v 12.8%), fasting glucose =120 mg/dL (23.8% v 15.9%) and uric acid =8 mg/dL (43.5% v 19.6%).
The CDP investigators concluded, “There is no evidence from the Coronary Drug Project that the use of niacin will prolong life in persons with CHD. Because of the effect of niacin in reducing the incidence of definite, nonfatal MI, the use of this drug may be of some slight benefit as a therapeutic agent for persons with CHD. However, the excess incidence in the niacin group of atrial fibrillation and other arrhythmias, along with the excess incidence of abnormal chemistry findings, as noted above, indicate that great care and caution must be exercised if this drug is to be used for treatment of patients with CHD.”

In the Atherothrombosis intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) trial (Boden et al., 2011) addition of extended release Niacin to simvastatin therapy did not result in a reduction of the clinical endpoints of cardiovascular mortality, nonfatal myocardial infarction, ischemic stroke, hospitalization greater than 23 hours for acute coronary syndrome or coronary or cerebral revascularization based on symptoms. In their systematic review of Niacin and cardiovascular disease (CVD) in primary and secondary prevention trials, Lavigne and Karas (2013) concluded that Niacin reduced CVD events. There were limitations to this review which included: A search of only one database. Limitation to published, English language articles (raising the possibility of publication and language bias). Heterogeneity of the included trials (related to patient characteristics, dosing regimens and combination therapies). Extraction of only trial level and not patient level data.

The authors concluded that additional trials were needed to determine the effects of Niacin and its role in cardiovascular disease prevention.

Landray et al. (2014) studied the outcomes of adding 2 grams of extended release Niacin and 40 mg of Laropiprant to patients with established CVD on statin therapy. Laropiprant is a prostaglandin antagonist that has been shown to effectively reduce symptoms of flushing related to Niacin therapy. Over a median follow up period of 3.9 years, addition of Niacin-Laropiprant to effective statin based therapy did not result in a reduction of study endpoints. Study endpoints were death from coronary causes, non-fatal myocardial infarction, stroke or revascularization (coronary or non-coronary). Adverse reactions to Niacin-Laropiprant included gastrointestinal, musculoskeletal and skin related effects. There was also a significant increase in blood sugars in patients with preexisting diabetes as well as an increase in newly diagnosed diabetes in the Niacin-Laropiprant treated group. Additional side effects included an increased risk of bleeding and infection.

References:


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