

Dyslipidemia: Causes, Symptoms and Treatment

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ABSTRACT

Deaths that are caused due to coronary heart disease (CHD) is a major cause of deaths in most of the population. Even though the mortality rate has been reducing, dyslipidemia is the major known risk factor in pathogenesis of CHD. In this paper we review the role of dyslipidemia and lipid changes that occur in men and women at different stages. We discuss about dyslipidemia causes symptoms and treatments and all the other issues that arise due to dyslipidemia. We talk about different drugs that are used in treating dyslipidemia and their side effects.

Abbreviations:

- high-density lipoprotein - HDL
- low-density lipoprotein – LDL
- coronary heart disease – CHD

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INTRODUCTION

Dyslipidemia refers to unhealthy levels of one or more kinds of lipid (fat) in your blood. Blood contains 3 main types of lipid.

- high-density lipoprotein (HDL)
- low-density lipoprotein (LDL)
- triglycerides

If the levels of low-density lipoprotein are too high or the levels of triglycerides are too high, then it means you have Dyslipidemia. It also means your high-density lipoprotein levels are too low. Having HDL is good because it helps remove LDL from blood. LDL cholesterol is bad type of cholesterol, as it can build up and form clumps in the artery walls. This builds up can cause heart attack. Triglycerides are formed from the food calories but don't burn right away. This is what you use when you need energy, but when you eat so many calories than what you need triglycerides get build up.

Dyslipidemia is divided into two types, primary and secondary. Primary dyslipidemia come through genes, and secondary dyslipidemia is acquired, which means its developed from other issues like obesity or diabetes. Hyperlipidemia is often confused with dyslipidemia. Hyperlipidemia is caused when LDL levels are high, but dyslipidemia is caused by blood fats being either low or high. Hyperlipidemia is a major cause of atherosclerosis and its included conditions like ischemic cardiovascular issues, coronary heart disease, peripheral vascular disease. The occurrence of these atherosclerosis related cardiovascular

issues has declined in United States, but mortality has raised in middle aged and older adults. Because of obesity issues happening more in the people these death rates were going to increase in the coming decade in US population. Some of the primary dyslipidemia are:

Familial combined hyperlipidemia:

This is the common type of dyslipidemia. And is caused mostly from inheritance, which is due to high levels of LDL cholesterol and high levels of triglycerides. If you have familial combined hyperlipidemia, you will develop these issues in twenties. You are also at risk of heart attack issues and early coronary artery disease.

Familial hypercholesterolemia and polygenic hypercholesterolemia:

The total cholesterol can be calculated by combining LDL and HDL, and half of your triglyceride. and these two types are caused due to high levels of total cholesterol. Total cholesterol levels should be less than 200 milligrams per deciliter.

Familial hyperapobetalipoproteinemia:

This condition means you have high levels of apolipoprotein B, a protein that is part of your LDL cholesterol.

As per 2018 guidelines on cholesterol and blood management published in Journal of the American College of Cardiology, these are the acceptable levels of cholesterol in adults. All the values are in mg/dL and are based on fasting conditions.

	Total cholesterol	HDL cholesterol	LDL cholesterol	Triglycerides
Good	Less than 200 (but the lower the better)	Ideal is 60 or higher; 40 or higher for men and 50 or higher for women is acceptable	Less than 100; below 70 if coronary artery disease is present	Less than 149; ideal is <100
Borderline to moderately elevated	200–239	n/a	130–159	150–199
High	240 or higher	60 or higher	160 or higher; 190 considered very high	200 or higher; 500 considered very high
Low	n/a	less than 40	n/a	n/a

Source: JACC (Journal of the American College of Cardiology)

Fig 1: Recommended cholesterol levels for adults

Cholesterol level is considered to be good if the total cholesterol level is less than 200 mg/dL. And if HDL cholesterol level is 60 it is considered ideal. And it is 40 or more it is ideal, and for women 50 or more is acceptable. LDL cholesterol level should be less than 100, and if the person has coronary artery disease it should be less than 70. And Triglycerides level should be less than 149, and less than 100 is ideal. The cholesterol level is considered to be moderate if the total cholesterol level combining LDL, HDL and half of triglycerides is between 200 to 239. and If the LDL cholesterol level alone is between 130 and 159 it is considered to be moderate. And triglycerides levels should be between 150 and 199 to be called as moderate.

Cholesterol levels is considered high if the total cholesterol combining HLD, LDL, and half of triglycerides all together is 240 or higher, and HDL cholesterol level if it is higher than 60 or 60 it is considered as high. And if the LDL concentration is 160 or higher cholesterol level in the body is considered to be high. And if the LDL levels are 190 cholesterol level in the body is considered to be very high. If the triglycerides levels are 200 or higher cholesterol levels are considered to be high, if it is 500 it is considered very high. Cholesterol level is considered low if the HDL levels are less than 40.

	Total cholesterol	HDL cholesterol	LDL cholesterol	Triglycerides
Good	170 or less	Greater than 45	Less than 110	Less than 75 in children 0–9; less than 90 in children 10–19
Borderline	170–199	40-45	110–129	75-99 in children 0–9; 90–129 in children 10–19
High	200 or higher	n/a	130 or higher	100 or more in children 0–9; 130 or more in children 10–19
Low	n/a	Less than 40	n/a	n/a

Source: JACC (Journal of the American College of Cardiology)

Fig 2: Recommended cholesterol levels for children

Cholesterol levels in children are considered to be good if the total cholesterol levels are 170 or less, and if the HDL cholesterol levels are greater than 45, and LDL cholesterol levels are less than 110.

If triglycerides are less than 75 in children from age 0 to 9, and less than 90 in children from 10 to 19. cholesterol levels are considered to be borderline if the total cholesterol levels are between 170 to 199, and if the HDL cholesterol levels are between 40 to 45 it is considered to be o border. If the LDL cholesterol levels are between 110 to 129 and if triglycerides in children from age 0 to 9 years should have cholesterol levels between 75 to 99, and if is between 90 to 129 for children of age between 10 to 19 it is considered moderate.

Cholesterol levels in children are considered high if the total cholesterol levels are more than 200, and if the LDL levels are 130 or higher, then the cholesterol levels are considered to be high in children's body.

Triglycerides levels in children should not be more than 100 in children from age 0 to 9 years and it should not be more than 130 in children from age 10 to 19. Cholesterol levels are considered low if the HDL levels are less than 40 in children.

Drug Therapy for Dyslipidemia:

There are natural ways to reduce LDL cholesterol levels by diet modifications. But one can achieve only 10 to 20 percent reduction in cholesterol levels. If lipid levels are on raise even after six months NCEP recommended that cholesterol lowering agents should be used for therapy. Patients with High LDL cholesterol level should start therapy by using drugs sooner [2] as it is unlikely that a patient with LDL level 130 mg per dL with only diet [3]. Drug therapy is never a substitute for diet and exercise, patient should always continue with that. IN patients with hypercholesterolemia HMG-CoA reductase inhibitors are the drugs of choice because they reduce LDL cholesterol most effectively [4-8].

Satins are the most commonly prescribed medications for high cholesterol. Cholesterol production is blocked from your liver.

Some examples of satins are:

- atorvastatin (Lipitor)
- fluvastatin (Lescol)
- rosuvastatin (Crestor)
- simvastatin (Zocor)

Doctors also may prescribe other medications for high cholesterol like:

- Niacin (Nicotinic acid)
- Bile acid resins like colesevalam, colestipol, Prevalite
- Cholesterol absorption inhibitors like ezetimibe

Some of the cholesterol lowering agents are Cholestyramine, and the maintenance dosage 4g, 8g, 12g, or 16g twice daily. Colestipol is another agent that can be used to reduce cholesterol lowering agents. There are of types Bile acid-binding resins. Bile acid binding resins reduce total cholesterol levels by approximately twenty percent, and LDL levels by 10 to 20 percent and they are expected to increase HDL levels by 3 to 5%. Some of the side effects of Bile acid binding resins are unpalatability, bloating, constipation and heartburn. On Triglycerides bile acid biding resins effect is neutral or slightly increased.

Nicotinic acid lowers the total cholesterol levels by 25% and reduce the LDL levels by 10 to 25%. It increases HDL levels by 15 to 35%. Reduces triglycerides by 20 to 50%. Some side effects of using Nicotinic acid are Flushing, nausea, glucose, intolerance, and abnormal liver function test. Nicotinic acid has short life of 1 to 3 hours. The dissolution-controlled system was developed for Nicotinic acid by encapsulating with natural phenolic antioxidant polymer. This approach will get stable drug level in plasma with drug release being slow and with low fluctuations reduction. A release percentage of 97.74% was achieved using F4 and 97.23% using F5 for 12 hours [10]. Trails in the days where of non statin era showed that managing HDL cholesterol levels low

and triglyceride levels with niacin caused a reduction of 11% reduction in mortality [10]. Taking 325 mg of aspirin for about thirty minutes before the drug is induces will minimize the flushing [13]. One should take nicotinic acid with meals, so that occurrence of gastrointestinal upset is reduced. With sustained release of nicotinic acid hepatotoxic side effects are common than compared to regular formulations. With sustained release preparations hepatitis like syndrome, followed by weakness and appetite lack is formed [14].

Fibric acid analogs reduces the total cholesterol levels by 15% and reduce the LDL levels by 5 to 15%. It increases the HDL levels by 14% to 20%. And it reduces triglyceride by 20% to 50%. some side effects of using fibric acid analogs are nausea, skin rash.

Using HMG-CoA reductase Inhibitors reduces the total cholesterol levels by 15 to 30%. and it reduces the LDL cholesterol levels by 20 to 60%. It increases the HDL levels by 5 to 15%. It reduces triglyceride by 10 to 40%. Some side effects of using HMG-CoA reductase Inhibitors is myositis, myalgia and elevated hepatic transaminases [12].

Lipid benefits

- Lowers total cholesterol
- Lowers LDL-C cholesterol (specifically low-density LDL-C)
- Lowers triglycerides
- Lowers Lp(a)
- Raises HDL-C (specifically apolipoprotein A-1)

Non-lipid benefits

- Inhibits vascular inflammation/reduces reactive oxygen species
- Reduces oxygenation of LDL-C
- Reduces intravascular adhesion molecules and monocyte chemo-attractant protein-1 (atherogenesis initiators)
- May reduce the size and functional recovery time of acute stroke

Even though there are many benefits using NA, but its utilization can be hampered by many side effects. But another good part is all the side effects are reversible or minimized or can also be eliminated by appropriate dosing and administration. One of the most common side effects of NA is flushing. Flushing is caused by release of prostaglandin D2 and prostaglandin E2 from Langerhans cells in the skin and macrophages [16]. IN most of the people flushing can be minimized by changing dosing and administration. One another side effect is impaired liver function with ERNA therapy. Methyl group depletion in hepatocytes is one of the reasons, and the second one is in the liver metabolic amidization [16]. In the people who have diabetes using NA

therapy increased blood glucose levels. There are some other common small that are negligible. As per the guidelines, the patient risk factor for the coronary event happening for the patient in the future need to be discussed before starting the treatment. The other NA lipid therapies, ERNA is more best tolerated and is effective for the other fractions.

Most of the PG-ERNA studies have used one time/day dosing at bedtime with a small snack for two reasons: (1) convenience (and it can be given at the time a statin is supposed to be given) and (2) to match the time of peak hepatic lipid synthesis. The PG-ERNAs (Niaspan and Slo-Niacin) also have a somewhat higher rate of flushing than the WM-ERNA (Endur-Acin) so giving it in a near fasting state may also reduce the chance of early breakdown of the polygel capsule that might happen with the increased peristaltic activity of a meal. Critics of the bedtime NA dosing used in the AIM-HIGH and HPS-2 THRIVE studies, however, point out that dosing NA in a fasting or near fasting state causes a drop in non-esterified fatty acids. This in turn can inadvertently cause a transient drop in blood glucose triggering release of epinephrine and hepatic gluconeogenesis which might have caused some of the negative results found in those studies [17] [18].

Conclusion:

Dyslipidemia is one of the reasons for cardiovascular events and mortality. There are drugs that are proved to have shown effectiveness like statin and nicotinic acid. The standard care for all the patients who have high risk of CVD are statins, and ezetimibe is also now proved to have effectiveness on CV risk along with statins. Human genetics and clinical trials have supported the role of LDL in CVD and in supporting treatments to reduce LDL-C. Several researchers are researching on targets that lower the TRL through human genetics.

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