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). A recent study of the incremental value of niacin in addition to statin treatment was stopped early due to lack of benefit. Some experts believe that niacin may benefit the subgroup of patients with low HDL/high triglycerides and/or those who cannot tolerate statins.

Summary:
In the only Level 1 study (Coronary Drug Project, CDP) niacin reduced the incidence of definite nonfatal MI (NNT=28 over 5 years) and increased the incidence of atrial fibrillation and other arrhythmias (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% vs 12.2%). Negative effects of niacin included increased incidence of atrial fibrillation (2.6% vs 1.3%), acute gouty arthritis (6.4% vs 4.3%), ichthyosis (3.1% vs 0.8%), acanthosis nigricans (3.6% vs 0.7%), hyperpigmentation (5.1% vs 2.0%), and any dermal abnormality (26.3% vs 15.8%) excluding flushing and itching that occurred in 92% and 48.9%, respectively, vs 4.3% and 6.2% of the placebo group. At some time during the study, niacin caused elevations in SGOT (50.2% vs 34.8%), alkaline phosphatase (32.8% vs 18.2%), CPK (18.4% vs 12.8%), fasting glucose ≥120 mg/dL (23.8% vs 15.9%) and uric acid ≥8 mg/dL (43.5% vs 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."

Seven smaller secondary prevention randomized trials have compared niacin in combination with other agents (a fibrate, colestipol, and/or a statin) to placebo, with mixed results, but there have been no further trials of niacin alone against placebo. A large NIH study of niacin as add-on therapy to a statin in secondary prevention of CHD was stopped early due to lack of niacin benefit and a slightly increased incidence of stroke.

We found no clinical trials of Niaspan, a sustained release version of niacin, versus placebo in the secondary prevention of CHD. It therefore cannot be concluded that Niaspan has superior benefit compared to niacin in the secondary prevention of CHD.

Niacin has not been studied as a therapeutic agent in the primary prevention of coronary artery disease.

Sources:
3. BMJ 2011;342:d3400 (News report)

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