INTRODUCTION

In 2002, CVDs contributed to approximately a third of entire global deaths, whereas, by the year 2020, it is expected that CVDs will become the leading cause of death and disability worldwide.\(^1\)\(^-\)\(^2\) At proper levels, lipids have been noted to perform important functions in the body, but may cause various health problems if present in excess amounts. The term hyperlipidemia refers to the elevated lipid levels in the body including high cholesterol and high triglyceride levels.\(^3\)\(^-\)\(^4\) Lipids have been considered as “fats” in the bloodstream, which is commonly divided into cholesterol and triglycerides. However, the cholesterol circulates in the bloodstream and is involved in the structure and function of cells, whereas, the triglycerides are either used immediately or stored in the fat cells.\(^5\)\(^-\)\(^6\) Further, high cholesterol levels in the body have been considered as a modifiable risk factor which is evident by the fact that plasma cholesterol at levels >200 mg/dL cause 4.4 million deaths in a year.\(^7\)\(^-\)\(^8\) Various types of cholesterol have been reported that include total cholesterol (TC), consisting of all the cholesterol combined; HDL cholesterol, often referred to as good cholesterol; and LDL cholesterol, often called bad cholesterol.\(^9\)\(^-\)\(^10\) The abnormal cholesterol levels are the result of an unhealthy lifestyle including taking high-fat diet and other lifestyle factors like being overweight, heavy alcohol use and lack of exercise.\(^11\) Moreover, diabetes and underactive thyroid gland have also been reported to cause high cholesterol levels.\(^12\)\(^-\)\(^13\) Other illnesses that may elevate cholesterol levels include polycystic ovary syndrome and kidney disease. The higher levels of female hormones like estrogen, have been noted to increase or change cholesterol levels. In addition, drugs like diuretics, beta-blockers and medicines used to treat depression have also been reported to raise cholesterol levels.\(^14\) Numbers of studies have shown statins, niacin analogues, fibrates, bile acid binding resins and cholesterol absorption inhibitors to possess certain modulatory roles in the treatment of hyperlipidemia.\(^15\)\(^-\)\(^17\) The present review highlights about the classification and treatments for hyperlipidemia.

CLASSIFICATION OF LIPID CONCENTRATIONS

It has been noted that cholesterol along with some other types of fats cannot be dissolved in the blood. Moreover, in order to be transported to and from cells, they have to be specially carried by certain molecules called lipoproteins, which consist of an outer layer of protein with an inner core of cholesterol and triglycerides.\(^18\)\(^-\)\(^19\) In addition, the lipoproteins have been found essential for cholesterol to move around the body. The lipids can be classified as TC, triglycerides, LDL, HDL and very low density lipoprotein (VLDL) cholesterol.

Total cholesterol: According to guidelines of National Cholesterol Education Program (NCEP), TC concentrations below 200 mg/dL have been regarded as desirable, whereas, concentrations greater than 240 mg/dL are referred to as hyperlipidemic. However, epidemiological evidence suggests that the risk of cardiac events decreases as TC levels fall approximately to 150 mg/dL. Moreover, TC should be less than 180 mg/dL for children.\(^20\)\(^-\)\(^21\)

Triglyceride: Triglycerides are another type of fat that is carried in the blood by VLDL. Moreover, it has also been shown that excess calories, alcohol or sugar in the body get converted into triglycerides and stored in fat cells throughout the body.\(^22\) The triglyceride concentration less than 150 mg/dL is regarded as normal, whereas, concentrations of 200-499 mg/dL are considered high. Moreover, concentrations of 500 mg/dL or higher are considered dangerous for the development and progression of various CVDs.\(^23\)

LDL cholesterol: LDL is commonly known as the bad cholesterol, which is produced by the liver and carry cholesterol and other lipids from the liver to different areas of the body like muscles, tissues, organs and heart. The high levels of LDL indicate much more cholesterol in the blood stream than necessary and hence, increase the risk of heart disease.\(^24\)\(^-\)\(^25\) According to NCEP guidelines, LDL cholesterol concentrations below 100mg/dL are considered optimal, whereas concentrations in the range of 160-189 mg/dL are considered to be the higher side.\(^26\) However, increasing evidence supports that normal human LDL cholesterol concentration can be as low as 50 to 70 mg/dL.\(^27\) Moreover, it has been comprehensively seen that the risk of CVDs decreases as LDL cholesterol concentration decreases.

HDL cholesterol: HDL is commonly referred to as the good cholesterol, which is produced by the liver to carry cholesterol and other lipids from tissues back to the liver for degradation.\(^28\) High levels of HDL cholesterol have been considered as a good indicator of a healthy heart. The concentrations of 60 mg/dL or higher have been considered as optimal, whereas, HDL concentrations below 40 mg/dL are considered as major risk factor for CVDs. However, HDL is often interpreted in the context of TC and LDL concentrations, and hence may be regarded as less significant when LDL is low.\(^29\)\(^-\)\(^30\)

VLDL Cholesterol: VLDL cholesterol is similar to LDL cholesterol in the sense that it contains mostly fat and not much protein. VLDL cholesterol is the lipoproteins that carry cholesterol from the liver to organs and tissues in the body.\(^31\) They are formed by a combination of cholesterol and triglycerides. Moreover, VLDLs are heavier than LDL, and are also associated with atherosclerosis and heart disease.\(^32\)

Keywords: Cardiovascular, Hyperlipidemia, Cholesterol.
RISK FACTORS ASSOCIATED WITH HYPERLIPIDEMIA

A variety of risk factors have been found to be associated with hyperlipidemia like cholesterol rich foods, obesity, diabetes and stress. Saturated fat and cholesterol in the food has been noted to increase cholesterol levels in the body. Further, in addition to being a risk factor for heart disease, being overweight also increases the cholesterol levels in the body. Moreover, it has been shown that losing weight can help lower LDL and total cholesterol levels and consequent increase the HDL cholesterol levels in the body. In addition, regular exercise has also been noted to lower LDL cholesterol and raise HDL cholesterol levels. Another modifying factors in the development and progression of hyperlipidemia are age and gender. It has been shown that cholesterol levels rise as the person gets older. However, before menopause, women tend to have lower TC levels than men of the same age, whereas, after menopause, LDL levels of women tend to rise. Furthermore, it has been comprehensively suggested that poorly controlled diabetes leads to increased cholesterol levels. The improvements in diabetes control have been demonstrated to decrease the cholesterol levels in the body. Heredity has also been a modifying factor for the progression of hyperlipidemia as it has been noted that the genes partly determine the amount of cholesterol body makes. Surprisingly, it has been reported that people under stress have been shown to console themselves by eating fatty foods ultimately leading to hyperlipidemic condition.

PATHOPHYSIOLOGY OF HYPERLIPIDEMIA

The pathophysiology of hyperlipidemia can be studied under two headings, i.e., primary hyperlipidemia and secondary hyperlipidemia. The pathophysiology of primary hyperlipidemia involve that the idiopathic hypercholesterolemia defect in lipid metabolism leads to hypertriglyceridemia and hypercholesterolemia which is caused by a defect in lipoprotein lipase activity or the absence of the surface apoprotein CII. Further, in primary hyperlipidemia, the LDL cholesterol is high which is supported by the results obtained in various studies showed that idiopathic hypercholesterolemia occur in many families of doberman pinchers and rottweilers. Moreover, hypercholesterolemia in cats with familial hypercholesterolemia defect in lipoprotein lipase (LPL) activity showed the occurrence of primary hyperlipidemia.

In secondary hyperlipidemia, the postprandial absorption of chylomicrons from the gastrointestinal tract occurs 30-60 min after ingestion of a meal containing fat that may increase serum triglycerides for 3-10 hours. The diabetes mellitus patients have been noted to possess low LPL activity which further caused high synthesis of VLDL cholesterol by the liver ultimately leading to hyperlipidemia. Moreover, hypothyroidism-induced low LPL activity and lipolytic activity has been noted to reduce hepatic degradation of cholesterol to bile acids. Furthermore, hypocholesterolemia has been noted to reduce the formation and increase the breakdown of cholesterol and triglycerides in the body, accounting for their hyperlipidemic potential. The common side effects of this drug is constipation. The potent members of the class include cholestyramine, colestipol and coles-velam. Furthermore, cholesterol absorption inhibitors have also been noted to reduce HDL cholesterol levels via unknown mechanisms. The common side effects of niacin drugs include flushing, hot flashes, itching and headache. The third potent class of agents for the treatment of hyperlipidemia is fibric acid derivatives which have been thought to reduce the formation and increase the breakdown of cholesterol and triglycerides in the body, accounting for their hypolipidemic potential.

CONCLUSION

Hyperlipidemia is a critical condition of elevated lipid levels in the body that ultimately lead to the development and progression of various CVDs. The link between hyperlipidemia and occurrence of CVDs has already been established. Various studies have reported the treatment of hyperlipidemic patients with statins, fibrates and niacinic acid derivatives. Moreover, the focus on dietary management should be done in order to prevent and treat the patients presented with hyperlipidemia. However, ample studies have provided the evidence for the efficacy of already reported treatments, but further studies are mandatory in order to provide more information about the safety and efficacy of novel antihyperlipidemic agents.
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