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Clinical Champion Update

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Hyperlipidemia Update:

If Treatment Is Indicated, What Should We Prescribe?

If you have been reading this series of occasional posts about hyperlipidemia, you're aware that the first "prescription" is actually lifestyle modification (see my post from 2/8/21), as cardiovascular disease remains the leading cause of death worldwide. For patients whose risk level remains high despite decreasing consumption of saturated fats, increasing exercise, and reaching / maintaining a healthy weight, a statin may be recommended (see When to Consider a Statin for Primary Prevention of Cardiovascular Disease, 5/18/21, and Lowering Lipids with a Heart-Healthy Lifestyle, 3/8/22). What about other options for patients who cannot tolerate a statin or for whom statins are inadequate or ineffective?

Current research, as summarized in UpToDate, continues to support lowering LDL-C to reduce cardiovascular risk. In the absence of diabetes, goal LDL-C is <100 (for patients ages 40-75 with diabetes and at least one other cardiovascular disease risk factor, goal LDL-C is <70). If intensification of statin therapy does not achieve the recommended reduction, oral ezetimibe (a cholesterol absorption inhibitor) can be added. Other oral nonstatin drugs include fibric acid derivatives gemfibrozil and fenofibrate (which decrease triglycerides and also lower LDL-C), bempedoic acid (an ATP citrate lyase inhibitor), and bile acid sequestrants (cholestyramine, colestipol, colesevelam). These medications can also be used if statins are not tolerated (and gemfibrozil should not be taken with a statin). Nicotinic acid has also been used to help lower LDL-C, but it is poorly tolerated due to flushing so not prescribed often. Rechecking LDL-C is appropriate four to six weeks after beginning any new treatment.

PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitors alirocumab and evolocumab (monoclonal antibodies) are injectable medications that lower LDL-C. They are most commonly prescribed for patients with LDL-C >190 and/or those who have familial hypercholesterolemia. These medications have low risk for potential medication interactions, and their most common side effects are injection site reactions. They do not increase the risk of intracerebral bleeding so are considered safer than statins for patients with a history of hemorrhagic stroke. PCSK9 inhibitors typically have been prescribed by cardiologists and lipid specialists for the indications noted. However, a new medication, inclisiran (a small interfering RNA agent), has received approval for use in primary prevention of cardiovascular disease and may be appropriate for

patients who cannot tolerate PCSK9 inhibitors. Inclisiran and PCSK9 inhibitors are still quite expensive, especially when compared with oral agents.

Although lowering LDL-C is an accepted strategy for both primary and secondary prevention of cardiovascular disease, not all patients are offered the same opportunities for treatment. Dyslipidemia is more prevalent among South Asian, Filipino, and Black patients, for instance, but they are prescribed lipid-lowering medications less frequently than are White patients and are less likely to reach optimal LDL-C goals. Women (particularly Black women) are also prescribed statin therapy less frequently than are men. Elevated LDL-C and triglyceride levels are more common among Hispanic adults, who also have a higher incidence of diabetes, metabolic syndrome, and visceral adiposity. Hypertension, stroke, heart failure, and cardiovascular mortality are more common among Blacks, who are less likely than Whites to receive appropriate preventive cardiovascular care.

--Lisa Appleton, FNP, clinical champion for hyperlipidemia and lifestyle medicine