This supplement is sponsored by Primary Care Education Consortium and the Primary Care Metabolic Group and was supported by an educational grant by Kowa Pharmaceuticals America, Inc. and Lilly USA, LLC. It has been edited and peer reviewed by *Clinician Reviews*.

SUPPLEMENT TO
Clinician Reviews®

FREE 1.0 CME/CE CREDIT

Available at clinicianreviews.com FEBRUARY 2013

Individualizing Statin Therapy

Michael Cobble, MD, AAFP, FNLA
Diplomate, American Board of Clinical Lipidology
Certified Hypertension Specialist
Private Practice
Sandy, Utah
Adjunct Faculty, University of Utah School of Medicine
Salt Lake City, Utah

Joyce Ross, MSN, CRNP, FNLA, FPCNA
Certified Clinical Lipid Specialist
Diplomate, Accreditation Council for Clinical Lipidology
Past President, Preventive Cardiovascular Nurses Association
University of Pennsylvania Health System - Retired
Philadelphia, Pennsylvania

LEARNING OBJECTIVES

1. Describe the use of the Framingham Risk Score and Reynolds Risk Score to assess 10-year risk of coronary heart disease
2. Describe the long-term benefits associated with statin therapy
3. Differentiate the statins with respect to efficacy and safety
4. Describe adverse events associated with statins and their management
5. Identify strategies to improve adherence to statin therapy

TARGET AUDIENCE

Nurse practitioners and physician assistants with an interest in the management of patients with hyperlipidemia.

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Release date: February 1, 2013

Expiration Date: January 31, 2014

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INTRODUCTION

Dyslipidemia is a common, important, and treatable cardiovascular risk factor. The pathophysiology of this disorder has become better understood over the past generations, but still remains a major contributor to premature death. The percentage of adults aged 20 years and older with high total cholesterol has declined substantially over the past decade. For 2009-2010, 13.4% of US adults had high total cholesterol (defined as ≥240 mg/dL), which meets the Healthy People 2010 target of 17% or less (**FIGURE**).[1,2] However, 31.4% of men and 11.9% of women were found to have low high-density lipoprotein cholesterol (HDL-C) (defined as <40 mg/dL).

In addition, only 68% of adults had their cholesterol level checked within the past 5 years, which is below the Healthy People 2010 target of 80%.[1] The low rate of cholesterol screening likely contributes to the estimated 8% of adults who have undiagnosed hypercholesterolemia. Among those with diagnosed hypercholesterolemia, fewer than half who qualify for lipid-modifying treatment receive it, including those with symptomatic coronary heart disease (CHD). Moreover, fewer than 20% of patients with CHD are at their low-density lipoprotein cholesterol (LDL-C) goal.[3] These statistics are a concern because of the health implications associated with dyslipidemia.

This article reviews risk factors and treatment goals for dyslipidemia characterized by high LDL-C. Emphasis is placed on statin therapy with a focus on recently published results of clinical trials with long-term follow-up, as well as pitavastatin, the newest statin. Differences among the statins, clinically important adverse events and drug interactions, and strategies to improve adherence are also discussed.

Case Study

HW is a healthy white male who has been a patient for 4 years. He recently turned 45 years old, which increases his risk of CHD based on criteria established by the National Cholesterol Education Program (NCEP). In addition, the American Diabetes Association recommends beginning screening for type 2 diabetes mellitus (T2DM) in asymptomatic persons at 45 years of age.

The results of the lipid panel reveal the following:

- Total cholesterol, 194 mg/dL (goal <200 mg/dL)
- LDL-C, 128 mg/dL (goal <100-130 mg/dL)
- HDL-C, 44 mg/dL (goal >40 mg/dL)
- Non–HDL-C, 146 mg/dL (goal <130-160 mg/dL)
- Triglycerides, 110 mg/dL (goal <150 mg/dL)

An in-office test shows his glycosylated hemoglobin (A1C) level to be 7.4%. To verify this result, the health care provider draws blood for a chemistry panel, including A1C, blood glucose, and thyroid-stimulating hormone (TSH).

Vital signs: blood pressure (BP), 146/94 mm Hg; heart rate (HR), 74/min; respiratory rate (RR), 18/min; temperature, 37.3°C; weight, 187 lb; body mass index (BMI), 26 kg/m^2

Past medical history: No significant history

Social history: Married, lives with wife and 3 children; never smoked; occasional alcohol; no illicit drugs; works around the house many weekends but no regular exercise program

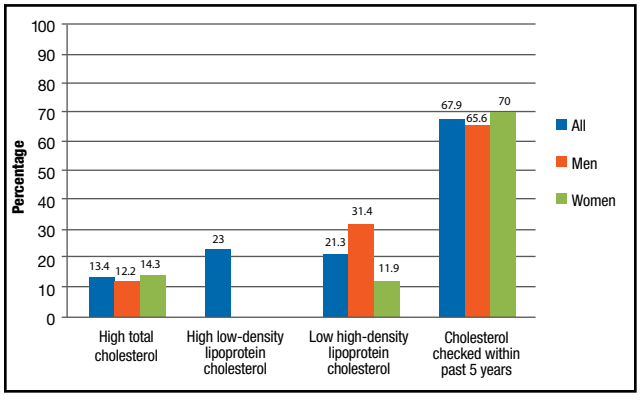
Family history: parents alive (father, T2DMx 6 years); 3 siblings (1 older brother, T2DM x 1 year)

(continued on page S3)

RISK FACTORS FOR CORONARY HEART DISEASE

Recognition that the age of the patient in the case study, 45 years (≥55 years for women), placed him at increased risk for CHD prompted his being screened for dyslipidemia and T2DM. Another non-modifiable risk factor would be a family history of premature CHD. Modifiable nonlipid risk factors for CHD include hypertension (BP ≥140/90 mm Hg on 2 occasions or on antihypertensive medication), cigarette smoking, thrombogenic/hemostatic state, diabetes mellitus, obesity, physical inactivity, and an atherogenic diet that includes a high intake of saturated fatty acids and fried fats.[4] In addition to age, the patient in the case study has hypertension as a risk factor and limited regular exercise. Among the lipid risk factors for cardiovascular disease, LDL-C is the best validated, and although it underestimates the atherogenic lipoprotein burden, it remains the principal treatment target.[5] If the patient had a triglyceride level of ≥200 mg/dL, non–HDL-C (total cholesterol minus HDL-C) would be a secondary target if elevated, as it takes into account all atherogenic lipoproteins and is a strong epidemiologic predictor of cardiovascular risk.

FIGURE Prevalence of lipid-related measures in persons aged ≥20 years, 2009-2010[1,2]



Calculating 10-year coronary heart disease risk

To determine the need for and goals of lipid-lowering therapy, the patient's 10-year risk of CHD can be determined using 2 risk calculators. The Framingham Risk Score [http://www.framinghamheartstudy.

org/risk/coronary.html or http://hp2010.nhlbihin.net/atpiii/calculator.asp] is commonly used. However, the Framingham Risk Score may underestimate CHD risk, especially in women and younger persons or those who appear to be healthy, but may be at risk for CHD.[6,7] In addition, the Framingham Heart Study did not show an increased risk of CHD based on positive family history, although other studies have shown an association, so family history is not included in the Framingham Risk Score. On the other hand, the Reynolds Risk Score [http://www.reynoldsriskscore.org], which is similar to the Framingham Risk Score, does include parental history of myocardial infarction before age 60 years, as well as other risk factors such as high-sensitivity C-reactive protein (hs-CRP).[8] The Reynolds Risk Score performs better than the Framingham Risk Score overall, particularly in discriminating the difference in risk between black and white women.[9,10] The Reynolds Risk Score has also been validated in healthy, nondiabetic men.[11] In practical terms, the Framingham Risk Score is a reasonable choice when the patient's family history of cardiovascular disease and hs-CRP level are not known. If, however, the family history and hs-CRP level are known, the Reynolds Risk Score is a better choice, especially if the family history and/or hs-CRP are positive.

STATIN THERAPY

Statins have become a key treatment option for reducing cardiovascular risk and have been widely used for more than 2 decades, yet their long-term efficacy and safety have been questioned.[14-16] In addition, there are important differences among the 7 statins commercially available in the United States. Understanding these differences is pertinent to individualize therapy and reduce the risk of statin-associated adverse events (AEs).

Recent clinical evidence

The short-term efficacy and safety of statins for primary prevention of CHD (ie, before the occurrence of a cardiovascular event) in persons without established disease, as in the case of patient HW, was reaffirmed in a meta-analysis of 10 randomized clinical trials involving 70 388 patients without CHD; 23% had diabetes mellitus.[17] Over a mean follow-up of 4.1 years, statins demonstrated significant reductions in all cardiovascular events. There was no evidence of an increased risk of cancer.

The long-term benefits of statin therapy without evidence of emerging safety concerns were recently confirmed in 2 randomized clinical trials.[16,18] Results from the Heart Protection Study showed that patients treated with simvastatin 40 mg/d for 5 years maintained a 23% reduction in vascular events at follow-up 6 years later.[16] Similar long-term benefits were observed at 8 years' follow-up in patients treated with atorvastatin 10 mg/d for 3 years in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT).[18] Patients treated with atorvastatin for primary prevention maintained a 14% reduction in all-cause mortality (P = .02) and a 15% reduction in non-cardiovascular death (P = .03) compared to placebo.

A recent meta-analysis evaluated the possible benefit of statin use in primary prevention populations. This analysis evaluated the results of 22 trials compar-

Case Study (continued from page S2)

Using either of these risk calculators (assuming hs-CRP level of 0.8 mg/L) shows that HW's 10-year CHD risk is 3%. This risk score, coupled with his 2 risk factors for CHD (age and hypertension), places him at moderate risk for a CHD event within 10 years. Based upon this, his target LDL-C goal is <130 mg/dL. Although HW is below the threshold for lifestyle management, the health care provider encourages HW to increase his physical activity and lose 3% of his body weight over the next 6 months. HW agrees.

HW returns 6 months later. He indicates that he and his wife now walk for about a half hour after dinner 2 to 3 evenings per week and that he has curtailed snacking between meals.

Vital signs: BP, 142/90 mm Hg; HR, 70/min; RR, 17/min; temperature, 36.9°C; weight, 183 lb; BMI, 26 kg/m^2

Laboratory results from previous visit 6 months ago: A1C, 7.3%; fasting plasma glucose (FPG), 151 mg/dL; TSH, 3.6 µIU/mL.

Current laboratory results:
- Total cholesterol, 189 mg/dL
- LDL-C, 122 mg/dL
- HDL-C, 46 mg/dL
- Non–HDL-C, 143 mg/dL
- Triglycerides, 116 mg/dL
- A1C, 7.2%
- FPG, 142 mg/dL

The health care provider commends HW for losing 4 pounds (2.1%) but notes that, based on the A1C and FPG levels, HW has T2DM. The finding of comorbid T2DM elevates his risk and places HW in the highest risk category for a CHD event. Consequently, because HW has no overt cardiovascular disease, the target goals are: LDL-C <100 mg/dL, HDL-C >40 mg/dL (>50 mg/dL in women), and apoB <90 mg/dL.[12] ApoB (and non–HDL-C) is especially important as it is the apoprotein attached to atherogenic lipoproteins and is a strong epidemiologic predictor of cardiovascular risk. Greater improvement in the lipid profile is recommended for those with overt cardiovascular disease.[13]

The health care provider discusses with HW further lifestyle management changes and lipid-lowering drug therapy directed at lowering LDL-C for primary prevention of CHD. Lisinopril 10mg/d is initiated to treat his hypertension, since several measurements at his local pharmacy following his last visit confirmed elevated BP. Low-dose aspirin is initiated as well. The health care provider and HW discuss options to lower his LDL-C.

(continued on page S6)

TABLE Range of LDL-C–lowering among statins[22]

LDL-C range (↓)	Atorvastatin	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
20%-25%	----	20 mg	----	----	----	----	----
25%-30%	----	40 mg	----	----	10 mg	----	----
30%-35%	----	80 mg	20 mg	1 mg	20 mg	----	10 mg
35%-40%	10 mg	----	40 mg	2 mg	40 mg	----	20 mg
40%-45%	20 mg	----	80 mg	4 mg	80 mg	5 mg	40 mg
45%-50%	40 mg	----	----	----	----	10 mg	----
50%-60%	80 mg	----	----	----	----	20 mg	----
>60%	----	----	----	----	----	40 mg	----

LDL-C, low-density lipoprotein cholesterol.

ing statin with control therapy (N = 134 537; mean age 63 years; 71% men; median follow-up in survivors, 4.8 years) on reductions in major vascular events.[19,20] Using statins to lower LDL-C by 39 mg/dL reduced the risk of a major vascular event (nonfatal myocardial infarction or coronary death, coronary revascularization, or stroke) regardless of baseline risk level (relative risk, 0.79).

Analysis of data from a subset of patients in ASCOT (N = 4853) with total cholesterol <250 mg/dL and followed for 5.5 years showed that baseline hs-CRP did not predict the magnitude of the atorvastatin effect on cardiovascular outcome (P = .54).[21] Furthermore, there was no difference in the incidence of cardiovascular events between those with hs-CRP below the median (1.83 mg/dL) compared with hs-CRP above the median (P = .60).

Typical reductions in LDL-C by dose for each of the currently available statins are provided in the TABLE.[22]

Pitavastatin

Available in Japan since 2003, pitavastatin (brand name Livalo) is the most recent statin to become available in the United States and was approved in 2009. Similar to atorvastatin and rosuvastatin, pitavastatin has a long elimination half-life.[23-30] In addition, similar to rosuvastatin, pitavastatin undergoes minimal hepatic metabolism without the formation of active metabolites. The limited hepatic metabolism that does occur is mediated by the cytochrome-P450 (CYP) 2C9 isoenzyme rather than the major CYP3A4 pathway, thereby reducing the occurrence of CYP-mediated drug interactions.[30]

The efficacy and safety of pitavastatin have been demonstrated in clinical trials from 12 weeks to 5 years. Comparable reductions in the LDL-C level have been observed over 12 weeks with pitavastatin 4 mg/d (-41%) and atorvastatin 20 mg/d (-43%),31 and over 16 weeks with atorvastatin 10 mg/d, rosuvastatin 2.5 mg/d, and pitavastatin 2 mg/d.[32]

The Japanese LIVALO Effectiveness and Safety (LIVES) study (N = 20,279) evaluated the effects of pitavastatin 1 to 4 mg/d over 2 years with an extension phase to 5 years.[33] At the end of 2 years, pitavastatin was associated with a 29.1% reduction in LDL-C and a 5.9% increase in HDL-C. At 5 years (N = 6582), LDL-C was reduced 30.5%, while HDL-C increased 29% compared to baseline. In those with abnormal HDL-C and triglyceride levels at baseline, pitavastatin increased HDL-C levels by 19.9% and reduced triglyceride levels by 22.7% at 2 years. Patients who achieved both LDL-C and HDL-C goals experienced the greatest reductions in cardiovascular and cerebrovascular risk.

Pitavastatin 4 mg/d has also demonstrated significant improvement comparable to atorvastatin 20 mg/d over 8 to 12 months in coronary plaque volume among patients with acute coronary syndrome undergoing intravascular ultrasound (N = 252).[34]

Adverse events

Statins have a favorable risk-to-benefit ratio, but have the potential to cause clinically important muscle- and liver-related AEs, while an increased risk of diabetes has been posited.

Myotoxicity

Myalgia, myositis, and rhabdomyolysis are well-recognized AEs associated with statin therapy. Myalgia refers to muscle symptoms without creatine kinase (CK) elevation; myositis refers to an increased CK level without muscle symptoms; myopathy refers to muscle symptoms with CK elevations, while rhabdomyolysis refers to severe myopathy.[4] A case-crossover comparison of myopathy/myalgia based on 16591 statin users (atorvastatin, cerivastatin, fluvastatin, pravastatin, rosuvastatin, simvastatin) from The Health Information Network database showed that the rate ratio (ie, ratio of the number of events when exposed divided by the number of events when not exposed) at 52 weeks for all statins was 24.9, with the lowest rate with rosuvastatin (14.9) and the highest rate with fluvastatin (35.6).[35] [Note: this study was performed before pitavastatin was approved in the

United States.] Rhabdomyolysis, the most severe form of muscle injury, has an estimated incidence of 3.4 cases per 100 000 person-years with standard statin doses, with an increased rate at higher doses.[36] Analysis of the Prediction of Muscular Risk in Observational Conditions (PRIMO) survey showed that 10.5% of patients receiving moderate- to high-dose statin therapy experienced muscle-related symptoms. Approximately 30% of patients with muscle-related symptoms associated with high-dose statin therapy in the PRIMO study reported starting a new medication as the cause.[37]

The increase in myotoxicity with higher doses is more apparent with specific statins, notably simvastatin,[38,39] which led the US Food and Drug Administration (FDA) to issue an advisory, including restricting the 80 mg dose of simvastatin.[40] While lower rates of myopathy and rhabdomyolysis have been reported with atorvastatin 80 mg, fluvastatin 80 mg, and rosuvastatin 40 mg in major trials,[41] a threshold also has been observed with an approximate 3-fold higher incidence of CK and hepatic transaminase elevations when titrating from moderate to maximal doses.[42]

In addition to higher doses, the incidence of statin-associated myotoxicity may be increased with concomitant use of drugs that inhibit or compete with similar metabolic pathways such as the liver CYP450 isoenzymes or organic anion-transporting polypeptides (OATPs) involved with uptake into hepatocytes. Since about half of all currently available drugs are biotransformed primarily by the CYP3A4 isoenzyme, statins that undergo CYP3A4 biotransformation (atorvastatin, lovastatin, simvastatin and, minimally, pravastatin) are the most likely to interact. As lovastatin and simvastatin undergo extensive CYP3A4 biotransformation, the labeling for both simvastatin and lovastatin was recently revised to include information on contraindications and dose limitations with concomitant agents [http://www.fda.gov/Drugs/DrugSafety/ucm293877.htm].[40,43] The labeling for atorvastatin was made less restrictive because a previous report of an interaction with lopinavir/ritonavir has not been validated; nonetheless, caution is advised when using atorvastatin with lopinavir/ritonavir and the lowest necessary dose of atorvastatin is used. Similar to other potent CYP3A4 inhibitors, protease inhibitors can increase lovastatin and simvastatin levels by 13- to 20-fold.

A recent FDA advisory provides specific dose limitations and contraindications for the statins.[44] However, no information is available for fluvastatin, while no dose limitations are needed for pitavastatin or pravastatin. Since statins have the potential to interact with a wide variety of medications, and there are differences among the statins, it is imperative that the possibility of a drug interaction be investigated whenever a statin is initiated or the dose changed, or any medication is initiated or discontinued.

Statins that undergo biotransformation via CYP450 isoenzymes other than CYP3A4 are also subject to important drug-drug interactions. For example, fluvastatin (and, minimally, pitavastatin and rosuvastatin) is metabolized primarily by CYP2C9, the same enzyme that metabolizes warfarin.[37] Appropriate monitoring of the international normalized ratio is suggested when fluvastatin, or any statin, is added to warfarin treatment. The combination of a statin with a fibrate, particularly gemfibrozil, is to be avoided because this combination inhibits CYP2CP and leads to a marked increase in statin blood level. A several-fold increase in the rate of hospitalization due to rhabdomyolysis has also been reported.[45] Similarly, the coadministration of a statin with cyclosporine is clinically relevant. Cyclosporine blocks OATP, another key step in statin metabolism, thereby resulting in elevated concentrations of nearly all statins. The concomitant use of cyclosporine with lovastatin, simvastatin, or pitavastatin is contraindicated, whereas most other agents require dose limitations.[26,40,43,46]

In addition to avoiding drug interactions, other steps can be taken to minimize the risk of statin-associated myotoxicity, if it is determined that the benefits of statin therapy outweigh the potential risks. These steps include not using high doses, using intermittent dosing (eg, every other day, twice weekly) with an extended half-life statin (eg, atorvastatin, pitavastatin, rosuvastatin), and switching to a non-statin.[37,47,48] Other possible contributing factors such as thyroid dysfunction, electrolyte and metabolic abnormalities, and recent muscle injury should be ruled out.

Hepatotoxicity

A review of AEs associated with statin use and involving the liver was finalized by the FDA in February 2012.[43] The conclusion of the review was that all 7 currently available statins appear to be associated with a very low risk of serious liver injury. The FDA further concluded that routine periodic monitoring of serum alanine aminotransferase does not appear to detect or prevent serious statin-related liver injury. As a consequence, routine periodic monitoring of liver enzymes is no longer recommended in patients taking a statin. However, liver enzyme tests should be performed prior to initiating statin therapy and as clinically indicated thereafter.

Other

Statin use has been reported to be associated with other AEs. Two recent meta-analyses examined a possible association between statins and cognitive function with one showing no association[15] and the other a neutral or beneficial effect on cognitive function.[49] These findings may be influenced by the presence or absence of

Case Study (continued from page S3)

HW returns 3 months later for dyslipidemia, hypertension, and T2DM follow-up. At his previous visit, he and his health care provider decided to begin a low-dose statin and metformin 500 mg twice daily.

Vital signs: BP, 135/85 mm Hg; HR, 68/min; RR, 16/min; temperature, 37.1°C; weight, 181 lbs; BMI, 26 kg/m^2

Current laboratory results:
- Total cholesterol, 164 mg/dL
- LDL-C, 90 mg/dL
- HDL-C, 52 mg/dL
- Non–HDL-C, 112 mg/dL
- Triglycerides, 119 mg/dL
- A1C, 6.8%
- FPG, 139 mg/dL

Because HW is not at the more aggressive LDL-C and non–HDL-C goals (<70 mg/dL and <100 mg/dL, respectively), his health care provider considers increasing the statin dose. With respect to HW's T2DM, the provider is surprised that there has only been a modest reduction in the A1C level and considers possible explanations (eg, medication and lifestyle adherence, low metformin dose, persistent postprandial hyperglycemia, statin-related effects).

(continued on page S7)

preexisting dementia. A prospective open-label trial involving 18 older adults with Alzheimer's disease found improvement in cognitive function as measured using the Mini-Mental State Examination (MMSE) upon discontinuation of statin therapy with a subsequent decline upon rechallenge.[50] A possible association with statin therapy and neuropathy, proteinuria, and cancer has been suggested by mostly case reports and epidemiologic studies. Review of the evidence and additional investigation have generally resulted in contradictory or inconclusive findings.[15,51-61]

Diabetes

While the West of Scotland Coronary Prevention Study (WOSCOPS) found statin therapy to provide a 30% reduction in the risk of becoming diabetic, the Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) study found a significantly elevated incidence of physician-reported diabetes with rosuvastatin compared with placebo.[62,63] A subsequent meta-analysis of 13 clinical trials involving 91 140 patients found that statin use was associated with a 9% increased risk for new-onset diabetes mellitus.[64] It was estimated that treatment of 255 patients for 4 years would result in 1 extra case of diabetes. No difference was observed in diabetes risk between lipophilic and hydrophilic statins. Further analysis indicated the risk was limited to patients older than 60 years. Another recent meta-analysis of 5 statin trials involving 32 752 patients examined the relationship between statin dose and new-onset diabetes mellitus and found a 12% increase with high-dose compared with moderate-dose statin therapy.[65] In absolute terms, this meant that there were 2 additional cases of diabetes mellitus per 1000 patient-years among those taking high-dose statin therapy. Taking cardiovascular benefit into consideration, the investigators determined that treating 498 patients with intensive-dose statin therapy for 1 year would result in 1 additional case of diabetes mellitus, while treating 155 patients for 1 year would prevent 1 additional case of a cardiovascular event.

Limited evidence from individual trials suggests that there may be differences in the increased risk for diabetes among the statins. A 16-week comparison showed that low-dose atorvastatin and rosuvastatin were associated with a 0.1% increase (P = NS) in the A1C level, while pitavastatin had no effect on A1C.[66] Similar findings were observed in another study showing no difference in fasting plasma glucose or A1C with atorvastatin 10 mg/d or pitavastatin 2 mg/d for 12 weeks.[67]

While further investigation is needed, the FDA recently added warnings to all statin labeling indicating that statins can raise blood glucose and A1C levels.[43] No definitive changes to clinical practice were recommended.

Selecting a statin based on ethnicity

Since there is some variability in the metabolic pathways involved in statin clearance and genetic variants in these pathways have been identified, there has been limited investigation to assess the possible impact of ethnicity on statin efficacy and safety. These investigations generally suggest that lipid changes and cardiovascular outcomes do not vary based on ethnicity. A substudy of ASCOT showed that there were no significant differences in the reductions in total cholesterol, LDL-C, or triglycerides among whites, blacks, and Asians.[68] Similar reductions in major cardiovascular events were noted for whites versus non-whites in the JUPITER study, with Hispanics and blacks experiencing comparable risk reductions.[69] Another study found no differences in the pharmacokinetics of pitavastatin between healthy Caucasian and Japanese men.[70] However, a 2-fold increase in pharmacokinetic parameters in patients of Asian ancestry compared with whites has been observed with rosuvastatin, thus leading to the recommendation that the dose of rosuvastatin, including the 5 mg starting dose, should be reduced in patients of Asian ancestry.[71]

Strategies to improve patient adherence

Patient adherence to statin therapy is sub-optimal, as only 75% of patients have a statin prescription filled upon hospital discharge for myocardial infarction.[72] Three years later, 44% continued taking the statin. Patients who are not adherent with statin therapy are twice as likely not to achieve

Case Study (continued from page S6)

Having eliminated the low-dose statin as the most likely cause for the less-than-expected reduction in the A1C level (7.2% to 6.8%), the health care provider asks HW if he has been taking his metformin as they discussed. HW admits that he hasn't because he is feeling overwhelmed with the impact that treating his dyslipidemia and T2DM has had on his life, especially because he feels well.

Plan:

- Discuss importance of treatment to reduce risk of long-term complications
- Encourage adherence; assure treatment will be modified as needed to achieve goals and meet his needs; provide support
- Encourage and support lifestyle changes; refer for nutrition counseling, if necessary
- Continue metformin 500 mg twice daily; reevaluate dose at next visit
- Continue statin at current dose
- Follow-up in 2 months ■

their identified LDL-C goal.[73] Furthermore, the absolute death rate in those who are prescribed a statin but who do not use it is 2.7 times that of regular statin users.[74]

Patients who regularly receive medical care or participate in a cardiac rehabilitation program are more likely to adhere to statin therapy.[72,75] Building on patient motivation through active collaboration that individualizes therapy based on patient's beliefs, needs, and capabilities is crucial.[73] Patient education is also important since many patients are misinformed and lack understanding regarding potential manifestations of dyslipidemia. For instance, patients often have an exaggerated sense of statin-induced hepatic and renal toxicity. Additionally, patients may comprehend that statins lower blood cholesterol, but do not make the connection to reduced CHD, stroke, and need for revascularizations with medication adherence and LDL-C goal attainment. Simple counseling sessions explaining the realistic benefits and risks of statins, as well as how to follow the prescribed treatment, are critically important.[4] One reported intervention that improved statin adherence from 65% to 91% over 6 months began with the health care provider completing a 1-page form with the patient, as well as providing education about a healthy lifestyle and written instructions to facilitate treatment goals, with monthly follow-up office visits.[76] The increase in statin adherence was also accompanied by significant improvement in total cholesterol, LDL-C, HDL-C, and triglyceride levels.

Health care provider factors also impact adherence. Practice patterns that negatively influence adherence include not adhering to or misunderstanding treatment guidelines, perceiving that patients will be nonadherent, and spending minimal time with patients. In contrast, a strong patient-health care provider relationship enhances adherence.[77]Another strategy shown to significantly improve adherence is prescribing fixed-dose combination lipid-lowering therapy compared with multi-pill therapy.[78]

CONCLUSION

Statins are widely used and remain a key treatment option for patients with elevated LDL-C. Differences among the statins allow for individualization of treatment, but require careful dosage selection and monitoring for AEs.

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