Indian Health Service
National Pharmacy and Therapeutics Committee
ACC/AHA Dyslipidemia Guideline Review
NPTC Updates
February 2014

Background:

In February 2014, the I.H.S. NPTC convened to review the November 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. This is the first update to the National Heart, Lung, and Blood Institute's Adult Treatment Panel (ATP III) recommendations in 10 years.

Discussion:

Epidemiology

Heart disease and stroke respectively represent the second and seventh leading causes of death in the American Indian and Alaska Native population. Dyslipidemia is a common and important major risk factor for the development of atherosclerotic cardiovascular disease (ASCVD).

Scope of the Cholesterol Treatment Guideline

The November 2013 cholesterol treatment guideline focuses almost exclusively on a strategy of fixed-dose statin therapy for both the primary and secondary prevention of atherosclerotic cardiovascular disease. Unlike ATP III, it is not intended as a comprehensive approach to management of lipid disorders.

Treatment Strategy

In a departure from prior guidelines, the expert panel found no clinical evidence to support popular strategies for lipid management based upon statin dose titration or treatment targets. Specifically, the panel concluded that "treat to target" or "lower (cholesterol) is better" strategies are not supported by the evidence. In addition, evidence was felt to be lacking regarding the use of non-statin pharmacologic treatment modalities for risk reduction for atherosclerotic cardiovascular disease. The panel did endorse lifestyle modification as a fundamental intervention both before and during statin treatment for at-risk persons. The NPTC notes that cholesterol treatment guidelines from other organizations, including the ADA, still support cholesterol treatment targets.

Major Statin Benefits Groups

The ACC/AHA panel defined 4 primary and secondary prevention groups for whom evidence was felt to support statin therapy and for whom relative risk reduction of ASCVD was felt to outweigh the risks of adverse statin effects. They were;

Secondary Prevention

1. Persons with clinical ASCVD (age < 75 years).

Primary Prevention

2. Persons with LDL cholesterol > 189 (age > 20 years).
3. Persons with diabetes mellitus and LDL cholesterol 70-189 (age 40-75 years).
4. Persons with LDL cholesterol 70-189 and calculated 10-year risk of ASCVD >7.4% using new Pooled Cohort Equations (age 40-75 years).

Risk Calculation

Pooled cohort equations, available for use at my.americanheart.org/cvriskcalculator were formulated for the guideline using 4 cohorts including African-American and non-Hispanic White study participants. Risk variables include age, total and HDL cholesterol, systolic BP (treated or untreated), diabetes mellitus, and current smoking status. The new risk calculator is intended for the calculation of ASCVD risk in the primary prevention statin-benefit subgroups.

Controversy About Risk Estimation

When applied to certain external cohorts for validation in the primary prevention subgroups, the risk calculator is known to overestimate risk by as much as double. Internal validation cohorts did not include American Indian or Alaska Native patients. The NPTC reviewed the controversial aspects of risk calculation, with input from I.H.S. subject matter experts and concluded that the potential for risk overestimation in the I.H.S service population was generally not clinically significant. The new Pooled Cohort Equations were deemed superior to other risk calculation methods including the Framingham and the Strong Heart calculators. This was based, in part, on health disparities in the service population. The NPTC endorses the use of the new Pooled Cohort Equations for risk calculation of ASCVD in the primary prevention subgroups for the I.H.S. service population.

Simplification of Statin Treatment and Monitoring

The ACC/AHA expert panel found little evidence for risk of hepatic dysfunction or myopathy in statin treated patients, except for those with known predisposing comorbid conditions or on drugs with known potential for interactions with statins (especially those competing for metabolism via the cytochrome P450 isoenzyme CYP3A4). The panel also found no evidence for dose titration of statins for a specific treatment target. This should greatly simplify therapy by guiding providers to use a fixed dose statin of appropriate intensity (see links) for the selected treatment group and by limiting the need for routine lab monitoring.

De-emphasizing the Use of Non-statin Medications

The guideline panel reviewed RCT's evaluating non-statins used as monotherapy or in combination with statin therapy and could find no data supporting the routine use of non-statin drugs combined with statin therapy to reduce further ASCVD events. The addition of non-statins to statin therapy has not demonstrated additional ASCVD prevention in RCT's. Adherence to lifestyle and to statin therapy should be re-emphasized before considering the addition of a non-statin drug in patients who have a less-than anticipated therapeutic response on statins. When non-statin drugs are added to statin therapy, preference should be given to non-statin cholesterol-lowering drugs shown to reduce ASCVD events in RCT's. The current guideline focused only on treatments proven to reduce ASCVD events. Once further RCT data becomes available for non-statin therapy, questions regarding the treatment of hypertriglyceridemia with non-statins, the use of non-HDL-C in decision-making, and whether on-treatment markers such as Apo B, Lp(a), and TGY are useful in guiding treatment may be further answered.

Findings:

There is strong clinical merit to use statins in the primary and secondary prevention of ASCVD in appropriate patients. The NPTC modified the National Core Formulary (NCF) to include both moderate and high intensity statins. The NTPC added the high intensity statin atorvastatin at the 40mg to 80 mg doses. This modified the NCF to currently include two low and moderate intensity statins with both cytochrome P450 and non-CYP3A4 metabolism, as well as, one high intensity statin for use as clinically indicated by the new cholesterol treatment guideline. Non-statin therapy was also modified with the removal of gemfibrozil and the addition of "fibric acid derivative - any product" to the NCF.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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