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Combating Dyslipidemia

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Approved for 1.0 CE unit by the Canadian Council on Continuing Education in Pharmacy. File #1065-2009-451-P-T. Not valid for CE credits after November 25, 2012.

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Learning Objectives:

Upon completion of this lesson, the pharmacy technician will:

1. Understand the difference between good and bad cholesterol
2. Describe nonpharmacologic ways patients can improve their cholesterol levels
3. Understand categories of medications used to treat dyslipidemia
4. Explain the various ways a pharmacy technician can help patients manage their dyslipidemia

Introduction

Dyslipidemia, or cholesterol disorder, is one the many risk factors—along with hypertension, diabetes, smoking and obesity—that increases the risk of cardiovascular disease (CVD). CVD includes heart disease, diseases of the blood vessels and stroke. CVD is the leading cause of mortality and morbidity in Canadians and despite its prevalence, the impact of the disease is still not fully appreciated.[1] In 2004, CVD accounted for 32% of all deaths in Canada, and it is estimated that every seven minutes a Canadian dies of heart disease or stroke.[2] About 40% of Canadians have dyslipidemia, and as many as 10 million Canadian adults have not reached their recommended cholesterol target levels.[2] Keeping cholesterol under control reduces the risk of heart disease and stroke. Studies have shown that a 1 mmol/L reduction in low-density cholesterol can decrease heart disease risk by 25%.[1] Both proactive prevention and treatment of dyslipidemia are required to maximize the health of Canadians and prevent the complications associated with this chronic disorder.

This lesson will provide an overview of "good and bad" cholesterol, prevention of CVD as it relates to cholesterol, risk factors, and aspects of nonpharmacological and pharmacological treatments.

What is dyslipidemia

Dyslipidemia is an asymptomatic disease that generally results from elevated blood cholesterol levels. Cholesterol, triglycerides and phospholipids are the major lipids found in the body. They are carried in the blood as complexes of lipids and proteins, known as lipoproteins. The various types of lipoproteins are based on their different densities, and they include low-density (LDL), high-density (HDL) and very-low-density lipoproteins (VLDLs). VLDL is carried in the blood as triglycerides. Each atherogenic lipoprotein particle also contains a molecule called apolipoprotein B (apoB). The blood concentration of apoB reflects the total number of these lipoprotein particles. Recent studies have found that apoB is a better marker of the risk of vascular disease than LDL.[1,3]

Dyslipidemia can present as elevated cholesterol, LDL or triglycerides, low HDL or a combination of these abnormalities. HDL is considered the "good" cholesterol because it transports extra cholesterol from the blood to the liver where it is then removed in the bile. Some experts have found that HDL may remove the cholesterol found in arterial plaques. There is evidence that HDL protects against the development of atherosclerosis

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(buildup of plaque in the artery walls, causing arterial narrowing) and that low HDL increases the risk for CVD.[3] LDL on the other hand, is considered "bad" cholesterol because this lipoprotein carries around most of the body's cholesterol, thus contributing to high cholesterol levels found in the blood. High levels of LDL promote the storage of cholesterol in the cells and result in atherosclerosis. Triglycerides are a common type of fat in the body and are linked to low levels of HDL, excess body weight and poorly controlled diabetes.[2,4]

Most patients with dyslipidemia remain asymptomatic for many years before their disease becomes clinically evident. There are several risks factors associated with dyslipidemia that together additively increase the risk for developing CVD (see Table 1). Primary (genetic) and secondary causes (i.e., low thyroid, pregnancy, lupus, kidney disease, beta-blockers, steroids, estrogens) are also involved in the development of dyslipidemia.

TABLE 1 – Major risk factors[1,9]

- Diabetes
- Hypertension (≥140/90)
- Smoking
- Low HDL ≤1
- Family history: 1st degree relative who developed coronary artery disease at an early age (Age: men <55, women <65)
- Age (men ≥45, women ≥55)
- Obesity
- Inflammatory biomarkers

Dyslipidemia is diagnosed when a patient is above their target cholesterol level, based on individual assessment for their risks of developing heart disease. It is recommended that all men over the age of 40 and women who are postmenopausal and/or 50 years or older should have their cholesterol measured every one to three years.[1] In addition, adults who have additional risk factors such as diabetes, smoking, hypertension, family history of premature heart disease, kidney disease, lupus, obesity, use of anti-retroviral medications and/or erectile dysfunction should be screened at any age.[1] The most well-known cardiovascular risk assessment tool is the Framingham Risk Score. This score takes into account risk factors, such as age, sex, blood pressure, smoking and presence of diabetes, to provide an estimate of a patient's 10-year risk of experiencing a nonfatal heart attack or cardiac death. Based on this score, patients are divided into high-, moderate- and low-risk categories, which have corresponding, different treatment targets[1] (see Table 2). Identifying patients who may be at risk for dyslipidemia and helping them understand the importance of measuring their cholesterol levels will empower them to work towards preventing CVD to better manage their health.

Nonpharmacological management

Implementing lifestyle modifications is the initial step in attaining healthy cholesterol levels for patients in the low and intermediate Framingham Risk Score categories. Patients should be advised to reduce dietary fat intake to 20-35% of their daily calories; this includes limiting the intake of saturated fats and choosing healthier fats such as polyunsaturated fats (e.g., omega-3 and -6 fatty acids) and monounsaturated fats. Polyunsaturated and monounsaturated fats are found in vegetable oils, nonhydrogenated margarines, nuts and fish, whereas saturated fats are found in red meat and high-fat dairy products. The fats to avoid are trans-fats, which are known to raise LDL and lower HDL. These are found in foods made with shortening or partially hydrogenated vegetable oil, hard margarines, fast foods and ready-prepared foods. Consuming a diet that includes plenty of fruit, vegetables and whole grains is ideal.[2]

A program that includes physical activity for at least 30 minutes a day, most days of the week, can lower cholesterol levels. Preventing obesity by maintaining a waist circumference of less than 94 cm for men and less than 80 cm for women, and striving for a healthy weight with a body mass index of less than 25 kg/m^2 is recommended. Low-fat diets are not sufficient in maintaining weight loss; rather one should also focus on reducing the intake of refined carbohydrates, which are found in processed white flour foods, crackers and rice, as this will help to achieve an optimal distribution of body fat. Limiting excessive alcohol intake and lastly, refraining from smoking is beneficial because smoking both decreases HDL and increases LDL.[1,2]

Pharmacological management — prescription agents

Although lifestyle modifications are beneficial, more often than not patients will require pharmacologic therapy to achieve their lipid targets. All patients in the moderate- to high-risk categories who have a calculated 10-year risk of coronary artery disease (CAD)-related death or nonfatal heart attack of at least 10-20% should start treatment (see Table 2). Patients in the low-risk category with a calculated Framingham risk score of less than 10% may be considered for treatment and managed according to the physician's clinical judgment. However, the presence of additional risk factors, such as family history of early CAD, abdominal obesity or borderline high blood sugars, may necessitate pharmacologic therapy in low-risk category patients.[1]

The choice of lipid-lowering agents is based on the severity of the LDL, HDL or triglyceride abnormalities measured in the blood. Patients who have a predominantly high LDL will be treated with a different agent compared to patients who present only with high triglycerides or very low HDL.

A variety of medications can be used to manage dyslipidemia. These include the

TABLE 2 – Lipid targets[1]

RISK LEVEL	PRIMARY TREATMENT TARGET
HIGH (10yr CAD risk ≥**20%**) *[ALL patients with coronary artery, cerebrovascular or peripheral arterial disease or chronic renal disease and most adults with diabetes]*	LDL<2.0 or ≥ 50% ↓LDL apoB<0.80g/L
MODERATE (10yr CAD risk **10-19%**)	LDL<2.0 or ≥ 50% ↓LDL apoB<0.80g/L
LOW (10yr CAD risk **<10%**)	≥ 50% ↓LDL

CAD = coronary artery disease; LDL = low density lipoprotein; HDL = high density lipoprotein; apoB = Apolipoprotein B

TABLE 3 – Drug therapies for dyslipidemia[7,9]

	Mechanism of Action	Therapeutic Effect
STATIN		
atorvastatin **fluvastatin** **lovastatin** **pravastatin** **rosuvastatin** **simvastatin**	Inhibits HMG-CoA reductase, which decreases production of cholesterol in the liver.	LDL ↓ 20-65% HDL ↑ 5-15% TG ↓ 7-30%
FIBRATES		
bezafibrate **fenofibrate** **gemfibrozil**	Stimulates the activity of a liver enzyme to increase the clearance of LDL from the blood.	LDL ↓ 5-20% HDL ↑ 10-20% TG ↓ 20-50 %
RESINS/BILE ACID SEQUESTRANTS		
cholestyramine **colestipol**	Binds bile acid cholesterol and prevents absorption of cholesterol from the gut.	LDL ↓ 15-30% HDL ↑ 3-5% TG ↑ 11-28%
OTHER		
ezetimibe	A cholesterol absorption inhibitor, stops the passage of dietary and biliary cholesterol across the intestine.	LDL ↓ 10-20% HDL ↑ 0-6% TG ↓ 7-15%
niacin	Inhibits VLDL production in the liver which reduces LDL production, also increases the clearance of LDL from the blood.	LDL ↓ 15-25% HDL ↑ 15-35% TG ↓ 30-60 %

LDL: low density lipoprotein HDL: high density lipoprotein TG: Triglyceride

statins, fibrates, resins, and other agents such as ezetimibe and niacin (see Table 3). Each drug class works via a different mechanism and varies in the degree of lowering specific lipoproteins. Depending on the severity of the lipid abnormality, patients may require drugs from more than one drug class. Lowering levels of LDL directly decreases CAD event rates, and this is why LDL is the primary target for treatment.[5]

Statins:

Statins are mainstay therapies in the treatment of dyslipidemia. They are the most potent lipid-lowering agent—effectively lowering LDL, modestly lowering triglycerides and increasing HDL. Various clinical trials have shown that statins can reduce the risk of heart attack or death in patients who have a high risk of developing heart disease or who have CAD. More recent evidence has found that starting statin therapy in relatively healthy patients at low to moderate risk may reduce future cardiovascular events.[6] Statins are very well tolerated; however, they have the potential to interact with some medications and foods. In particular, atorvastatin, simvastatin and lovastatin are known to interact with grapefruit juice and therefore patients on those particular statins should be advised to avoid grapefruit juice. The combination of these statins and grapefruit juice will increase the risk of myopathy, a muscle disease that causes weakness, or rarely rhabdomyolysis, a condition where the muscle breaks down (see Table 4).

Combination therapy:

In patients who do not respond to statin monotherapy, combination therapy with other lipid-lowering agents may be required; however, this increases the risk for adverse drug interactions and side effects. Thus, these patients need to be monitored closely. Patients who present with high triglyceride levels despite being on a statin usually respond well to the addition of niacin or fibrate therapy.[1]

Fibrates:

These agents are very effective in lowering triglycerides, but have a modest effect in lowering LDL and increasing HDL.[4] Gemfibrozil is associated with a higher risk of muscle toxicity when used with statins and therefore concurrent use of these two agents should be avoided.[1,4]

Niacin:

Niacin, also known as vitamin B3 or nicotinic acid, has the most potent effect on increasing HDL. It is important to note that niacin comes in four different formulations: immediate release; extended release; long-acting/sustained /controlled release; and "flush-free" niacin. Niaspan and the new Niaspan film-coated tablets are available by prescription, other sustained-release products are Schedule II and immediate-release products are unscheduled. Most formulations are effective in lowering cholesterol except the flush-free formulation, as it contains very little active niacin. High doses of niacin should be used cautiously in patients with diabetes because they can increase blood glucose levels. The most common side effects of niacin are flushing, itching and dry skin; taking this drug with meals, pretreating with acetylsalicylic acid (ASA) and slowly increasing the dose will minimize these adverse effects.[1]

Resins:

Resins (e.g., cholestyramine, colestipol) are other agents that lower LDL, but to a lesser degree than statins. These drugs can be difficult to tolerate due to their gastrointestinal side effects resulting in poor compliance. Through pharmacists' interventions and proper patient education, adherence rates can improve. Resins can interact with medications and impair their absorption. This can be avoided by separating the administration times of resins and other drugs by at least four to six hours.[4]

Cholesterol absorption inhibitors:

Ezetimibe is often combined with a statin to further reduce LDL by an additional 10-20%, particularly in patients who have not achieved their target LDL levels.[6,7]

Nonprescription agents

Several nonprescription agents are used to manage dyslipidemia. Fish oils (e.g., salmon oil), and compounds containing omega-3 fatty acids may lower triglycerides and minimally increase HDL. Epidemiological studies have found that diets high in fish may

TABLE 4 – Significant drug interactions with lipid-lowering agents[7,9]

DRUG INTERACTIONS	
LIPID-LOWERING AGENTS Lovastatin, Atorvastatin, Simvastatin	**STATINS** • toxicity when used with amiodarone, clarithromycin, erythromycin, gemfibrozil, grapefruit juice, verapamil
All statins	• efficacy when used with cholestyramine, colestipol
All fibrates	**FIBRATES** • toxicity when used with statins • efficacy when used with cholestyramine, colestipol • effect of pioglitazone, repaglinide, rosiglitazone, sulfonylureas and warfarin
Cholestyramine/ Colestipol	**RESINS** • absorption of various drugs and vitamins

NOTE: Pharmacy technicians should alert the pharmacist if a patient is receiving or about to start any above combination of medication.

decrease CVD. Garlic, flaxseed, lecithin and grape seed are other alternative agents that minimally lower cholesterol; however, their effects are not consistent. In general, these agents are not recommended to be used alone to manage dyslipidemia, as there is little evidence available to support their effectiveness.[7] For patients who have moderately high triglyceride levels, the addition of salmon oil to statin therapy may be beneficial to further lower triglycerides and achieve targets. Consultation with the pharmacist is important when selecting alternative nonprescription medications such as salmon oil, because the pharmacist can ensure that a safe and appropriate agent is chosen, one with minimal drug interactions and side effects. Patients who also have low HDL levels can significantly increase HDL with lifestyle modifications such as smoking cessation and increased exercise, or combining either niacin or fibrates with a statin.

Patient adherence

Dyslipidemia is a chronic disorder necessitating life-long medication use. Since it is an asymptomatic condition, adherence rates to cholesterol-lowering drugs are poor. Pharmacy technicians and pharmacists are easily accessible and well placed to encourage medication adherence and help in the provision of preventive cardiovascular care.[8] Pharmacy staff can work with the patient and their physicians to simplify medication regimens by suggesting combination products. However, patients should first be titrated on the individual components before switching to a combination product. Other methods that can enhance patient adherence include encouraging patients to associate medication-taking with a specific activity (e.g., dinner) to help them remember to take it, reminding patients of their next refill dates, providing education on how to lessen drug side effects and preparing medications in blister packs. Encouraging patients to regularly check their cholesterol levels is a necessary step to ensuring that they achieve their cholesterol targets. More importantly, knowing their own cholesterol levels will empower patients to use this knowledge to play a more active role when working with their pharmacist and physician to achieve their cholesterol targets and prevent future cardiovascular events.

Role of the Pharmacy Technician

The pharmacy technician plays an important role in assisting the pharmacist to help patients better manage dyslipidemia. Some examples of how pharmacy technicians can work within this collaborative environment include:

- Identifying patients who are late in getting their lipid medications refilled
- Reminding patients who have no further refills to see their doctors for a reassessment
- Detecting patients who are late for their refills, thus demonstrating non-adherence with their medications and alerting the pharmacist
- Noting any side effects that patients mention, which may be related to their lipid medications, and letting the pharmacist know
- Supporting prevention of dyslipidemia by advocating good lifestyle choices, and ensuring that patient information pamphlets on weight loss, proper nutrition and exercise are well stocked in the pharmacy
- Encouraging interested patients to speak to the pharmacist about smoking cessation
- Making patients aware of online resources from the Heart and Stroke Foundation available at www.heartandstroke.com. This website contains comprehensive information, tools and support for patients living with CVD.

Dyslipidemia is a significant risk factor in the development of CVD, a disease that causes death and disability worldwide. The pharmacy technician can play a major role in encouraging patients to adhere both to lifestyle modifications and lipid-lowering medications in order to achieve the optimal benefit of cardiovascular risk reduction and protection.

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➤QUESTIONS

Please select the best answer for each question or answer online at www.pharmacygateway.ca for instant results.

1. Which statement is true?
a) CVD is the second leading cause of death in Canadians
b) Risk factors for CVD are additive
c) Symptoms of dyslipidemia are always evident early in the disease
d) Stress is a proven risk factor in the development of dyslipidemia
e) CVD only affects the heart

2. Which statement is true?
a) Genetic abnormalities and/or drugs can cause dyslipidemia
b) A 25-year-old woman with diabetes should have her cholesterol measured
c) Carol is a healthy 45-year-old non-smoker with no diabetes or hypertension. Her mom died of a heart attack at age 50 and her dad has diabetes, Carol should measure her cholesterol after age 50
d) b and c
e) a and b

3. Which statement(s) is (are) true regarding lipids?
a) HDL, LDL, triglycerides are types of lipoproteins
b) VLDL, HDL, LDL are types of lipoproteins
c) Triglyceride is a type of cholesterol
d) a and b are true
e) a, b and c are true

4. The Framingham Risk Score takes into account:
a) smoking status, diabetes, sex, height and weight
b) diabetes, smoking status, sex, age, blood pressure
c) blood pressure, ethnicity, sex, weight, smoking status
d) age, smoking status, alcohol consumption, weight, diabetes

5. Which statement(s) is (are) correct?
a) HDL is good cholesterol because it carries the body's cholesterol, promoting cholesterol storage cells
b) High LDL levels prevents the development of atherosclerosis
c) a and b
d) HDL> 1.0 is considered protective against atherosclerosis
e) all of the above

6. In which situation(s) would you alert the pharmacist regarding a patient's anti-lipid therapy?
a) A patient mentions that he takes rosuvastatin with grapefruit juice
b) On a patient's profile you notice that she has been started on atorvastatin and gemfibrozil
c) When filling Mrs. Jones' prescription for clarithromycin, you notice that is she is also on atorvastatin
d) b and c should be brought to the pharmacist's attention
e) There are no concerns

7. Regarding pharmacologic therapy, which statement is most correct?
a) Immediate release, extended-release and flush-free niacin are available as non-prescription drugs
b) Flush-free niacin is very effective in controlling cholesterol levels
c) Niacin is a form of vitamin B3
d) Immediate-release niacin causes less flushing than extended-release niacin
e) None of the above

8. What advice would best benefit a patient wanting to implement lifestyle modifications to manage their dyslipidemia?
a) Increase intake of saturated and polyunsaturated fats
b) Encourage intake of healthier fats like trans-fat and Omega-3,-6 fatty acids
c) Patient must abstain from all alcohol
d) All fats are created equal as long as fat intake is less than 20-35% of one's daily calories
e) Consume a diet low in saturated and trans fat

9. Which lifestyle change(s) can help manage cholesterol levels?
a) Limiting excessive alcohol intake
b) 30 to 60 minutes of moderate physical activity most days of the week
c) Smoking cessation
d) Healthy body weight
e) all of the above

10. Bile acid sequestrants
a) are the most effective agents to decrease LDL
b) inhibit the absorption of cholesterol from the gut
c) do not interact with any drugs
d) are very well tolerated with no side effects

11. Which statement(s) regarding statins are true?
a) Symptoms of mild muscle pain are common
b) Myopathy and rhabdomyolysis are very common side effects
c) Statins are the most effective agent for lowering LDL
d) all of the above
e) a and c

12. Which of the following is true of statins?
a) Atorvastatin is not known to interact with grapefruit juice
b) Increase clearance of LDL from the blood
c) Effect on HDL is modest
d) Can always be safely combined with any fibrate
e) none of the above

13. Which agent is least likely to decrease triglycerides?
a) Pravastatin
b) Cholestyramine
c) Ezetimibe
d) Niacin IR

14. Harry wants to purchase salmon oil so you offer to direct him to where such products are kept. Which of the following statements is true?
a) Every alternative and herbal medication is well regulated by the government in terms of its active ingredients and safety
b) Salmon oil, being a source of omega-6 fatty acid, decreases triglycerides and slows progression of atherosclerosis
c) Omega-3 and -6 are monounsaturated fats
d) Omega-3 fatty acids are found in fatty fish, such as sardines, salmon, mackerel

15. Treatment with anti-lipid agents can completely cure dyslipidemia
a) true
b) false

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