

Review Paper

Risk factors and management of Hyperlipidemia (Review)

Abstract

Hyperlipidemia involves abnormally elevated levels of any or all lipids and/or lipoproteins in the blood. Hyperlipidemia may basically be classified as either familial hyperlipidemia or acquired hyperlipidemia. There are two types of hyperlipidemia; modifiable and non-modifiable risk factors. Management of hyperlipidemia requires multi-team intervention include medical, nutritional and lifestyle modifications. Searching on the internet using the Google search engine was the main source of data as well as books. This review will try to draw a picture about hyperlipidemia; its risk factors and management.

Key Words: Hyperlipidemia, Risk factors, Management

Introduction

Hyperlipidemia, hyperlipoproteinemia, or hyperlipidemia involves abnormally elevated levels of any or all lipids and/or lipoproteins in the blood. It is the most common form of dyslipidaemia (which includes any abnormal lipid levels). The lipoprotein density and type of apolipoproteins it contains determines the fate of the particle and its influence on metabolism.⁽¹⁻²⁾ Hyperlipidemia is a heterogeneous group of disorders characterized by an excess of lipids in the bloodstream. These lipids include cholesterol, cholesterol esters, phospholipids, and triglycerides.⁽¹⁻⁴⁾ The intestine absorbs dietary fat and packages it into chylomicrons, which are transported to peripheral tissues through the blood. The enzyme lipoprotein lipase breaks down chylomicrons, and fatty acids enter muscle and adipose tissues. The chylomicron remnants are subsequently taken up by the liver to start the process of very-low-density lipoproteins (VLDLs) synthesis. The liver secretes VLDL, which undergo lipolysis by lipoprotein lipase to form Low Density Lipoprotein "LDLs". LDLs are then taken up by the liver and by the peripheral tissues. High Density Lipoprotein HDL is produced by the liver. Its function is to transport cholesterol from the body back to the liver. That is why it is called "good cholesterol" lipoprotein.^(1-3,5) Hyperlipidemia may basically be classified as either familial (primary) caused by specific genetic abnormalities, or acquired (secondary) when resulting from another underlying disorder that leads to alterations in plasma lipid and lipoprotein metabolism. Hyperlipidemia may be idiopathic, that is, without known cause. Hyperlipidemia is also classified according to

which types of lipids are elevated, that is hypercholesterolemia, hypertriglyceridemia or both in combined hyperlipidemia. Elevated levels of Lipoprotein (a) may also be classified as a form of hyperlipidemia.⁽²⁻⁶⁾ Acquired hyperlipidemia often mimics primary forms of hyperlipidemia and can have similar consequences. They may result in an increased risk of premature atherosclerosis or, when associated with marked hypertriglyceridemia, may lead to pancreatitis and other complications of the chylomicronemia syndrome.⁽⁷⁾ The most common causes of acquired hyperlipidemia are diabetes mellitus, use of drugs such as thiazide diuretics, beta blockers, and estrogens, hypothyroidism, renal failure, nephrotic syndrome, alcohol consumption, some rare endocrine disorders, and metabolic disorders. Treatment of the underlying condition, when possible or discontinuation of the offending drugs usually leads to an improvement in the hyperlipidemia.^(6,8) Another acquired cause of hyperlipidemia, although not always included in this category, is postprandial hyperlipidemia, a normal increase following ingestion of food.^(8, 9) The mean total cholesterol in 30 countries varied from 158 mg/dl in China-Beijing to 246 mg/dl in Luxemburg among men and from 162 mg/dl in China-Beijing to 246 mg/dl in United Kingdom (UK) among the women.⁽¹⁰⁾ Dyslipidemia covers the broad spectrum of lipid abnormalities. However, elevations of T-C and low density lipoprotein cholesterol (LDL-C) have received the most attention.^(8, 10, 11,12) An estimated 53% (105.3M) of United States (US) adults have lipid abnormalities: 27% (53.5M) have high LDL-C, 23% (46.4M) have low HDL-C, and 30% (58.9M) have high

TG. ⁽¹¹⁾ The prevalence of dyslipidemia among adults in the Kingdom Saudi Arabia KSA ranges from 20% to 44%. ⁽¹³⁾ In Iran, according to the report of Tehran Lipid Glucose Study which was held in the metropolitan city of Tehran among nearly half of Tehranian adults, mean T-C level was 210 mg/dl. ⁽¹⁴⁾ In China, the pooled prevalence estimates of hypercholesterolemia, hypertriglyceridemia, mixed hyperlipidemia (TC, TG), low levels of high-density lipoprotein cholesterol (HDL-C), and high levels of low-density lipoprotein cholesterol (LDL-C) are 10.1%, 17.7%, 5.1%, 11.0%, and 8.8% respectively. ⁽¹⁵⁾ Worldwide dyslipidaemia affects about 1 in every 3 women and 1 in every 8 men. ^(11,13,15) Studies have shown that health care for

dyslipidaemia exorbitant cost yearly. In the US \$12 to 18 billion dollar is used in dyslipidaemia direct healthcare costs each year. While in Saudi Arabia, with a population of 1,461,401 persons aged 50 years or more, 8768 would suffer dyslipidaemia and it consequence diseases yearly at a cost of \$1.14 billion, and also found that has an impact on the workforce and reduces the private country output. ^(3,11,14,16) All these reasons have made dyslipidaemia an important issue to review and worthwhile topic to study. The paper is aiming to review the risk factors, and management of hyperlipidemia.

Material and Method

Searching on the internet using the Google search engine was the main source of data. The keywords include risk factor, management of dyslipidaemia. The search has generated about 88 sources, of which 37 sources have actually used. These 37 articles were considered relevant because they answered the

aim and objective of the review. All included articles were written in English. The inclusive criteria included studies of epidemiology, risk factors, pathogenesis, diagnosis, prevention, and management. The study period has extended from first October 2016 to end of March 2017.

Discussion

Risk factors

Overproduction and defective clearance of the cholesterol, TG and LDL is the result of the mutations of single or multiple genes. This is called non modifiable Risk Factors. it is also known as primary causes. ^(9,11)

The primary disorders are the common dyslipidemia causes to the children, although it may not affect in the most cases of adult dyslipidemia.

Although unhealthy lifestyle choices are the main cause of hyperlipidemia, patient can also inherit it. Once a man reaches age 45 and a women reaches age 55, the risk naturally goes up due to age-related changes in the body. ^(13,15,17) With age, the heart muscle doesn't work as well as it once did. This can increase pressure on arteries. ^(18,19) For women it happens later, after they go through menopause and their cholesterol levels tend to rise. Although there is nothing people can do about age or genetic makeup, this does not mean the condition cannot be controlled. ^(10, 12, 20) Chronic diseases that make the cardiovascular system work harder can also cause high cholesterol levels. If the test

positive for high cholesterol and the cause is not obvious, the physician may look for an underlying disease. This includes kidney problems and liver disease, conditions that affect your thyroid, a malfunction of the pituitary gland, and diabetes. ^(16,17,20) In many cases, when these conditions are controlled, cholesterol levels improve. High blood sugar contributes to higher LDL cholesterol and lower HDL cholesterol. High blood sugar also damages the lining of the arteries. Other cholestatic liver diseases and primary biliary cirrhosis increase the risk of dislipidemia. Drugs like thiazides, retinoids, estrogens and glucocorticoids, among others also increase the risk of dislipidemia. ^(10, 12, 20,21) Unhealthy diet raises the risk for hyperlipidemia in two ways. First is what the diet is made up of. Eating high amounts fat and cholesterol contribute to higher lipid levels in the blood. In addition, consuming more calories leads to the excess calories being stored in the body as fat. ^(11,17,19) According to the National Cholesterol Education Program (NCEP), losing weight and eating healthy lowers the

bad cholesterol that gets stored in the body and raises the good kind of cholesterol that tends to be excreted from the body.^(19,21) Being active also tends to lower the bad cholesterol numbers and raise the good. In addition, physical inactivity can lead to weight gain. This is why physical inactivity is also considered a risk factor for hyperlipidemia.⁽²¹⁻

Global Risk Assessment

Identify risk factors is the first step in dyslipidaemia prevention.^(10, 19, 22) It recommends more frequent assessments for all patients with a family history of premature coronary artery diseases [CAD] (definite myocardial infarction [MI] or sudden death before age 55 years in father or other male first-degree relative, or before age 65 years in mother or other female first-degree relative). Moreover, it is necessary to have annual screening for all adult patients with diabetes mellitus for dyslipidaemia. In the absence of CAD risk factors, screen middle-aged persons for dyslipidaemia at least every 1 to 2 years.

Pathogenesis, Symptoms, and Diagnosis

Adiposopathy is promoted by unhealthy nutrition and a sedentary lifestyle in genetically and environmentally predisposed individuals. With impaired adipogenesis of peripheral, subcutaneous adipose tissue during positive caloric balance, existing fat cells may hypertrophy, circulating free fatty acids may increase, and lipids may be deposited in nonadipose tissue organs (e.g., liver, muscle, possibly pancreas) resulting in lipotoxicity.^(13,25,26) Adiposopathic endocrine and immune responses may be directly pathogenic to the cardiovascular system or otherwise interact with other body systems. If not mitigated by these other body organs, adiposopathy may indirectly cause or promote major atherosclerotic risk factors (type 2 diabetes mellitus, high blood pressure, or dyslipidemia).^(22,27) Adipocytes typically constitute the majority of adipose tissue cellular content. Fat-containing adipocytes constitute, by far, most of the adipose tissue volume. Adipose tissue's supporting framework contains "stromal vascular fraction" cells, which include mesenchymal cells, fibroblasts, preadipocytes, endothelial precursor cells, smooth muscle cells, blood cells, and immune cells. Adipose tissue-associated mesenchymal cells are especially

²³⁾ Cigarette smoking damages the walls of the blood vessels, making them likely to accumulate fatty deposits. Smoking may also lower your level of HDL.^(12, 13) The risk increases if the patient is a man with a waist circumference of at least (102 cm) or a woman with a waist circumference of at least (89 cm).⁽²¹⁾

^(15,23) Screening is used with children older than 2 years every 3 to 5 years if they have CAD risk factors or a family history of premature CAD or dyslipidaemia, are overweight or obese, have other elements of the insulin resistance syndrome, or have no available family history. On the other hand, screening should apply for adolescents older than 16 years every 5 years or more frequently if they have CAD risk factors, are overweight or obese, have other elements of the insulin resistance syndrome, or have a family history of premature CAD.⁽²⁴⁾

applicable to cardiovascular medicine because cardiovascular and adipose tissue cells share a common lineage.^(11,17,28-30) After fertilization of the ovum and mitotic divisions of the zygote, the subsequent pluripotent stem cells give rise to endoderm, ectoderm, and mesoderm. The mesoderm may differentiate into hematopoietic tissue, kidney, and sex organs, as well as mesenchymal stem cells. Mesenchymal stem cells may differentiate into skeletal myoblasts, osteoblasts, chondroblasts, tenoblasts, marrow stromal cells, neuron-like cells, and importantly, into cardiomyocytes, angiocytes, and adipocytes. Thus, adipose tissue is a rich, nonembryonic source of mesenchymal cells whose relative ease in accessibility and capacity for differentiating into heart and blood vessel cells have medical applications to CVD regenerative medicine, tissue engineering, and cell replacement therapies and represents a potential therapeutic modality to repair post-ischemic or infarcted heart tissue.^(22,23) Most patients are asymptomatic for many years prior to the appearance of physical findings. Physical findings can include corneal arcus of the eye and, tuberous xanthomas in the Achilles tendon, hands, feet, elbows, and/or knees. Symptoms of dyslipidemia can include

paresthesias, dyspnea, and confusion. Dyslipidemia does not have symptoms at all, but it can cause other symptomatic vascular disease, like coronary artery disease. Eyelid xanthelasma, tendinous xanthomas at the

Management of Dyslipidaemia

The main indication for dyslipidaemia treatment is prevention of atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes, stroke, transient ischemic attack, or peripheral arterial disease presumed caused by atherosclerosis. ⁽²⁶⁾

Treatment is indicated for all patients with ASCVD (secondary prevention) and for some without (primary prevention). ^(11,17,23,27)

Treatment options depend on the specific lipid abnormality, although different lipid abnormalities often coexist. ^(13,25,28) In some

patients, a single abnormality may require several therapies; in others, a single treatment may be adequate for several abnormalities.

Treatment should always include treatment of hypertension and diabetes, smoking cessation. ^(10, 24,25,29-31)

Treatment options to lower LDL cholesterol in all age groups include lifestyle changes (diet and exercise), drugs, dietary supplements, procedural interventions, and experimental therapies. ^(10, 14,25)

Many of these options are also effective for treating other lipid abnormalities. Dietary changes include decreasing intake of saturated fats and cholesterol; increasing the proportion of dietary fiber, and complex carbohydrates; and maintaining ideal body weight. ^(6, 21,29) Referral to a dietitian is often useful, especially for older people. Exercise lowers LDL cholesterol in some people and also helps maintain ideal body weight. Dietary changes and exercise should be used whenever feasible but using drug treatment for certain groups of patients after discussion of the risks and benefits of statin therapy. ^(10, 24,25)

For drug treatment in adults, American Heart Association [AHA] recommends treatment with a statin for 4 groups of patients, comprised of those with any of the clinical ASCVD, LDL cholesterol ≥ 190 mg/dL, age 40 to 75, with diabetes and LDL cholesterol 70 to 189 mg/dL, age 40 to 75, LDL cholesterol 70 to 189 mg/dL, and estimated 10-yr risk of ASCVD $\geq 7.5\%$. ^(10, 24,25,32)

Treatment of children is controversial; dietary changes may be difficult to implement, and no data suggest that lowering lipid levels in childhood effectively prevents heart disease in adulthood. Moreover, the safety and

elbow, knee tendons and Achilles and arcus cornea are caused by high levels of LDL. Acute pancreatitis is caused by high levels of TGs. ^(10, 24,25)

effectiveness of long-term lipid-lowering treatment are questionable. Nevertheless, the American Academy of Pediatrics (AAP) recommends treatment for some children who have elevated LDL cholesterol levels. ^(1, 14,15)

Children with heterozygous familial hypercholesterolemia should be treated beginning at age 10. Children with homozygous familial hypercholesterolemia require diet, medications, and often LDL apheresis to prevent premature death; treatment is begun when diagnosis is made. ⁽³¹⁾

For children, the AAP recommends dietary treatment for children with LDL cholesterol > 110 mg/dL (> 2.8 mmol/L). Drug therapy is recommended for children > 8 yr and with either of poor response to dietary therapy, LDL cholesterol ≥ 190 mg/dL (≥ 4.9 mmol/L), and no family history of premature cardiovascular disease, LDL cholesterol ≥ 160 mg/dL (> 4.13 mmol/L) and a family history of premature cardiovascular disease or ≥ 2 risk factors for premature cardiovascular disease, drugs used in children include many of the statins. ^(10, 24,33)

Children with familial hypercholesterolemia may require a second drug to achieve LDL cholesterol reduction of at least 50%. ⁽³³⁾ Although it is unclear whether elevated TGs independently contribute to cardiovascular disease, they are associated with multiple metabolic abnormalities that contribute to CAD (eg, diabetes, metabolic syndrome). Consensus is emerging that lowering elevated TGs is beneficial. No target goals exist, but levels < 150 mg/dL (< 1.7 mmol/L) are generally considered desirable. No guidelines specifically address treatment of elevated TGs in children. The overall treatment strategy is to first implement lifestyle changes, including exercise, weight loss, and avoidance of concentrated dietary sugar and alcohol. Intake of 2 to 4 servings/wk of marine fish high in omega-3 fatty acids may be effective, but the amount of omega-3 fatty acids is often lower than needed; supplements may be helpful. ^(10, 24,25,29,34)

In patients with diabetes, glucose levels should be tightly controlled. If these measures are ineffective, lipid-lowering drugs should be considered. Patients with very high TGs may need to begin

drug therapy at diagnosis to more quickly reduce the risk of acute pancreatitis.⁽³¹⁾ Fibrates reduce TGs by about 50%. They appear to stimulate endothelial LPL, leading to increased fatty acid oxidation in the liver and muscle and decreased hepatic VLDL synthesis. They also increase HDL by up to 20%. Fibrates can cause GI adverse effects, including dyspepsia, abdominal pain, and elevated liver enzymes. They uncommonly cause cholelithiasis. Fibrates may potentiate muscle toxicity when used with statins and potentiate the effects of warfarin.⁽³²⁾ Statins can be used in patients with TGs < 500 mg/dL (< 5.65 mmol/L) if LDL cholesterol elevations are also present; statins may reduce both LDL cholesterol and TGs through reduction of VLDL. If only TGs are elevated, fibrates are the drug of choice.⁽³¹⁾ Omega-3 fatty acids in high doses (1 to 6 g/day of eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) can be effective in reducing TGs.^(10, 24,35) The omega-3 fatty acids EPA and DHA are the active ingredients in marine fish oil or omega-3 capsules. Adverse effects include eructation and diarrhea. These effects may be decreased by giving the fish oil capsules with meals in divided doses (eg, bid or tid). Omega-3 fatty acids can be a useful adjunct to other therapies. Prescription omega-3 fatty acid preparations are indicated for triglyceride levels > 500 mg/dL (> 5.65 mmol/L).^(33,35) Although higher HDL levels are associated with lower cardiovascular risk, it is not clear whether treatments to increase HDL cholesterol levels decrease risk of death. ATPIII guidelines define low HDL cholesterol as < 40 mg/dL [< 1.04 mmol/L]; the guidelines do not specify an HDL cholesterol target level and recommend interventions to raise HDL cholesterol only after LDL cholesterol targets have been reached. Treatments for LDL cholesterol and TG reduction often increase HDL cholesterol, and the 3 objectives can sometimes be achieved simultaneously. No guidelines specifically address treatment of low HDL cholesterol in children. Treatment includes lifestyle changes such as an increase in exercise and weight loss. Alcohol raises HDL cholesterol but is not routinely recommended as a therapy because of its many other adverse effects. Drugs may be successful in raising levels when lifestyle changes alone are insufficient, but it is uncertain whether raising HDL levels reduces mortality.^{((17, 28,36)}

Nicotinic acid (niacin) is the most effective drug for increasing HDL. Its mechanism of action is unknown, but it appears to both increase HDL production and inhibit HDL clearance; it may also mobilize cholesterol from macrophages. Niacin also decreases TGs and, in doses of 1500 to 2000 mg/day, reduces LDL cholesterol. Niacin causes flushing, pruritus, and nausea; premedication with low-dose aspirin may prevent these adverse effects.^(10, 24,35) Extended-release preparations cause flushing less often. However, most OTC slow-release preparations are not recommended; an exception is polygel controlled-release niacin. Niacin can cause liver enzyme elevations and occasionally liver failure, insulin resistance, and hyperuricemia and gout. It may also increase homocysteine levels. The combination of high doses of niacin with statins may increase the risk of myopathy. In patients with average LDL cholesterol and below-average HDL cholesterol levels, niacin combined with statin treatment may be effective in preventing cardiovascular disorders. In patients treated with statins to lower LDL cholesterol to < 70 mg/dL (< 1.8 mmol/L), niacin does not appear to have added benefit.^(32, 35) Fibrates increase HDL. Fibrates may decrease cardiovascular risk in patients with TGs > 200 mg/dL (< 2.26 mmol/L) and HDL cholesterol < 40 mg/dL (< 1.04 mmol/L). Infusion of recombinant HDL (eg, apoprotein A-1 Milano, an HDL variant in which a cysteine is substituted for an arginine at position 173 allowing for dimer formation) appears promising as a treatment for atherosclerosis but requires further study.^(10, 12,13) The upper limit of normal for Lp(a) is about 30 mg/dL (0.8 mmol/L), but values in African Americans run higher. Few data exist to guide the treatment of elevated Lp(a) or to establish treatment efficacy. Niacin is the only drug that directly decreases Lp(a); it can lower Lp(a) by $\leq 20\%$ at higher doses. The usual approach in patients with elevated Lp(a) is to lower LDL cholesterol aggressively. LDL apheresis has been used to lower Lp(a) in patients with high Lp(a) levels and progressive vascular disease.^(14, 16-19) Treatment of diabetic dyslipidemia should always involve lifestyle changes and statins to reduce LDL cholesterol.^(30, 34,35) To decrease the risk of pancreatitis, fibrates can be used to decrease TGs when levels are > 500 mg/dL (> 5.65 mmol/L). Metformin lowers TGs, which may be a reason

to choose it over other oral antihyperglycemic drugs when treating diabetes. Some thiazolidinediones (TZDs) increase both HDL cholesterol and LDL cholesterol.⁽³⁴⁻³⁶⁾ Some TZDs also decrease TGs. These antihyperglycemic drugs should not be chosen over lipid-lowering drugs to treat lipid abnormalities in diabetic patients but may be useful adjuncts. Patients with very high TG levels and less than optimally controlled diabetes may have better response to insulin than to oral antihyperglycemic drugs.^(10, 24,25) Treatment of dyslipidemia in patients with hypothyroidism, renal disease, liver disease, or a combination of these disorders involves treating the underlying disorders primarily and lipid abnormalities secondarily. Abnormal lipid levels in patients with low-normal thyroid function (high-normal TSH levels) improve with hormone replacement. Reducing the dosage of or stopping drugs that cause lipid abnormalities should be considered.^(22, 29) Lipid levels should be monitored periodically after starting treatment. No data support

Treatment Goals and recommendations

In adults of both sexes, a target LDL-C concentration less than 100 mg/dL and less than 70 mg/dL in *all* patients at very high risk. For patients with diabetes mellitus, LDL-C goal of less than 100 mg/dL, and in those with one or more additional risk factor(s) (for example, existing CVD), the recommended LDL-C goal is less than 70 mg/dL.^(6, 20,35) Raising HDL-C levels as much as possible is another goal, but minimally to greater than 40 mg/dL in both men and women. However, it does not recommend increasing HDL-C levels alone (i.e., low HDL-C without any accompanying risk factors) because it is difficult to determine from clinical trials whether increasing HDL-C levels alone is clinically beneficial.^(11,25) It is also recommended that an optimal apolipoproteins “apo B” level for patients at risk of CAD, including those with diabetes, is less than 90 mg/dL, while patients with established CAD or diabetes plus one or more additional risk factor(s) should have an apo B goal less than 80 mg/dL. Triglyceride levels less than 150 mg/dL in both men and women are recommended.^{((10,24,25,35)} It is recommended to follow a comprehensive strategy to control lipid levels and to address associated metabolic abnormalities and modifiable risk

specific monitoring intervals, but measuring lipid levels 2 to 3 mo after starting or changing therapies and once or twice yearly after lipid levels are stabilized is common practice. Despite the low incidence of liver and severe muscle toxicity with statin use (0.5 to 2% of all users), current recommendations are for baseline measurements of liver and muscle enzyme levels at the beginning of treatment.^(10, 14,28) Routine monitoring of liver enzyme levels is not necessary, and routine measurement of CK is not useful to predict the onset of rhabdomyolysis. Muscle enzyme levels need not be checked regularly unless patients develop myalgias or other muscle symptoms. If statin-induced muscle damage is suspected, statin use is stopped and CK may be measured. When muscle symptoms subside, a lower dose or a different statin can be tried. If symptoms do not subside within 1 to 2 wk of stopping the statin, another cause should be sought for the muscle symptoms (for example, polymyalgia rheumatica).⁽³⁶⁾

factors such as hypertension, diabetes, obesity, and cigarette smoking. The first-line approach to primary prevention in patients with lipid disorders involves the implementation of lifestyle changes, including physical activity and medical nutrition therapy.^(10, 24,25) Treatment may also involve pharmacotherapy, as well as patient education programs, to promote further risk reduction through smoking cessation and weight loss.^(10, 12,13) The international guidelines recommend a reasonable and feasible approach to fitness therapy (for example, exercise programs that include at least 30 minutes of moderate-intensity physical activity [consuming 4-7 kcal/min] 4 to 6 times weekly, with an expenditure of at least 200 kcal/day). Suggested activities include brisk walking, riding a stationary bike, water aerobics, cleaning/scrubbing, mowing the lawn, and sporting activities. Daily physical activity goals can be met in a single session or in multiple sessions throughout the course of a day (10 minutes minimum). For some patients, breaking activity up throughout the day may help improve adherence to physical activity programs. In addition to aerobic activity, muscle-strengthening activity is recommended at least two days a week.⁽³⁰⁾ For adults, international guidelines recommend a reduced-

calorie diet consisting of fruits and vegetables (≥ 5 servings/day), grains (≥ 6 servings/day, one-third of those as whole grains), fish, and lean meats. Intake of saturated fats, trans fats, and cholesterol should be limited, while LDL-C-lowering macronutrient intake should include plant stanols/sterols (~ 2 g/day) and soluble fiber (10-25 g/day).⁽³⁰⁾ Every effort should be made to support patients in their efforts to cease smoking. Cigarette smoking is a powerful risk factor, especially for MI, peripheral vascular disease, and stroke. Smoking accelerates coronary plaque development and may lead to plaque rupture and is particularly dangerous in persons with advanced coronary atherosclerosis. Numerous studies have shown that smoking has a substantial, negative effect on HDL-C levels and the LDL-C to HDL-C ratio. Smoking also appears to have a negative effect on postprandial lipids, including triglycerides. However, smoking cessation significantly increases HDL-C, with improvement observed in as few as 30 days.^(22, 28) It is recommended to consume aggressive lipid-modifying therapy to lower LDL-C to less than 100 mg/dL in patients with average or elevated LDL-C. This has been shown to reduce vascular mortality in

patients at high risk and to decrease coronary death, MI, or any cardiovascular events in patients on aggressive statin therapy. Additionally, medical guideline recommends an LDL-C goal less than 70 mg/dL as an appropriate goal for all patients with established CAD.^(1,14,27) Current evidence indicates that LDL-C can be aggressively lowered with statin therapy regardless of baseline levels and suggests that there is no threshold below which LDL-C lowering ceases to be effective. Fibrates is recommended for treatment of severe hypertriglyceridemia (triglycerides > 500 mg/dL). Adjunct use of 2 to 4 g of omega 3 fish oil can be used, if necessary, to achieve satisfactory triglyceride lowering.^(29,30,36,37) It is recommended to reassessing patients' lipid status 6 weeks after therapy initiation and again at 6-week intervals until the treatment goal is achieved. Thereafter, it is recommended that patients be tested at 6- to 12-month intervals. The specific interval should depend on patient adherence to therapy and lipid profile consistency. If adherence is a concern or the lipid profile is unstable, the patient will probably benefit from biannual assessment.^(36,37)

Conclusion

Lipid disorders, also called dyslipidaemia, are abnormalities of lipoprotein metabolism and include elevations of total cholesterol, LDL-C, or triglycerides (TG), or deficiencies of HDL-C. These disorders can be acquired or familial. The disorder become one of the most three common disorders in the world during the last five years due to several modifiable and none modifiable risk factors. The modifiable risk factors include diet, physical activity level and smoking. While the none modifiable factors include age and gender. Adiposopathy is promoted by unhealthy nutrition and a sedentary lifestyle in genetically and environmentally predisposed individuals. With impaired adipogenesis of peripheral, subcutaneous adipose tissue during positive caloric balance, existing fat cells may

hyperlipidemia, circulating free fatty acids may increase, and lipids may be deposited in nonadipose tissue organs (e.g., liver, muscle, possibly pancreas) resulting in lipotoxicity. Most patients are asymptomatic for many years prior to the appearance of physical findings. Treatment options depend on the specific lipid abnormality, although different lipid abnormalities often coexist. Many countries or regions have developed their own dyslipidaemia guidelines. Prevention and treatment of dyslipidaemia consists of many procedures. These procedures include risk assessment, establishment of treatment goal, increase activity level, dietary modification, medical therapy, follow up, re-assess and modifying the procedure as necessary.

References

1. Block, E.R., Edwards, D. Effect of plasma membrane fluidity on serotonin transport by endothelial cells. *American Journal of Physiology*; 1987;253: 672-678.

2. Brunner, L.J., Vadieli, K., Luke, D.R. Cyclosporine disposition in the hyperlipidemic rat model. *Research Community*. 1988; 59:339-348.
3. Diebold, K., Michel, G., Schweizer, J., Diebold-Dorsam, M., Fiehn, W., Kohl, B. Are

psychoactive-drug-induced changes in plasma lipid and lipoprotein levels of significance for clinical remission in psychiatric disorders? *Pharmacopsychiatry*. 1998; 31:60–67.

4. Dursun, S.M., Szemis, A., Andrews, H., Reveley, M.A. The effects of clozapine on levels of total cholesterol and related lipids in serum of patients with schizophrenia: a prospective study. *Journal of Psychiatry Neurosciences*. 1999;24:453–455.

5. Yeragani, V.K., Balon, R., Pohl, R., Ramesh, C. Imipramine treatment and increased serum cholesterol levels. *Canadian Journal of Psychiatry*. 1989;34:845

6. World Health Organization, “Quantifying Selected Major Risks to Health,” World Health Organization, Geneva, 2002.

7. D. Smith, “Epidemiology of Dyslipidemia and Economic Burden on the Healthcare System,” *American Journal of Managed Care*, Vol. 13, No. S3, 2007, pp. S68-S71.

8. J. Stamler, M. L. Daviglus, D. B. Garside, A. R. Dyer, P. Greenland, et al., “Relationship of Baseline Serum Cholesterol Levels in 3 Large Cohorts of Younger Men to Long-Term Coronary, Cardiovascular, and All-Cause Mortality and to Longevity,” *The Journal of the American Medical Association*, Vol. 284, No. 3, 2000, pp. 311-318. doi:10.1001/jama.284.3.311

9. WHO, “Country Cooperation Strategy for WHO and Saudi Arabia 2006-2011,” 2012. http://www.who.int/countryfocus/cooperation_strategy/ccs_sau_en.pdf

10. M. M. Al-Nozha, M. R. Arafah, M. A Al-Maatouq, M. Z. Khalil, N. B. Khan, K. Al-Marzouki, Y. Y. Al-Mazrou, M. Abdullah, A. Al-Khadra, S. S. Al-Harthi, M. S. Al-Shahid, A. Al-Mobeireek and M. S. Nouh, “Hyperlipidemia in Saudi Arabia Saudi,” *Medical Journal*, Vol. 29, No. 2, 2008, pp. 282-287.

11. D. O. Ogbeide, A. Karim, I. M. Al-Khalifa and S. Siddique, “Population Based Study of Serum Lipid Levels in Al-Kharj Health Center, Saudi Arabia,” *Saudi Medical Journal*, Vol. 25, No. 12, 2004, pp. 1855-1857.

12. S. N. Al-Shehri, Z. A. Saleh, M. M. Salama and Y. M. Hassan, “Prevalence of Hyperlipidemia among Saudi School Children in Riyadh,” *Annals of Saudi Medicine*, Vol. 24, No. 1, 2004, pp. 6-8.

13. B. A. Abalkhail, S. Shawky, T. M. Ghabrah and W. A. Milaat,

“Hypercholesterolemia and 5-Year Risk of Development of Coronary Heart Disease among University and School Workers in Jeddah, Saudi Arabia,” *American Journal of Preventive Medicine*, Vol. 31, No. 4, 2000, pp. 390-395. doi:10.1006/pmed.2000.0713.

14. R. Bonita, M. de Courten, T. Dwyer, K. Jamorzik and R. Winkelmann, “Surveillance of Risk Factors for NonCommunicable Diseases,” The WHO Stepwise Approach, WHO, 2001.

15. WHO, EMRO, “STEPwise WHO,” 2005. http://www.who.int/chp/steps/2005_Saudi_Arabia_STEPS_Report_EN.pdf

16. W. T. Friedewald, R. I. Levy and D. S. Frederickson, “Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, without Use of the Preparative Ultracentrifuge,” *Journal of Clinical Chemistry*, Vol. 18, No. 6, 1972, pp. 499-502.

17. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III),” *The Journal of the American Medical Association*, Vol. 285, No. 19, 2001, pp. 2486-2497. doi:10.1001/jama.285.19.2486

18. H. Saadi, S. G. Carruthers, N. Nagelkerke, et al., “Prevalence of Diabetes Mellitus and Its Complications in a population-Based Sample in Al-Ain, United Arab Emirates,” *Diabetes Research and Clinical Practice*, Vol. 78, No. 3, 2007, pp. 369-377.

19. Jackson, Z. Al-Mousa, M. Al-Raqua, P. Prakash and A. N. Muhanna, “Multiple Coronary Risk Factors in Healthy Older Kuwaiti Males,” *European Journal of Clinical Nutrition*, Vol. 56, No. 8, 2002, pp. 709-714.

20. S. Al-Moosa, S. Allin, N. Jemai, J. Al-Lawati and E. Mossialos, “Diabetes and Urbanization in the Omani Population: An Analysis of National Survey Data,” *Population Health Metrics*, Vol. 4, No. 5, 2006, p. 5-17.

21. A. Bener, M. Zirie, I. M. Janahi, O. A. Al-Hamaq and M. Musallam, “Prevalence of Diagnosed and Undiagnosed Diabetes Mellitus and Its Risk Factors in a Population Based Study of Qatar,” *Diabetes Research and Clinical Practice*, Vol. 84, No. 1, 2009, pp. 99-106.

22. Y. S. Khader, A. Batieha, M. El-Khateeb, M. Al Omari and K. Ajlouni, "Prevalence of Dyslipidemia and Its Associated Factors among Jordanian Adults," *Journal of Clinical Lipidology*, Vol. 4, No. 1, 2010, pp. 53-58. doi:10.1016/j.jacl.2009.12.004 .
23. C. Pongchaiyakul, P. Hongprabhas, V. Pisprasert and C. Pongchaiyakul, "Rural-Urban Difference in Lipid Levels and Prevalence of Dyslipidemia: A Population-Based Study in Khon Kaen Province, Thailand," *Journal of the Medical Association of Thailand*, Vol. 89, No. 11, 2006, pp. 1835-1844.
24. W. H. Zhao, J. Zhang, Y. Zhai, Y. You, Q. Q. Man, et al., "Blood Lipid Profile and Prevalence of Dyslipidemia in Chinese Adults," *Biomedical and Environmental Sciences*, Vol. 20, No. 4, 2007, pp. 329-335.
25. W. M. Kang, J. S. Zhang, X. X. Liu, M. S. Wang and M. L. Zhao, "Prevalence of Abnormality of Blood Lipid and Associated Factors in Health Examination Population in Beijing," *Chinese Medical Sciences Journal*, Vol. 24, No. 3, 2009, pp. 142-146. doi:10.1016/S1001-9294(09)60078-X
26. C. Erem, A. Hacihasanoglu, O. Deger, et al., "Prevalence of Dyslipidemia and Associated Risk Factors among Turkish Adults: Trabzon Lipid Study," *Endocrine*, Vol. 34, No. 1-3, 2008, pp. 36-51. doi:10.1007/s12020-008-9100-z
27. F. Azizi, M. Rahmani, A. Ghanbarian, H. Emami, P. Salehi, P. Mirmiran and N. Sarbazi, "Serum Lipid Levels in an Iranian Adults Population: Tehran Lipid and Glucose Study," *European Journal of Epidemiology*, Vol. 18, No. 4, 2003, pp. 311-319. doi:10.1023/A:1023606524944
28. R. W. Mahley, K. E. Palaoglu, Z. Atak, J. Dawson-Pepin, A. M. Langlois, V. Cheung, H. Onat, P. Fulks, L. L. Mahley, F. Vakar, S. Ozbayrakci, O. Gokdemir and W. Winkler, "Turkish Heart Study: Lipids, Lipoproteins, and Apolipoproteins," *The Journal of Lipid Research*, Vol. 36, No. 4, 1995, pp. 839-859.
29. V. Grabauskas, I. Miseviciene, J. Klumbiene, J. Petkeviciene, Z. Milasauskiene, A. Plieskiene and L. Margeviciene, "Prevalence of Dyslipidemias among Lithuanian Rural Population (CINDI Program)," *Medicina (Kaunas)*, Vol. 39, No. 12, 2003, pp. 1215-1222.
30. E. Polychronopoulos, D. B. Panagiotakos and A. Polystipioti, "Diet, Lifestyle Factors and Hypercholesterolemia in Elderly Men and Women from Cyprus," *Lipids in Health and Disease*, Vol. 4, No. 17, 2005, pp. 1-7.
31. L. J. de Souza, J. T. Souto Filho, T. F. de Souza, et al., "Prevalence of Dyslipidemia and Risk Factors in Campos dos Goytacazes, in the Brazilian State of Rio de Janeiro," *Arquivos Brasileiros de Cardiologia*, Vol. 81, No. 3, 2003, pp. 249-264.
32. R. Pradeepa, R. Deepa, S. S. Rani, G. Premalatha, R. Saroja and V. Mohan, "Socioeconomic Status and Dyslipidaemia in a South Indian Population: The Chennai Urban Population Study (CUPS 11)," *National Medical Journal of India*, Vol. 16, No. 2, 2003, pp. 73-78.
33. S. Wang, L. Xu, J. B. Jonas, Q. S. You, Y. X. Wang, et al., "Prevalence and Associated Factors of Dyslipidemia in the Adult Chinese Population," *PLoS One*, Vol. 6, No. 3, 2011, p. e17326.
34. R. W. Mahley, S. Can, S. Ozbayrakci, T. P. Bersot, S. Tanir, K. E. Palaoglu and G. M. Pepin, "Modulation of High-Density Lipoproteins in a Population in Istanbul, Turkey, with Low Levels of High-Density Lipoproteins," *American Journal of Cardiology*, Vol. 96, No. 4, 2005, pp. 547-555.
35. J. Yarnell, S. Yu, E. McCrum, D. Arveiler, B. Hass, J. Dallongeville, M. Montaye, P. Amouyel, J. Ferrieres, J. B. Ruidavets, A. Evans, A. Bingham, P. Ducimetiere and PRIME Study Group, "Education, Socioeconomic and Lifestyle Factors, and Risk of Coronary Heart Disease: The Prime Study," *International Journal of Epidemiology*, Vol. 34, No. 2, 2005, pp. 268-275. doi:10.1093/ije/dyh267
36. Z. R. Guo, X. S. Hu, M. Wu, M. H. Zhou and Z. Y. Zhou, "A Prospective Study on the Association between Dyslipidemia and Hypertension," *Chinese Journal of Epidemiology*, Vol. 30, No. 6, 2009, pp. 554-558.
37. Z. H. Liu, X. B. Xue and Z. Zhi, "Prevalence of Dyslipidemia and Associated Factors among the Hypertensive Rural Chinese Population," *Archives of Medical Research*, Vol. 38, No. 4, 2007, pp. 432-439.