

## **Dyslipidemia**

By: Raymond Lengel, FNP, MSN, RN

Purpose: The purpose of this course is to provide an overview of abnormal cholesterol levels. The course will include an explanation of the different components of cholesterol, what levels are abnormal, risks of abnormal cholesterol and treatment options.

### **Objectives**

1. Define optimal cholesterol levels
2. List four diseases associated with abnormal cholesterol levels
3. Discuss three non-pharmacological options in the management of dyslipidemia
4. Discuss the use of medications in the management of dyslipidemia
5. Discuss how to monitor the patient with dyslipidemia

### **Introduction**

Hyperlipidemia – high cholesterol - is defined as a blood cholesterol reading of greater than 240 mg/dl (1). It is a major risk factor for a variety of cardiovascular diseases and other diseases.

A better term to use when describing abnormal cholesterol is dyslipidemia, which are abnormal blood lipid levels. This more accurately defines the problem as a lipid panel that has total cholesterol in the normal range but a low level of high-density lipoproteins (HDL) (also known as good cholesterol) is still considered abnormal even though the total cholesterol level is not high.

Approximately 17% of adult Americans have total cholesterol levels over 240 mg/dl (2). The average total cholesterol level for Americans is 203 mg/dl. Less

than 50% of the population has desirable lipid levels. Over sixty-five million American adults have lipid levels in the range that qualifies them for lifestyle changes, while 36 million have levels that indicate the need for drug therapy (3).

### **Who has dyslipidemia?**

Race affects cholesterol levels. White Americans have the highest rate of dyslipidemia followed by non-Hispanic blacks and Mexican Americans.

Approximately 17% of white Americans have high total cholesterol. Slightly over 16% of African American females have high cholesterol while 12.5% of African American men have high cholesterol (2). Among Mexican Americans, 17.6 % of men have high cholesterol, 12.7% of women have high cholesterol (2).

Age is the strongest risk for dyslipidemia. The older one becomes the more likely they are to be afflicted with dyslipidemia.

Men are more commonly afflicted with dyslipidemia before the age of 55 and men and women are more evenly affected after the age of 55. Estrogen has a positive effect on overall cholesterol levels. Despite this, estrogen replacement therapy is not recommended in the management of cholesterol and cardiovascular disease in post-menopausal women because of the increased risk coronary events and some cancers (4).

### **Consequences**

Dyslipidemia can lead to many medical problems including coronary heart disease, cerebrovascular disease and peripheral artery disease. There is a strong relationship between elevated LDL levels and cardiovascular mortality and cardiovascular event rates.

Coronary heart disease (CHD) is the main type of heart disease and it was responsible for 445,687 deaths in 2005 (5). Coronary heart disease (CHD) is a blockage of the arteries that supply blood to the heart. Lipids, low-density lipoproteins (LDL) being the main fat involved in this process, accumulate in the lining of the blood vessel wall. It is believed that atherosclerosis begins when the endothelium is injured. The injured endothelium is susceptible to the buildup of fats in the coronary artery (3). The LDL enters the vessel wall and causes inflammation and plaques to form.

In addition to lipid accumulation, there is also a thickening or hardening of the arterial intima (the inner layer of the coronary artery). These changes lead to a reduction in blood flow to the areas distal to the blockages.

Some of the plaques remain stable; this means they are stuck to the side of the blood vessel wall and do not move. Many of the plaques continue to grow and gradually obstruct the vessel wall leading to the typical signs and symptoms of CHD. Some of the plaques break off and lodge in a smaller blood vessel downstream, which can result in a heart attack.

Plaques usually do not develop in isolation around the heart. If one is unfortunate enough to have plaques around the heart it is likely that plaques have developed in other areas of the body. Some other common areas of plaque development include the carotid arteries, which can lead to stroke and vessels of the legs, which can lead to peripheral vascular disease.

Cerebrovascular disease is strongly related to dyslipidemia. Ischemic stroke and transient ischemic attacks (TIAs) are the two major risks of dyslipidemia.

Research has shown that treatment of lipid levels significantly reduces the risk of ischemic stroke and TIAs.

Peripheral vascular disease is atherosclerosis of the extremities (usually the legs). It results in reduced blood flow that leads to tissue and nerve damage. It is strongly related to dyslipidemia.

### **Lipid Panel**

A standard lipid panel consists of reporting on a total cholesterol level, a low density lipoprotein, high density lipoprotein and triglyceride level. It should be run after a 9-12 hour fast.

The total cholesterol is the sum of all the cholesterol in the blood. The higher the cholesterol, the higher the risk of heart disease. Ideal levels for total cholesterol are less than 200 mg/dl. High levels are considered 240 mg/dl.

The LDL particles carry the majority of cholesterol in the blood. High levels of LDL cholesterol can be from elevated LDL production or a decrease in the liver's uptake of the cholesterol. Diets that are high in cholesterol, saturated fat and trans fat reduce the LDL receptors in the liver. This slows the catabolism of LDL cholesterol. Generally speaking the lower the LDL cholesterol the better, but there is some evidence that extremely low levels may be associated with higher death rates (6). See table 1 for an interpretation of LDL levels.

### **Table : LDL Levels**

<b>LDL level reported in mg/dl</b>	<b>Interpretation</b>
Less than 100	Optimal
100-129	Near Optimal

130-159	Borderline High
160-189	High
Greater than 190	Very High

The HDL carries cholesterol in the blood from other parts of the body back to the liver. HDL keeps cholesterol from accumulating in the walls of the arteries. An ideal HDL cholesterol level is greater than 60 mg/dl and above this level is considered to be protective against heart disease. Levels less than 40 mg/dl is a risk factor for heart disease.

Triglycerides are another blood fat reported on the lipid panel. The role of triglycerides is less clear in the development of heart disease, but elevated levels are likely related to an increased cardiovascular risk. This number on the lipid panel is most variable from day to day. Extremely high levels increase the risk of pancreatitis. Data is sparse on the cardiovascular benefits of lowering triglycerides independent of LDL cholesterol. High levels of triglycerides are often associated with other abnormalities such as low HDL and high risk for diabetes which are associated with heart disease.

Optimal triglycerides are below 150 mg/dl. Borderline high triglyceride levels are 151 to 199 mg/dl and high triglycerides are 200-499 mg/dl. Very high levels of triglycerides are over 500 mg/dl.

**Some lipid panels report special lipids, including a small-dense LDL. This is a type of LDL cholesterol that is smaller and heavier than the typical LDL cholesterol and is a bigger risk. Small, dense LDL cholesterol can be inherited or can be increased by a diet high in carbohydrates or trans fats.**

**It is also highest in uncontrolled diabetes mellitus, and those with low HDL cholesterol or high triglycerides.**

### **Work up**

Abnormal cholesterol levels rarely results in symptoms. Long standing elevated cholesterol levels increase the risk of disease (especially cardiovascular disease) and needs to be identified.

After dyslipidemia is recognized it is important to detect those with clinical cardiovascular disease or situations that confer high risk of coronary heart disease. This includes peripheral artery disease, symptomatic carotid artery disease, abdominal aortic aneurysm and clinical coronary heart disease.

Next, the clinician should look for other major risk factors for coronary heart disease. These risk factors include: blood pressure greater than 140/90 mmHg or someone on antihypertensive medication, diabetes, cigarette smoking, family history of early cardiovascular disease (less than 55 in males and less than 65 in females who are a first degree relative), an HDL level below 40 mg/dl, and older age (men over 45 years and females over 55). An HDL level of more than 60 mg/dl acts as a negative risk factor (it erases a risk factor).

Assessing the 10-year risk of having a heart attack is a critical part of the work-up of abnormal cholesterol. A large database using years of information from the Framingham heart study should be used to evaluate risk for cardiovascular death and myocardial infarction based on cholesterol levels and other risk factors. The tool is available on-line and should be used in everyone 20 years-old and older.

This tool looks at age, gender, total cholesterol, HDL cholesterol, smoking status and systolic blood pressure.

To check out your or your patient's risk check out:

<http://hp2010.nhlbi.nih.net/atp/iii/calculator.asp>

This tool breaks risk down into three categories.

- Those with a greater than 20% risk of having a coronary event in the next ten years
- Those who have between a 10-20% chance
- Those who have less than a ten percent chance

Next, determine the LDL goal and how to achieve it. Using this tool and the guidelines the clinician will be able to determine if the patient needs lifestyle changes or medications or both. The intervention that will be required depends on the degree of dyslipidemia as well as other risk factors.

Individuals with coronary heart disease or coronary heart disease risk equivalents (diabetes, history of a stroke or documented peripheral artery disease) have a 10-year risk of greater than 20% and have an LDL goal of less than 100 mg/dl. Some high-risk individuals should attain a LDL of less than 70 mg/dl.

In this population, if the LDL level is below 130 mg/dl the use of therapeutic lifestyle changes alone can be tried. When levels rise above 130 mg/dl, strong consideration of pharmacological intervention should be considered. Levels below 130 mg/dl may consider drug therapy.

When there are two or more risk factors, but no coronary heart disease or equivalents than the LDL goal should be at least below 130 mg/dl. Lifestyle changes should be considered for anyone above 130 mg/dl.

When the 10-year risk is between 10-20% than drug therapy should be considered when LDL is greater than 130 mg/dl. When the 10-year risk is less than 10%, drug therapy should be considered when LDL is at or above 160 mg/dl.

Individuals with 0-1 risk factors have a target LDL level of less than 160 mg/dl. Lifestyle changes should be implemented when LDL is at or above 160 mg/dl. When LDL is greater than 190 mg/dl drug therapy should be strongly considered and it should be considered for some with LDL levels over 160 mg/dl.

Routine screening is the major method of identifying abnormal cholesterol levels. For the healthy population, routine screening should occur every five years starting at the age of 20 (7). Some organizations do not recommend testing until age 35 (8).

Recommendations vary but for those with established heart disease or multiple risk factors should have a lipid profile every 1-2 years.

The physical exam rarely gives hints to dyslipidemia. The most prevalent physical exam feature to predict abnormal cholesterol levels is abdominal obesity.

Tendon xanthomas can be seen on rare occasion. A xanthoma is a buildup of cholesterol rich material in the tendon (and sometimes other body parts) that is

yellowish. Xanthelasma (small yellow deposits around the eye) can also be seen at times, but do not always indicate dyslipidemia

## **Causes**

The most common cause of dyslipidemia is genetics, poor lifestyle factors or a combination of these two. Less commonly, there are some disease states that may lead to dyslipidemia. These include:

- Hypothyroidism
- Alcohol abuse
- Primary biliary cirrhosis
- Liver disease
- Kidney disease

In addition, some medications are related to dyslipidemia. These include:

- Thiazide diuretics
- Beta-blockers
- Highly active antiretroviral agents
- Anabolic steroids
- Glucocorticoids
- Progestins
- Estrogen

## **Treatment**

## **Medical Care**

The first step in the treatment of dyslipidemia is to determine cholesterol levels and determine the risk of the individual as described above. If LDL levels are elevated, this should be treated first.

While LDL is the primary target in the management of dyslipidemia, other numbers should be considered. If the LDL target is met and the triglycerides remain greater than 200 mg/dl then the non-HDL goal is determined. The non-HDL goal is the LDL cholesterol goal plus 30.

For high risk individuals, getting LDL levels below 70 mg/dl is reasonable when high dose statins do not have to be used. The use of high dose statins is associated with more side effects and the benefit may not be worth the risk (10).

Targeting low HDL, when LDL is elevated, is a matter of debate. Certain drugs are more effective in the management of low HDL such as niacin. There is data to show that the use of a statin in a patient with low HDL and high LDL reduces the risk of coronary heart disease (9). One study did show positive angiographic effect on the combination of niacin and low dose statin (10).

It is still a question of debate if targeting low HDL in those with high LDLs is necessary beyond the use of therapeutic lifestyle interventions and statins.

## **Monitoring levels**

Those individuals with abnormal cholesterol levels who are undergoing treatment with lifestyle changes should have their lipid profile rechecked in 6 to 12 weeks and those being treated with medications should have their lipid profile rechecked in 6-12 weeks (8, 9).

Those taking medications – statins - should have their liver enzymes tested 6-12 weeks after medications are started or if the dose is adjusted.

### **Lifestyle**

Lifestyle modifications include changes in nutrition, exercise and toxic habits.

The term therapeutic lifestyle change (TLC) is often used in cholesterol literature. This is a fancy way of saying: improve your diet, exercise, lose weight and don't smoke.

### **Dietary Changes**

The National Cholesterol Education Program (14) has made suggestions to reduce cholesterol levels. These guidelines apply to everyone over two years old. They include:

- Maintain a body mass index below 25
- Reduce total fat intake to less than 30% of energy intake
- Reduce saturated fat to less than 7% of energy intake
- Reduce polyunsaturated fat to less than 10% of energy intake
- Consume 10-15% of energy intake from of monounsaturated fat
- Keep cholesterol intake to less than 200 mg/dL
- Keep carbohydrate intake between 50-60% of energy intake
- Consume 10-25 grams of soluble fiber a day
- Minimize trans-fatty acids

- Add plant sterols/stanols to the diet (Benecol, Take Control).

Some evidence suggests that plant stanols may reduce LDL levels by 10-15 percent (8).

### **Other Dietary Changes**

Flaxseeds have been shown to reduce total cholesterol. A recent study (11) showed that flaxseed lignans and flaxseeds reduced total and LDL cholesterol. These studies showed no effect on HDL levels or triglyceride levels. While this investigation showed an improvement in some cholesterol parameters, it did not look at flaxseed effect on cardiovascular mortality.

Omega-3 fatty acids (which are also discussed under supplements) are helpful in the treatment of dyslipidemia. Many studies show that docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in fish and fish oil do reduce triglycerides as well as reduce the risk of heart attack, stroke, slightly reduces blood pressure, slows the accumulation of atherosclerotic plaques, reduces some arrhythmias, and lowers death rates (12, 13).

The strongest evidence for the beneficial effects of omega-3 fatty acids is lowering triglycerides. Fish oil supplements may also slightly improve HDL cholesterol. There is some evidence that fish oil may improve C - reactive protein levels (CRP). CRP is a marker of inflammation that is linked to cardiovascular disease (15).

Fish and fish oils need to be used with some caution. High levels can increase the risk of bleeding. Some species of fish contain high levels of methylmercury which may cause neurotoxicity.

### **Other Foods and Food Products**

Some evidence suggests that cranberries lower LDL cholesterol. A double blind study showed that a 12.1 % reduction in LDL was noted on those who were treated with a cranberry extract. This study was done on diabetics (16). It is unknown how cranberries lower LDL cholesterol. Cranberries contain high levels of flavonoids, which have antioxidant effects and may improve cholesterol. In theory, cranberries may inhibit LDL oxidation and reduce inflammation, but research has not demonstrated this (17).

Garlic has shown some positive effects on cardiovascular health. It may reduce blood pressure, reduce platelet aggregation and enhance fibrinolytic activity (18). A reduction in total cholesterol and LDL cholesterol is another benefit. Most evidence for this effect is in the short term (less than 12 weeks). More research is needed in this area to fully understand the role of garlic in the treatment of cholesterol. Specific questions that need to be addressed include:

- What is the long-term effect of garlic on cholesterol?
- What is the role of garlic on HDL and triglycerides?

## **Exercise**

Exercise has many beneficial effects on lipid levels. It increases HDL levels and lowers triglyceride levels. Regular aerobic exercise has been shown to raise HDL levels up to 5% and can lower triglycerides by 30-40% (8, 9).

Exercise does not directly affect LDL levels, but it may result in weight loss that may indirectly lower LDL levels.

## **Toxins**

Smoking adversely affects cholesterol levels. Stopping smoking may raise HDL cholesterol up to 10% (19).

Moderate use of alcohol can positively affect lipid levels. Those individuals who drink alcohol moderately, which is defined as 0-1 drinks per day in women and 1-2 drinks per day in men, may raise HDL cholesterol up to 12% (20). Heavy drinking can adversely affect cholesterol as well as cause many other health problems.

## **Medications**

The statins (also known as the HMG-CoA reductase inhibitors) have changed the way dyslipidemia is managed. This class of drug is highly effective, safe and associated with minimal side effects.

Statins inhibit the HMG-CoA enzyme, which is the enzyme that catalyzes the rate-limiting step in making cholesterol. It therefore lowers the amount of cholesterol that the body makes.

This class of drug has much data that suggests it can reduce rates of heart disease, heart disease death and total death rates. This class is most effective at lowering LDL levels, but can affect all cholesterol parameters.

Statins are generally the first drug added when LDL levels are elevated. Therapeutic lifestyle changes should be continued when statin therapy is started.

Statins have different degrees of effectiveness. The most potent drug in regard to lowering LDL levels is rosuvastatin (45-63% reduction in LDL) followed by atorvastatin (39-60%), simvastatin (38-47%), lovastatin (24-42%), fluvastatin (22-36%) and pravastatin (22-34%) (8, 9).

While most individuals are able to take statins, some groups of patients should not use statins. These include those with an allergy to statin drugs, those with active liver disease, those who consume high levels of alcohol or pregnant women.

### **Treatment of Triglycerides and Low HDL Cholesterol**

The primary aim in the management of dyslipidemia is the treatment of elevated LDL cholesterol. When triglycerides are above 200 mg/dl, after the LDL goal is reached, the treatment of non-HDL cholesterol is targeting. This is calculated by taking total cholesterol and subtracting HDL cholesterol. The goal for non-HDL cholesterol is the same as the LDL goal plus 30. In the individual with CHD with a 10-year risk of 20% or more, the LDL goal is less than 100 mg/dl; the non-HDL goal is therefore less than 130 mg/dl.

Treatment of triglycerides first involves TLC. Specifically, weight loss and increasing physical activity are important in the management of elevated

triglycerides. Certain dietary changes are effective in the management of elevated triglycerides. These include limiting fats and sugars, limiting alcohol and weight loss.

Drug treatment to lower triglycerides may include the intensification of LDL lowering therapy or adding a fibrate, nicotinic acid or omega-3 fatty acids.

When the triglycerides are greater than 500 mg/dl, the primary goal is lowering triglycerides. This can be done with a very-low fat diet, weight loss, exercise, fibrates, nicotinic acid, omega-3 fatty acids or a combination of these methods.

Low HDL cholesterol is another secondary goal that should be focused on after LDL has reached goal. HDL can be raised with weight loss, stopping smoking, exercise, moderate alcohol consumption (1 drink per day in women and 1-2 drinks per day in men) nicotinic acid and fibrates.

## **The Medications**

### **Statins**

#### **Atorvastatin (Lipitor)**

**This drug is dosed between 10 and 80 mg in the adult. This is a popular anti-lipidemia agent and may lead to a 60% reduction in LDL cholesterol (8, 9). It may have interactions with triazole antifungal, CNS depressants or macrolide antibiotics.**

#### **Simvastatin (Zocor)**

Simvastatin is dosed at 5-40 mg per day Simvastatin reduces heart events in those with heart disease, high cholesterol and those with type 2 diabetes

mellitus. It may interact with rifampin, clofibrate, itraconazole, erythromycin, cyclosporine, niacin, warfarin and levothyroxine.

### **Rosuvastatin (Crestor)**

**Rosuvastatin is dosed from 5-40 mg per day and it should not be given with the triazole anti-fungals. Rosuvastatin is the most potent statin in regard to lowering LDL cholesterol.**

### **Pravastatin (Pravachol)**

Pravastatin is dosed 10-80 mg once a day and is typically dosed at night. It may interact with antiretroviral protease inhibitors, cyclosporine, erythromycin, clofibrate, gemfibrozil, fenofibrate, azole antifungal (e.g., fluconazole, itraconazole, ketoconazole), or antilipemic doses of niacin (vitamin B-3)

### **Side effects**

As a group statins carry similar side effects. Elevated liver enzymes, myopathy and rhabdomyolysis are three side effects that need to be considered in all patients on statins.

Statins at times increase liver enzymes. It is typically only a mild increase but significant elevations may occur. Elevated liver enzymes are not common with statin use, but liver enzymes need to be routinely monitored for. Typically liver enzymes are checked 6-12 weeks after starting statin therapy and then every 3-6 months. Persistent high levels may lead to permanent liver damage.

Certain groups of individuals are more commonly affected with elevated liver enzymes. Individuals who take other medications (e.g., gemfibrozil/niacin) The elevation of liver enzymes are six times more common in those on high dose

statin therapy (atorvastatin 80 mg) when compared to low dose statin therapy (atorvastatin 10 mg) (21).

Myopathy is a muscle disease that presents with muscle weakness, muscle pain, tenderness and impaired function due to the disease. The symptoms can range from mild discomfort to severe discomfort that impacts daily living.

Myopathy is the most common side effect of statin therapy. It can take a while for this side effect to show up. The average length of time it takes to appear is about 6 months after the initiation of statin therapy (22).

When statins are used alone the risk of myopathy is small but when certain drugs are added the risk increases. Niacin, fibrates, imidazoles, macrolides and protease inhibitors may increase the risk of myopathy. Patients who develop myalgias or muscle weakness should have their creatinine kinase levels checked.

Treatment of myopathy may include lowering the statin dose, switching the medication or trying a different class of medication to manage cholesterol. The addition of ezetimibe to a statin may allow a lower dose of the statin and may resolve the myopathy.

Another strategy that has been proposed includes the use of supplemental coenzyme Q10. Statins are known to reduce the production of coenzyme Q10. Theoretically it is a helpful intervention, but little evidence demonstrates its effectiveness.

Rhabdomyolysis is a rare life threatening condition that can occur with the use of statin drugs. Certain conditions, such as chronic renal failure and hepatic

cirrhosis, increase the risk of this condition. When certain drugs are combined there is an increased risk. Common drugs that pose a risk when combined with statins include: fibrates, verapamil, amiodarone, erythromycin and cyclosporin.

Rhabdomyolysis may lead to kidney failure, liver failure and even death.

### **Cholesterol Absorption Inhibitors**

There is only one drug in this class – Ezetimibe (Zetia). This drug stops the absorption of cholesterol at the intestine. It lowers LDL levels by 12-19 percent, but some individuals may have a reduction of up to 40% (8, 9),

This drug is dosed 10 mg once a day. This drug comes in a combination product called Vytorin. This is the combination of ezetimibe plus simvastatin. This combination product can lower LDL levels 45-60% (8, 9).

Ezetimibe can interact with cholestyramine, fenofibrate, gemfibrozil and cyclosporine. It is category C in pregnancy with some fetal risk shown in animal studies. It should be used cautiously in those with renal insufficiency, those with liver dysfunction and those who drink large amounts of alcohol.

### **Niacin**

Niacin is highly effective at raising HDL cholesterol and can lower triglycerides. It is not as good at lowering LDL cholesterol. This drug is sometimes combined with statin drugs to optimize cholesterol levels.

Major side effects include flushing, itching and rash. To reduce the risk of side effects the dose should be started low and titrated upwards. An aspirin can be taken 30-60 minutes prior to taking the dose. Other recommendations include: taking niacin with a small, low-fat snack, avoiding hot or spicy foods and not

taking a hot shower around the time of taking the medicine. Diphenhydramine can be used to reduce the severity of an attack.

Niacin can bring on a gout attack and should not be used by those with a history of gout. It may increase insulin resistance and should be used with caution in those with diabetes.

Niacin should also not be used in those with active liver disease, excessive alcohol consumption, or peptic ulcer disease.

It should be used extremely cautiously in doses above the RDA (which is needed for lipid control) in pregnant women – it is category C.

The dose needed to improve dyslipidemia is 1-2 grams per day. Because of side effects the dose is often titrated up by 500 mg every 30 days. Niacin can be given as a prescription (Niaspan or combined with statins) or as an over-the-counter product.

### **Fibrates**

Two popular fibrates are gemfibrozil (Lopid) and fenofibrate (Tricor). These agents are used for triglyceride lowering. They are not as effective as statins for pure LDL lowering, but fenofibrate is more effective at lowering LDL than older agents.

Fenofibrate is beneficial in those with mixed dyslipidemia especially in those with type 2 diabetes. There may be some stabilization of atherosclerosis when compared to placebo (9).

Gemfibrozil was shown to reduce triglycerides about 30% and raise HDL about 6% in one study (9).

Fenofibrate is dosed 145 – 200 mg per day with meals. When there is renal insufficiency the dose is lowered.

When this drug is combined with the statins there is an increased risk of rhabdomyolysis and myoglobinuria (which can lead to renal failure).

**It should not be used in those with liver, kidney or gallbladder disease. It should also not be used by those who are breastfeeding. It is category C in pregnancy – use with extreme caution.**

Any muscle tenderness or weakness should be evaluated with a lab draw for creatinine kinase level and kidney function tests.

Gemfibrozil (Lopid) is used to lower serum triglyceride levels (9). It may slightly increase HDL cholesterol. This drug is dosed 600 mg, given twice a day 30 minutes before meals. There is a higher risk of rhabdomyolysis with this drug than fenofibrate. It should not routinely be used in combination with statins. It also may potentiate warfarin and other blood thinners. It should not be used in those with gallbladder, kidney or liver disease. It is pregnancy category C. The drug should be stopped if there is no effect after 3 months. Liver function tests need to be monitored.

### **Bile Acid Sequestrants**

Bile acid sequestrants (BAS) are used in those who need to lower LDL in addition to statin therapy. These drugs work by stopping the enterohepatic reuptake of intestinal bile salts.

BAS can also be used in those who are intolerant of statins and need to lower LDL levels. They are also useful in pediatric patients. These drugs do slow the progression of atherosclerosis (9).

**Cholestyramine (Questran, Questran Light) is dosed four grams given once or twice a day. The maximum dose is 24 grams in 24 hours. This drug interacts with thyroid hormone, non-steroidal anti-inflammatory drugs, warfarin, niacin, amiodarone, digitalis, phenytoin, and hydrocortisone. It is pregnancy category C.**

**Colesevelam (WelChol) is a newer agent that is better tolerated. As a single agent it can lower LDL by 15-18% (9). It does not lower triglycerides and minimally affects HDL levels. It is dosed as 6 tablets once or divided twice a day. It has few interactions, but may interact with verapamil SR. It should not be used in those with a complete bowel or biliary obstruction. It is pregnancy category B. It should be used cautiously in those with dysphagia, after major GI surgery or in those with gastrointestinal motility disorders.**

## **Diabetics**

Diabetes mellitus is considered a cardiovascular equivalent and has the same goals for LDL (<100 mg/dL, or, <70 mg/dL) as those with established coronary heart disease.

Those who have diabetes type II are more likely to have a combination of LDL elevations, low HDL and triglyceride elevation. The use of statins are still the primary option in the management of disease. Some experts add other agents

such as fibrates or niacin to target triglycerides. The addition of other medications increase the risk of adverse events such as elevation in liver enzymes and rhabdomyolysis.

The addition of the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can be considered to lower triglyceride in this population. To lower triglycerides the optimal dose is three grams per day.

### **Postmenopausal women**

The risk of cardiovascular disease in women becomes equal to men after menopause. This suggests that estrogen is associated with some protection to the heart partly through its improvement in lipid parameters. Recent research does not support the use of estrogen therapy for cardio protection. The use of estrogen actually increases the risk of adverse events (23).

The use of statins is recommended for the management of abnormal lipid levels in postmenopausal women instead for estrogen.

## **Supplements**

**A few supplements are available for the management of elevated lipid levels. The use of long-chain omega-3 polyunsaturated fatty acids have some positive effects on the cardiovascular system. The benefits of omega-3 fatty acids include: reduced risk of arrhythmias, reduced rate of atherosclerotic plaques, reduced platelet aggregation, lower triglycerides and lower blood pressure. They are generally considered safe for adults in doses up to 3 grams/day.**

Omega-3 fatty acids are found in fish, some plant/nut oils and some supplements. Fish oil has both docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), while some nuts and vegetable oils (olive, flaxseed, canola, and soybean) have alpha-linolenic acid (ALA). DHA and EPA are most beneficial to cardiovascular health. Alpha-linolenic acid may have similar benefits, but research has not proven the benefits are as pronounced.

The American Heart Association recommends that patients without heart disease eat a variety of fatty fish at least twice a week and add oils that are high in alpha-linolenic acids. Those with heart disease should consume one gram of EPA/DHA each day. To lower triglycerides it is necessary to consume two to four grams of EPA and DHA each day. This amount requires the use of supplements (24). DHA and EPA reduce triglycerides up to 20-30 % (13).

Risks are increased as the dose is increased. When over 3 grams a day are taken the risk of bleeding is increased. It may also lead to vitamin E deficiency if high doses are taken for long periods of time (15).

Red yeast rice is another supplement that helps control dyslipidemia. It has its most profound effect on LDL cholesterol (25).

Short-term studies show effectiveness. Similar side effects are noted with this product when compared to statins. It can increase liver enzymes and possibly cause myopathy and rhabdomyolysis. Long-term use has not been studied.

One study looked at 83 patients and it showed that red yeast rice lowered LDL cholesterol about 20% over 12 weeks. It also lowered triglycerides 7%, but had no effect on HDL cholesterol (25).

A more recent study showed similar benefits. Over a 12 week period LDL cholesterol was reduced 27.3 percent and at 24 weeks it was 21.3 percent lower. No differences were noted in HDL or triglyceride levels in this study (26)

Red rice yeast contains a substance that inhibits the HMG-CoA enzyme. It should not be used in pregnant women.

Interestingly, in one study, there was no difference in reports of body pain, liver enzyme elevation and creatinine phosphokinase levels between those on placebo and those on red rice yeast (26). None-the-less, there are case reports of liver damage, rhabdomyolysis and significant drug interactions with the use of red yeast rice. Caution must be used with this supplement.

Despite its effect on cholesterol, red rice yeast does not have as much evidence as statins in its ability to lower cardiovascular events. Although, one study showed that red rice yeast reduced the risk of heart attack by 62% and decreased cardiovascular death rates by 31% (27).

## **Summary**

Cardiovascular disease is a major health concern. Controlling risk factors for cardiovascular disease may significantly reduce its impact. Abnormal cholesterol is a prevalent risk factor that can be managed to reduce the risk of cardiovascular disease. The nurse's role in the management of dyslipidemia is to act as educator. To do this effectively the nurse needs to understand dyslipidemia including how to read and interpret a lipid panel and understand lifestyle interventions that can have a positive effect on lipid levels. In addition, they need to understand common drugs used in the management of dyslipidemia including side effects and how to monitor them.

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