The Adult Treatment Panel III (ATP III) guidelines continue to emphasize intensive treatment for persons at risk for coronary heart disease (CHD). The newest feature is a focus on primary prevention in persons with multiple risk factors; the updated guidelines recognize diabetes as a CHD risk equivalent. These groups of people already are at high risk and can benefit from increased intensive treatment to lower serum low-density lipoprotein cholesterol (LDL-C) levels. The ATP III guidelines establish lower targets for LDL-C and triglyceride levels and higher targets for the high-density lipoprotein cholesterol level. The guidelines also combine several risk factors to estimate the probability of CHD with use of the Framingham risk point-scoring formula and emphasize the multifactorial benefits of drug therapy as an adjunct to lifestyle changes.

(Key words: comprehensive evaluation, diabetes, dyslipidemia, Framingham risk point-scoring formula, hypertension, lipid profile)

Implementing diagnostic and therapeutic principles has assumed greater importance in recent years because of the rapid growth in the number of Americans with metabolic syndrome (MBS). A concomitant increase in the rates of stroke and other cardiovascular diseases can be expected to follow unless much more is done to recognize and treat excess weight, hypertension, diabetes, and dyslipidemia.

Three representative case studies illustrate how the Adult Treatment Panel III (ATP III) recommendations can be applied. The cases focus on patients who have not yet had their first coronary event but who, because of their risk factors, have a moderate to very high likelihood of having coronary heart disease (CHD) develop within the next decade of their lives (Figure 1).

Case study 1

A 47-year-old Mexican American woman is seen for a comprehensive evaluation of CHD risk shortly after her type 2 diabetes mellitus had been diagnosed (Figure 2). She is currently taking no medications and has no history of CHD. However, she is considerably overweight at 189 pounds, with a body mass index (BMI) of 30. Her blood pressure is also elevated at 148/92 mm Hg. Her lipids are as follows: total cholesterol, 260 mg/dL (high); low-density lipoprotein-C (LDL-C), 157 mg/dL (borderline high); high-density lipoprotein cholesterol (HDL-C), 37 mg/dL (low); and triglyceride concentration, 320 mg/dL (high). Diabetes mellitus is reflected in her fasting glucose level of 160 mg/dL and her glycosylated hemoglobin (HbA1c) level of 8.2%.

This patient’s dyslipidemia and hypertension are both CHD risk factors, and her uncontrolled diabetes counts as a CHD risk equivalent. Therefore, according to the ATP III guidelines, the next appropriate step is to assess her 10-year probability of having an acute coronary event, based on the Framingham risk point-scoring formula for women. She is assigned 3 points for her age, 8 points for her high total cholesterol level, 2 points for her low HDL-C level, and 3 points for her untreated hypertension. This patient has a point total of 16, which translates to a 4% risk of a coronary event during the next 10 years.

The ATP III guidelines state that patients with a CHD risk equivalent (in this case diabetes) are in a risk category that warrants an LDL-C target level of less than 100 mg/dL. Although the guidelines advise a 3-month trial of therapeutic lifestyle changes (TLC) alone for patients whose LDL-C level is within 30 mg/dL of the target, immediate initiation of drug therapy is recommended for those whose LDL-C level is more than 30 mg/dL above the goal level. For this patient, both lifestyle changes and drug therapy are indicated.

If baseline LDL-C is ≥ 130 mg/dL, intensive lifestyle therapy and maximal control of other risk factors should be started. Moreover, for most patients, an LDL-lowering drug will be required to achieve an LDL-C level of < 100 mg/dL; thus, an LDL-C-lowering drug can be started simultaneously with TLC to attain the goal of therapy.

Management strategy for this patient begins with a recommendation for increased physical activity and referral to a dietitian with a suggestion for a type IV diet of a daily energy (caloric) intake of 5020.8 kJ (1200 kcal) to 6276.0 kJ (1500 kcal). She should be given a biguanide, a thiazolidinedione, and a secretagogue to normalize her blood glucose level. Her response should be monitored closely, and she should be given insulin if these measures fail after adequate titration. To control her blood pressure, she should

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Figure 1. New features of Adult Treatment Panel III.

Figure 2. Clinical considerations in estimating risk for coronary heart disease (CHD): case study 1.

Figure 3. Clinical considerations in estimating risk for coronary heart disease (CHD): case study 2.

**Checklist**

- **Focus on multiple risk factors**
  - Raises persons with diabetes without coronary heart disease (CHD), most of whom have multiple risk factors, to the risk level of CHD risk equivalent
  - Uses Framingham projections of 10-year absolute CHD risk (ie, the percent probability of having a CHD event in 10 years) to identify certain patients with multiple (2+) risk factors for more intensive treatment
  - Identifies persons with multiple metabolic risk factors (metabolic syndrome) as candidates for intensified therapeutic lifestyle changes

- **Modifications of lipid and lipoprotein classification**
  - Identifies low-density lipoprotein cholesterol (LDL-C) <100 mg/dL as optimal
  - Raises categorical low high-density lipoprotein cholesterol (HDL-C) from <35 mg/dL to <40 mg/dL because the latter is a better measure of a depressed HDL-C level
  - Lowers the triglyceride classification cutpoints to give more attention to moderate elevations

- **Support for implementation**
  - Recommends a complete lipoprotein profile (total, LDL, and HDL cholesterol and triglycerides) as the preferred initial test, rather than screening for total cholesterol and HDL-C alone
  - Encourages use of plant sterols/stanols and viscous (soluble) fiber as therapeutic dietary options to enhance lowering of LDL-C level
  - Presents strategies for promoting adherence to therapeutic lifestyle changes and drug therapies
  - Recommends treatment beyond lowering LDL-C level for persons with triglyceride concentrations ≥200 mg/dL

**Case study 1**

- Type 2 diabetes mellitus (CHD risk equivalent)
- Hypertension (major risk factor, modifies low-density lipoprotein cholesterol [LDL-C] goal)
- Excess weight
- High total cholesterol level
- Borderline-high LDL-C level
- Low level of high-density lipoprotein cholesterol (major risk factor, modifies LDL-C goal)
- High triglyceride concentration

**Case study 2**

- Cigarette smoking (major risk factor, modifies low-density lipoprotein [LDL-C] goal)
- Excess weight
- Hypertension (major risk factor, modifies LDL-C goal)
- Family history of CHD (major risk factor, modifies LDL-C goal)
- High total cholesterol level
- Very high LDL-C level
- Low level of high-density lipoprotein cholesterol (major risk factor, modifies LDL-C goal)

Also be given an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker to delay the nephrotic changes of diabetes.

Once this patient’s diabetes is controlled, many of her CHD risk factors will be reduced or eliminated, but her triglyceride and LDL-C levels will probably not change. A statin should be prescribed to improve her lipid profile, but if her triglyceride level does not drop below 150 mg/dL, a fibric acid derivative can be added. However, the combination of a statin and a fibrate can occasionally produce adverse effects. If the patient cannot tolerate both, she should remain on the statin therapy and discontinue the fibrate therapy. Both patient and physician should be realistic about the time needed to reach all these metabolic goals—at least 6 months—and probably much longer where body weight is concerned.

The healthcare team should also anticipate that major changes in diet and exercise habits will not occur immediately and that compliance with a lifelong multidrug regimen requires a dedicated patient-physician relationship with ongoing reinforcement and support. For patients whose compliance is limited by income, some drug manufacturers offer reduced-price programs. Generic products should also be considered.

**Case study 2**

On a routine annual physical examination, a 53-year-old Scottish American man is found to have numerous CHD risk factors (Figure 3). He reports a smoking habit of 2 packs of cigarettes a day for 35 years, and he is markedly overweight at 235 pounds, with a BMI of 31. In addition, this patient is severely hypertensive, with a blood pressure of 165/104 mm Hg. His family history is significant for his father’s fatal myocardial infarction at the age of 49 years and his brother’s cerebrovascular event at the age of 51 years.

His lipid profile also raises serious concerns: total cholesterol level is 265 mg/dL (high); LDL-C, 207 mg/dL (very high); HDL-C, 30 mg/dL (low); his triglyceride level is in the normal range (140 mg/dL). Although his blood glucose levels are currently within the normal range, his obesity and other metabolic abnormalities make him highly likely to have diabetes develop in the future.

Although this patient has neither CHD nor a CHD risk equivalent, he has several important CHD risk factors in addition to his elevated LDL-C level, including his tobacco use, untreated hypertension, low HDL-C level, and family history of premature CHD. According to the Framingham risk points-scoring formula for men, he is assigned 6 points for his age, 4 points for his total cholesterol level, 3 points for his smoking status, 2 points for his HDL-C level, and 2 points for his systolic blood pressure. With a total of 17 points, his 10-year risk of a coronary event is more than 30%.

Case study 3

□ Advanced age
□ Mother’s hypertension during pregnancy
□ Hypertension/use of antihypertensive agent (major risk factor, modifies low-density lipoprotein cholesterol [LDL-C] goal)
□ Slightly elevated total cholesterol level
□ Borderline-high LDL-C level
□ Low level of high-density lipoprotein cholesterol (major risk factor, modifies LDL-C goal)
□ Slightly elevated triglyceride concentration

This risk level definitely warrants immediate and aggressive intervention. The ATP III guidelines state that patients with a 10-year risk greater than 20% should have a target LDL-C level of less than 100 mg/dL. Because this patient's LDL-C level is so far above the target, drug therapy should be initiated immediately in conjunction with TLC.1

The patient should be strongly advised to quit smoking, with medical assistance if necessary. Dietary changes should be instituted immediately, but an exercise regimen should be delayed until the results of a stress test are obtained. Drug therapy should include both a statin and an ACE inhibitor. If the triglyceride level remains within normal parameters, additional medications may not be needed.

Case study 3

This patient, a 65-year-old white American man, presents interesting diagnostic and therapeutic dilemmas (Figure 4). He is not a smoker, is not diabetic, and has no family history of cardiovascular disease except for his mother’s hypertension during pregnancy. His total cholesterol level is 205 mg/dL (barely elevated over the desirable level); his LDL-C level is 137 mg/dL (borderline high); his HDL-C level is 38 mg/dL (low), and his triglyceride concentration is 150 mg/dL (just between normal and borderline high).1 Despite treatment with amlodipine besylate, 10 mg/d, his blood pressure remains somewhat elevated at 142/88 mm Hg.

At first glance, the CHD risk suggested by his blood pressure and lipid profile is ambiguous. However, applying the Framingham risk point-scoring formula shows that his global risk score is actually quite high. His age accounts for 11 points, his total cholesterol level adds 1 point, his HDL-C level adds 2 points, and his treatment-refractory hypertension contributes another 2 points. With a total of 16 points, his 10-year risk of a primary coronary event is an estimated 25%.1

This is the type of patient for whom the ATP III guidelines differ from the ATP II guidelines. Whereas ATP II would have specified an LDL-C goal of less than 130 mg/dL for this patient (given that he had no prior history of CHD), ATP III dictates a more stringent goal of less than 100 mg/dL because his 10-year CHD risk is greater than 20%, which is considered a CHD risk equivalent.1 Because his LDL-C level is almost within 30 mg/dL of the target, the physician may choose to try TLC alone for 3 months or initiate drug therapy immediately as an adjunct to TLC. If lifestyle changes are not sufficient to improve his lipid profile, a trial of a low dose of a statin may be considered. Nicotinic acid or a fibrate may also be useful for increasing his HDL-C level.

Although calcium channel blockers are often prescribed out of habit, they are not the ideal choice for this type of patient because they offer no benefits other than reducing blood pressure (and are not fully effective in this particular patient). He should be switched to an ACE inhibitor because this class of drugs has clinical benefits beyond its antihypertensive effects.

Comment

From both a clinical and a pharmacoeconomic perspective, it is essential that patients at risk for CHD be identified early and treated aggressively. Encouraging patients to quit smoking and adopt healthy diet and exercise habits is relatively cost-free. Furthermore, the cost of treating patients for MBS is minimal compared with the economic and personal expenditure associated with a cardiovascular event or diabetic complication. It has been shown that even patients with existing CHD can be offered effective therapy to prevent progression, so that they can maintain or improve their health status and productivity for many years.

Reference