Cochrane for Clinicians

Putting Evidence into Practice

Use of Niacin for Primary or Secondary Prevention of Cardiovascular or Cerebrovascular Events

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Clinical Question

Is niacin effective for primary or secondary prevention of cardiovascular or cerebrovascular events?

Evidence-Based Answer

Prescription niacin (nicotinic acid, vitamin B_3) does not reduce myocardial infarctions, strokes, or overall mortality when used for primary or secondary prevention.[1] (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Prescription niacin is one of the most effective agents in increasing serum levels of high-density lipoprotein (HDL) cholesterol.[2] Previous research has shown that lower levels of HDL cholesterol are independently associated with an increased risk of cardiovascular disease (CVD), and that use of prescription niacin could raise HDL cholesterol levels and may reduce cardiovascular events.[3,4] The objective of this review was to assess the effectiveness of niacin therapy (monotherapy or in addition to statin therapy) vs. placebo in terms of overall mortality, cardiovascular events, cerebrovascular events, and adverse effects.

This Cochrane review included 23 randomized controlled trials (published between 1968 and 2015) involving 39,195 participants.[1] The authors looked for studies including patients who were considered at risk of CVD as well as those with known CVD. The primary outcome examined was overall mortality, as discussed in 12 high-quality studies. Niacin did not appear to lower overall mortality. Concurrent statin use, comorbidities, and duration of niacin treatment did not change the impact on the primary outcome. Niacin also had no apparent impact on the secondary outcomes of myocardial infarctions, strokes, or need for revascularization procedures.

Niacin did appear to increase the risk of several adverse effects, including flushing (relative risk [RR] = 7.69; 95% confidence interval [CI], 4.14 to 14.28; number needed to harm [NNH] = 3.5), pruritus (RR = 5.26; 95% CI, 2.68 to 10.32; NNH = 4.8), rash (RR = 3.15; 95% CI, 1.94 to 5.13; NNH = 77), and gastrointestinal symptoms (RR = 1.69; 95% CI, 1.37 to 2.07; NNH = 125). Niacin users were at risk of discontinuing the medication because of these adverse effects (RR = 2.17; 95% CI, 1.70 to 2.77; NNH = 8 [95% CI, 5 to 14]). Alarmingly, there was also an apparent increased risk of developing diabetes mellitus in patients who used niacin (RR = 1.32; 95% CI, 1.16 to 1.51; NNH = 143).

Although current guidelines mention that niacin is used to potentially lower the risk of CVD, it is only discussed insofar as to caution physicians regarding the adverse effects associated with its use.[5] Based on this review, niacin should not be used for primary or secondary prevention of cardiovascular or cerebrovascular events.

The practice recommendations in this activity are available at http://www.cochrane.org/CD009744.

The views expressed reflect the opinions of the authors alone and do not reflect the opinion of the Department of the Army, Air Force, Defense Health Agency, Department of Defense, or the U.S. government.

Editor's Note: The numbers needed to harm reported in this Cochrane for Clinicians were calculated by *AFP* medical editors based on raw data provided in the original Cochrane review.

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CME **This clinical content** conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 439.

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DPP-4 Inhibitors and GLP-1 Receptor Agonists for Prevention or Delay of Type 2 Diabetes Mellitus and Associated Complications

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Clinical Question

Are dipeptidyl-peptidase-4 (DPP-4) inhibitors or glucagon-like peptide-1 (GLP-1) receptor agonists effective in preventing type 2 diabetes mellitus and its associated complications in patients at increased risk?

Evidence-Based Answer

There is only limited-quality evidence that at-risk patients taking GLP-1 receptor agonists are less likely to progress to diabetes (number needed to treat [NNT] = 23). Serious adverse events were more likely in patients taking GLP-1 receptor agonists than in patients taking placebo (number needed to harm [NNH] = 42). There is insufficient evidence to evaluate the effect of DPP-4 inhibitors on at-risk patients. There is no evidence that either medication class affects the development of diabetes-associated complications.[1] (Strength of Recommendation: C, based on low-quality, disease-oriented evidence.)

Practice Pointers

In the United States alone, an estimated 30.3 million persons have diabetes and 84.1 million have prediabetes,[2] and 70% to 90% of those with prediabetes progress to diabetes.[3] Microvascular and macrovascular complications of diabetes begin to occur while patients are still in the prediabetic stage.[3,4] Metformin and acarbose (Precose) have been shown to decrease the risk of some of these complications, but data for other medications are lacking.[5,6]

This Cochrane review included seven randomized controlled trials.[1] Because of the limited number of participants—only 98 patients—and the lack of patient-oriented outcomes data from the two DPP-4 inhibitor trials, no conclusions could be drawn about that class of medication. The remaining five trials included 1,620 participants randomized to monotherapy with a GLP-1 receptor agonist.

In a single randomized, double-blind, placebo-controlled trial, authors studied the effect of liraglutide (Victoza; a GLP-1 receptor agonist) in patients with prediabetes and obesity. After 160 weeks, fewer patients treated with liraglutide developed diabetes than those treated with placebo (1.8% vs. 6.2%; absolute risk reduction = 4.3%; NNT = 23). Because of limited data, no conclusions could be drawn regarding the effect of GLP-1 receptor agonists to decrease the risk of complications associated with diabetes.

Patients receiving GLP-1 receptor agonists may experience serious adverse events including, but not limited to, myocardial infarction, cholelithiasis, cholecystitis, pancreatitis, intervertebral disk protrusion, abdominal and hiatal hernia, infection, and neoplasm.[7] More individuals who received liraglutide had serious adverse events than those who received placebo (15.1% vs. 12.7%; absolute risk increase = 2.4%; NNH = 42). It is noteworthy that most of the data on GLP-1 receptor agonists came from the same large industry-sponsored study. Because of the small number of participants in the other GLP-1 receptor agonist studies, no comparisons among the different agents and thus no conclusions regarding their relative benefit could be made.

Current guidelines for treating patients with prediabetes advocate lifestyle modification, optimizing comorbid conditions, and—in high-risk individuals—metformin to decrease progression to diabetes.[5,6] The American Diabetes Association acknowledges that other medications, including acarbose, orlistat (Xenical), GLP-1 receptor agonists, and thiazolidinediones, can decrease the incidence of progression to diabetes,

but recommends metformin based on the strong evidence and long-term safety data.[5]

The practice recommendations in this activity are available at http://www.cochrane.org/CD012204.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the U.S. government.

Editor's Note: The number needed to treat, number needed to harm, absolute risk reduction, and absolute risk increase reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

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