

Treatment of Dyslipidemias: Change of Paradigm

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Dyslipidemia is a major risk factor for coronary artery disease and ischemic stroke. A great number of clinical trials of cholesterol lowering treatment have demonstrated the benefits for patients diagnosed with cardiovascular diseases and for those patients with dyslipidemia/hypercholesterolemia without established cardiovascular diseases. There are different guidelines for cholesterol treatment and lifestyle management in patients with dyslipidemia, starting from the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III (2001) and the 2004 Update and continuing with the 2011 European Society of Cardiology Guidelines for the management of dyslipidemias, 2013 American College of Cardiology/American Heart Association Guideline on the treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, 2013 American Heart Association/American College of Cardiology Guideline on Lifestyle Management to Reduce Cardiovascular Risk and 2013 American College of Cardiology/American Heart Association on the Assessment of Cardiovascular Risk.

In patients with triglycerides level greater than 500 mg/dL (especially >1000 mg/dL) first triglycerides should be lowered in order to prevent pancreatitis [1]. A very low-fat diet (15% of calories from fat), without alcohol, should be recommended, together with weight management and an appropriate level of physical activity. The secondary causes should be identified and corrected. The pharmacologic therapy consists in fibrin acid derivatives, omega 3 fatty acids and/or nicotinic acid [1]. When triglycerides become <500 mg/dL, the attention can be turned to LDL-lowering therapy [1]. The 2013 American College of Cardiology (ACC)/American Heart Association (AHA) Cholesterol Treatment Guideline is not meant to be a comprehensive treatment guideline for lipid disorders, but to answer specific critical questions and to identify treatment groups that would benefit from statin therapy, as demonstrated in randomized clinical trials. This guideline emphasizes that a heart healthy lifestyle is foundation of prevention. The diet should aim for 5-6% of calories from saturated fat and no Trans fats, with an emphasis on vegetables, fruits, whole grains, low-fat dairy, fish and nuts [2]. If arterial hypertension is present, a low sodium intake (<2.4 g/day) is recommended [2]. Cardio exercises 3-4 times per week, 40 minutes per session, at moderate to vigorous intensity, are also recommended. The 2013 ACC/AHA Cholesterol Treatment Guideline identifies 4 statin benefit groups [3]:

1. Secondary prevention in patients with clinical atherosclerotic cardiovascular diseases (ASCVD);
2. Primary prevention for patients with LDL-cholesterol >190 mg/dL;
3. Primary prevention in diabetics aged between 40-75 years old with LDL-cholesterol between 70-189 mg/dL;
4. Primary prevention in patients without diabetes, aged between 40-75 years old, with LDL-cholesterol 70-189 mg/dL and 10-year ASCVD risk >7.5%.

If patients have clinical ASCVD (acute coronary syndromes, history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke or transient ischemic attack,

peripheral arterial disease) and are less than 75 years old, high intensity statin treatment should be started [3]. If age is greater than 75 years old or not a high-dose statin candidate, a moderate dose statin is recommended. In adult patients with LDL-cholesterol >190 mg/dL a high intensity statin treatment should be initiated [3]. In diabetic patients aged between 40-75 years old, at least a moderate intensity statin is recommended; if the 10-year ASCVD risk is >7.5%, a high dose statin must be used [3]. In other patients aged between 40-75 years old, the 10-year risk for a first ASCVD event is calculated; elevated risk is >7.5%. If decision is uncertain, the guideline recommends considering revising risk upward if any of the following are present: family history of premature coronary artery disease, Hs-CRP >2 mg/dL, coronary artery calcium score >300, ankle-brachial index <0.9 [3].

The category of risk dictates the statin intensity. High intensity statin treatment is used in patients with clinical ASCVD, LDL-cholesterol >190 mg/dL, diabetics with 10-year ASCVD risk >7.5% [3]. Moderate intensity statin treatment is used in ASCVD and contraindication to high intensity statin, diabetics with 10-year ASCVD risk <7.5%, in primary prevention of patients without diabetes and with 10-year ASCVD risk >7.5% [3]. High intensity statin treatment (>50% LDL reduction) is considered atorvastatin 40-80 mg/day, rosuvastatin 20-40 mg/day. The moderate intensity statin treatment (30-50% LDL reduction) is considered atorvastatin 10-20 mg/day, fluvastatin 80 mg/day, lovastatin 40 mg/day, pitavastatin 2-4 mg/day, pravastatin 40-80 mg/day, rosuvastatin 5-10 mg/day, simvastatin 20-40 mg/day.

Currently, there are major paradigm shifts from older guidelines: newer guidelines target ASCVD risk instead of LDL-cholesterol levels, put an emphasis on statin therapy and avoidance of non-statin agents in most patients, lower risk calculator cut point for statin therapy initiation.

A simplified approach to lipid treatment in dyslipidemic patients may follow the next steps: first, look at triglycerides and decide on treatment to reduce the risk of pancreatitis, next assess patient's risk using the 4 risk categories. If ASCVD risk or other very high risk state is present, aim for LDL-cholesterol <70 mg/dL and/or non-HDL-cholesterol <100 mg/dL using statins as first line. If diabetes mellitus is present, moderate dose statin is reasonable. Next steps are risk calculator and clinical judgement; if risk is unclear, we may consider additional info.

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Received October 05, 2015; Accepted October 06, 2015; Published October 08, 2015

Citation: Diaconu CC (2015) Treatment of Dyslipidemias: Change of Paradigm. Pharm Anal Acta 6: e180. doi:[10.4172/2153-2435.1000e180](https://doi.org/10.4172/2153-2435.1000e180)

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