Brief Communication

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Atherosclerosis Dyslipidemia: A Mini Review

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Atherosclerosis dyslipidemia (AD) is a major risk factor for cardiovascular diseases such as myocardial infarction and stroke. Low-density lipoprotein cholesterol (LDL-C) is the main cause of atherosclerosis dyslipidemia. Thus, an individual's risk of AD is strongly related with their lifelong diet of LDL-C. Accordingly, a significant increase of risk for coronary heart disease and mortality to cardiovascular events has been reported in adults with long-term LDL-C ≥ 100 mg/dL. To prevent atherosclerosis and the sequelae (including myocardial infarction, ischemic stroke and peripheral arterial occlusion disease), it is necessary to change our lifestyle as early as possible. Statin can directly protect cardiovascular tissues by reducing inflammation and improving endothelial function of blood vessels.

Key words: atherosclerosis dyslipidemia, secondary prevention, cardiovascular disease, stroke

Introduction

Atherosclerosis dyslipidemia (AD) is an increase in total cholesterol and triglycerides in the blood. Dyslipidemia, such as the condition of hypercholesterolemia, hypertriglyceridemia, or a combination of the two, is a major cause of AD.

Hyperlipidemia is the risk factor of coronary heart disease. There are primary and secondary causes of AD. Atherosclerosis dyslipidemia is divided into primary and secondary types. Primary atherosclerosis dyslipidemia is congenital, while secondary dyslipidemia is an acquired condition, which means that it develops from other causes, such as obesity, diabetes, etc. Atherosclerosis is a disease characterized by endothelial dysfunction of large and medium-sized arteries, where vascular inflammation and accumulation of modified lipid, inflammatory cells and cell debris in plaques within the vascular wall are observed.[1] In addition to the effectiveness of lowering low-density cholesterol (LDL-C). Triglycerides are the remnant of cholesterol, which is small enough to enter the arterial intima. As expected, atherosclerosis dyslipidemia is strongly associated with ischemic stroke or acute coronary syndrome but not with cardioembolic conditions. These remnants of cholesterol cause low-grade inflammation and lead to the development of atherosclerotic plaques and thrombosis. Moreover, changes in cholesterol level have been found to be directly associated with cardiovascular diseases in patients. In addition, there are total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides, etc., that one can measure in human body. Indeed, the atherosclerotic condi-

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tion becomes more observable in the thirties of an individual's age, which is even more of a stark reality for a person to face early morbidity and mortality associated with familial hypercholesterolemia. These changes in human cholesterol level are also linked with the development of cardiovascular diseases in adults of any ages. Sugary drinks are rich in fructose, which by itself can cause high blood sugar and obesity. Fructose increases lipid conversion in the human body, produces triglycerides and cholesterol, and further causes hyperlipidemia and insulin resistance, that will eventually lead to AD. Long-term consumption of high fructose elicits a series of correlated changes that further boost the level of lipid synthesis from fructose. And the increase in hepatic steatosis and plasma lipid concentration may contribute to insulin resistance and promote cardiovascular diseases.[2] Due to the increasing adoption of Western diet, the proportion of cardiovascular and cerebrovascular diseases and atherosclerosis among Chinese people is increasing on an annual basis. The results of many epidemiological investigations showed that hyperlipidemia not only affects the health and physical fitness of an individual, but also affects the heart and blood vessels. Cardiovascular diseases, type 2 diabetes, hypertension, hyperuricemia and other diseases are often associated with high incidence and mortality. Among obese patients with high cholesterol, low HDL-C, high LDL-C, and high triglycerides, they showed a decrease in serum lipids that is frequently observed in arterial injuries. The American College of Cardiology (ACC) and American Heart Association (AHA) Guidelines recommend the first-line therapy of Statins when the 10-year risk is calculated to be > 7.5% (for non-diabetic patients with LDL-C > 70 mg/dL and the presence of other risk factors).[3]

Treatments

The ACC and AHA Guidelines of 2019 recognize that the benefits of lipid pharmacotherapy remain uncertain in persons whose risk of developing atherosclerotic cardiovascular disease in 10 years is 5 to 20%. In the present study, for people who were receiving the medication, those with AD carried a 2 to 3 folds of residual risk of developing major adverse cardiovascular events (MACE) than those without AD. In 2019, the ESC and EAS (European Society of Cardiology/European Atherosclerosis Society), which originally recommended a modified lifestyle as sufficient therapy, have now considered pharmacological intervention for individual with LDL-C > 115 mg/dL. The risk groups include people with stable atherosclerotic cardiovascular disease who are treated with high potency Statin. Very high-risk patients with atherosclerotic cardiovascular disease (ASCVD) are all potential candidates to the combinatory therapy of maximum dose of Statin with two non-Statin drugs, such as Ezetimibe or Proprotein convertase subtilisin/Lexin type 9 inhibitor (PCSK9) inhibitor (Proprotein convertase subtilisin/Lexin type 9). The risk of (ASCVD) in diabetic patients is higher than that of non-diabetic individuals. The Guidelines for lipid treatment published by ACC and AHA in 2013 abolish the absolute target level of LDL, but focus on the risks of ASCVD, as well as identifying four groups of patients (including those with ASCVD disease history, LDL > 190 mg/dL, age 40 – 75 years old with diabetes or 10 years of ASCVD risk > 7.5%) to receive drug treatment for obvious therapeutic benefits. AD is defined by high level of triglycerides, low-density lipoprotein cholesterol, and total cholesterol, while with low level of high-density lipoprotein cholesterol at the same time. The blood total cholesterol (TC) and LDL-C of the elderly population have shown to decrease, which may be caused by changes in body fat distribution, systemic inflammation, chronic diseases, and malnutrition. The first-line treatment strategy for hyperlipidemia still relies on adjusting the personal lifestyle, such

as the dietary habit (by increasing water-soluble high-fiber intake) and physical exercises. If such standard therapy does not resolve the condition within 3 to 6 months, drugs will then be considered. Hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors have a significant effect on the course of disease, and at the same time can stabilize atherosclerotic plaques formed by smooth muscle cells, fibrinogen, and intravascular cells. Statins are the most effective lipid-lowering agent, which has been shown to reduce the mortality rate of coronary heart disease. Recent studies have also found that in addition to a strong lipid-lowering function, Statin can also strengthen the protection of vascular endothelial cells, regulate the inflammatory response in the body, maintain the plaque stability, and inhibit platelet aggregation, besides other positive cardiovascular effects. AD contributes to the residual risk for patients with LDL-C level of < 100 mg/dL, which is a recommended goal for prevention of stroke or acute coronary syndrome by the current guidelines. Further LDL reduction using PCSK9 inhibitor or Ezetimibe with Statin may have additive cardiovascular benefits. Overall, it is beneficial for the prevention and treatment of coronary heart disease, and can be an alternative approach to improve condition for those with AD. According to the literature review, reducing triglycerides by 1 mmol/L using fibrates will reduce the chance of cardiovascular (CV) event by 50%, which is comparable with the benefits of LDL reduction (Table 1).[4,5]

Discussion

Increased incidence of cardiovascular diseases is often countered by suggesting changing the dietary habit and increasing physical exercises as the best treatment strategy. If drug treatment were required, HMG-CoA reductase inhibitor is considered the most effective lipid-lowering agent, which can significantly help patient to reduce the incidence and mortality of coronary heart disease (CHD). High LDL-C is a major risk factor for atherosclerosis, which plays an important role in CHD and other cardiovascular diseases. High-density lipoprotein cholesterol concentration, plasma viscosity, fibrinogen and high-sensitivity C-reactive protein are all correlated with cardiovascular diseases, especially coronary heart disease. This significant association is predictive of MACE regardless of whether the patient achieves the ideal target level of LDL-C (< 100 mg/dL). Management includes treating secondary causes and modifiable risk factors, such as changing lifestyle. Assessing 10-year risk of coronary arterial disease is recommended as primary prevention before starting treatment in patient, but once confirmed, treatment is always indicated for

Table 1. Comparison of ACC/AHA and ESC/EAS guidelines on lipid treatment.

ACC/AHA guidelines	First prevention	Diabetes mellitus	Severe hypercholesterolemia	Clinical ASCVD
	↓ 30 – 49%	↓ ≥ 50%	LDL-C < 100 mg/dL	LDL-C < 70 mg/dL
ESC/EAS guidelines	Very high risk	High risk	Moderate risk	Low risk
	↓ ≥ 50% and LDL-C < 55 mg/dL	↓ ≥ 50% and LDL-C < 70 mg/dL	LDL-C < 100 mg/dL	LDL-C < 115 mg/dL

ACC: American College of Cardiology; AHA: American Heart Association; ASCVD: atherosclerotic cardiovascular disease; ESC: European Society of Cardiology; EAS: European Atherosclerosis Society; LDL-C: Low-density lipoprotein cholesterol.

this type of patient. Statin is always the first choice of treatment for hypercholesterolemia. Treatment by PCSK9 inhibitor is a relatively new and effective lipid-lowering management. In hypertriglyceridemia, management options include Statin or fibrates, and the decision will be determined by the level of triglycerides and the presence of mixed dyslipidemia. Risk assessment tools may not be used in patients with high cerebral vessel disease (CVD) risks who need lipid-lowering agents. Statin is the first option of treatment for hypercholesterolemia, while PSCK9 inhibitor is a relatively new lipid-lowering agent that, as per NICE (National Institute for Health and Clinical Excellence) guideline, can be used in the primary prevention of CVD in familial hypercholesterolemia and the secondary prevention of familial and non-familial hypercholesterolemia. Hypertriglyceridemia is known to cause acute pancreatitis and the risk factors are significantly high when the concentration is > 180 mg/dL. Glucagon-like peptide-1 receptor agonist (GLP1-RA) with proven cardiovascular benefit is recommended for the second-line treatment in diabetic patients with ASCVD or sodium-dependent glucose cotransporters-2 inhibitor (SGLT2i). SGLT2 inhibitor can be used when renal function permits and GLP1-RA is considered if renal function is poor. DPP4 inhibitor (Dipeptidyl peptidase 4 inhibitor) can be used in patients without GLP1-RA. Most physicians agree with the role of GLP1-RA and SGLT2i as the preferential treatment for patients of atherosclerosis dyslipidemia and cardiovascular diseases, since the concentration of total cholesterol or LDL-C in blood is closely related to myocardial infarction and ischemic stroke.

Conclusion

Atherogenic dyslipidemia is a common human lipid disorder of primary (inherited) or secondary cause. Patient should always be probed of any possible secondary causes. Atherogenic dyslipidemia is one of the major risk factors for atherosclerosis, CHD, myocardial infarction (MI), and ischemia stroke. Treatment of dyslipidemia can reduce the incidence and mortality rate.[6] Several prospective epidemiological studies have shown that there is a clear inverse relationship between serum HDL-C concentration and the risk of developing coronary heart disease, even with low-density lipoprotein-cholesterol (LDL-C) below 70 mg/dL. Thus, it is apparent that HDL-C plays a more important role in arterial protection than circulating HDL-C in blood. The cholesterol efflux capacity of serum HDL is a key metrics of HDL functionality and is shown to inversely related with the likelihood of developing coronary artery disease, but independent of its concentration, as some of more recent clinical studies have challenged the notion of higher HDL-C level as beneficial and vice versa for low HDL-C concentration.[7] Many studies have confirmed that high total cholesterol and LDL-C resulted in higher chance of developing cardiovascular diseases (such as coronary artery disease [CAD], stroke, etc.), while the evidence showed the opposite for HDL-C. Low level of HDL-C increases the risk of cardiovascular diseases. Therefore, it is recommended that healthy adults can also use Statin for primary prevention, since studies have shown that low LDL-C is associated with less chance of getting atherosclerotic cardiovascular diseases in life.[7]

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Conflicts of Interest

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