

Hyperlipidemia: A Review of the Innovative Approaches for the Management of Lipid

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Abstract

The most prevalent modifiable cause of atherosclerotic cardiovascular disease is hyperlipidemia. The notion of the inverse link between the onset of a major adverse cardiovascular event and non-high-density lipoprotein (non-HDL) and low-density lipoprotein (LDL-C) cholesterol has emerged from our understanding of controlling hyperlipidemia. An overview of lipids and their metabolism will be given in this review. It will also address hyperlipidemia and therapeutic strategies for it.

Keywords: low density lipoprotein-cholesterol; statin-induced myopathy; lipid metabolism

Introduction and background

Atherosclerosis develops as a result of both hypertriglyceridemia and hypercholesterolemia. One medical issue that is closely linked to ischemic heart disease (IHD) is atherosclerosis [1].

Globally, cardiovascular disease (CVD) is the leading cause of death. Treatment for hyperlipidemia is therefore essential for the global management of individuals with coronary artery disease (CAD) or those who are at high risk for developing CAD. Since lipids are the fundamental components of all biological cells, they have a wide range of important and varied roles [2]. A disorder called hyperlipidemia causes elevated levels of lipoproteins and plasma lipids. Triglycerides (TGs), cholesterol esters, phospholipids, and cholesterol are a few types of plasma lipids. Conversely, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and decreased amounts of high-density lipoprotein (HDL) are among the lipoproteins seen in plasma. Lipids and proteins combine to form macromolecules called lipoproteins. Their arrangement allows the lipids to mix easily with other bodily fluids that are watery. They are divided into three groups: polar lipids, non-polar lipids, and certain proteins. Choleryl esters and TGs are examples of non-polar lipids, whereas phospholipids and unesterified cholesterol are examples of polar lipids. Apolipoproteins is another name for the particular proteins. Amphiphilic proteins, known as apolipoproteins, bind to plasma and lipids alike [3]. Densities are another factor used to categorise lipoproteins. Chylomicrons (CM), VLDL, LDL, and intermediate-density lipoproteins (IDL) are examples of non-HDL and HDL particles, respectively.

Types of Lipo Proteins

1	Chylomicrons (CM),
2	Verylow-densitylipoproteins (VLDL),
3	Low-density lipoproteins (LDL),
4	Intermediate-density lipoproteins (IDL)
5	High-densitylipoproteins (HDL)11

Chylomicrons

These are the biggest particles in terms of density and size, and there is a direct relationship between their concentration with the amount of triglycerides in food.

Very low-densitylipoproteins

The liver secretes very low-density lipoproteins, which are smaller particles that include more chylomicrons than triglycerides. Sterol is transported from the liver to the body's organs and tissues via very low density lipoprotein. They are created by a combination of triglycerides and cholesterol [4].

Low-density lipoproteins

Both Lee et al. and Galeano et al. claim that low-density lipoproteins are partially synthesised in the intestinal chyle and partially following lipolysis of very low density lipoproteins. It and CHD are intimately correlated.

Intermediate-density lipoproteins

After being lysed by the lipase enzyme in the capillaries of muscle and adipose tissue, VLDL particles produce intermediate-density lipoprotein.

High-densitylipoproteins

HDL is commonly referred as good cholesterol. Highdensity lipoproteins are synthesized in the liver. It carries cholesterol and other lipids from tissues back to the liver for degradation. HDL plays an antiatherogenic role [5].

Classification of Hypelipidemia

On the idea of causing factor (fig.1).

Primary (Familial: hyperlipidemia)

Due to a genetic flaw, it is also known as familial. The deficiency might be polygenic, meaning it has numerous genes, or monogenic, meaning it has just one gene. The majority of the time, primary hyperlipaemia may be resolved into an aberrant lipoprotein pattern summary.

Type I-Raised cholesterol with high triglyceride levels.

Type II-High cholesterol with normal triglyceride levels.

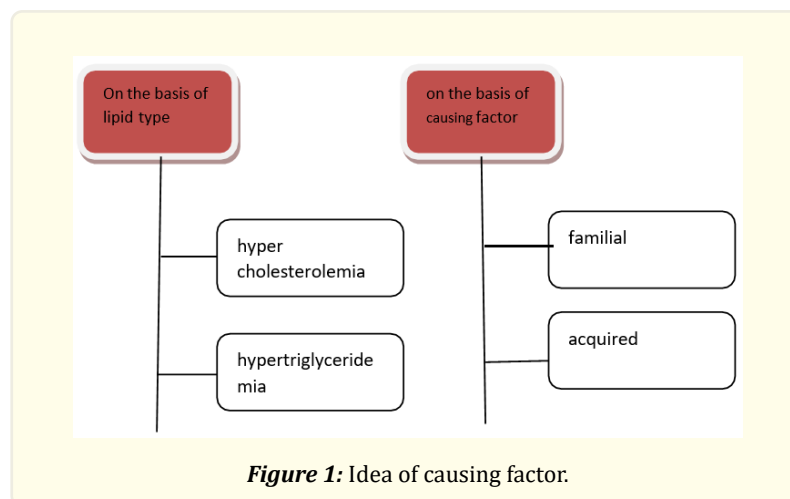
Type III-Raised cholesterol and triglycerides.

Type IV-Raised triglycerides, atheroma and uric acid.

Type V-Raised triglycerides.

Secondary (Acquired hyperlipidemia)

It is acquired because it is brought on by the use of medications such as corticosteroids, beta blockers, and oral contraceptives, as well as conditions including diabetes, glomerular syndrome, chronic alcohol use, hypothyroidism, and chronic alcohol intake. Pancreatitis can result from substantial hypertriglyceridemia associated with secondary hyperlipidemia.



Complications of Hyperlipidemia

Atherosclerosis

The primary cause of atherosclerosis, the main risk factor for cardiovascular disease, is hyperlipidemia. The pathological process known as atherosclerosis is typified by the build-up of lipids, cholesterol, and calcium as well as the formation of fibrous plaques inside the walls of large and medium-sized arteries [6].

Coronary Artery Disease

The main cause of coronary artery disease is atherosclerosis, which is characterised by the buildup of extra lipid and the development of fibrous plaques inside the artery walls. This causes the arteries supplying the myocardium to narrow, which restricts blood flow and leaves the heart with insufficient oxygen to meet its needs [7].

Ischemic stroke or cerebrovascular accident

The fourth most common cause of mortality is stroke. Strokes typically result from an artery being blocked by a blood clot or an atherosclerotic block fragment that breaks off in a tiny blood vessel inside the brain. Reducing total cholesterol and low-density lipoprotein by 15% was shown in several clinical trials to dramatically lower the risk of having a first stroke.

Pathogenesis of Hyperlipidemia

Blood monocytes and platelets adhere to a vascular wall at the locations of endothelial damage in the early stages of hyperlipidemia. The proliferation of smooth cells in the intimal and medial lining of the artery, collagen synthesis, cholesterol absorption, and the first signs of hyperlipidemic plaque are caused by the release of mediators such as platelets produced from growth factors. Acute syndromes including myocardial infarction, unstable angina, and abrupt cardiac death are being caused by plaque ruptures [8].

Significance

Because of the well-established link between lipid concentrations and the risk of cardiovascular disease (CVD), the nation's leading cause of death, health care practitioners are worried about hyperlipidemia [9-11]. The landmark study, the Lipid Research Clinics Coronary Primary Prevention Trial, published in two parts in 1984 (each using a different statistical analysis), helped establish that therapeutic interventions to lower cholesterol levels result in reduced risk of cardiovascular morbidity or mortality [12, 13]. A three-year-long, multi-part online review that was published in the Journal of Lipid Research provides a comprehensive history of the cholesterol dispute [14-20].

Pharmacological Treatment

There are several hypolipidemic medications on the market to treat hyperlipidemia. Drug Project showing that, in individuals with pre-existing coronary heart disease, the medications are comparatively inefficient in preventing myocardial infarction [21].

Drug therapy

Elevate LDL, risk factor presence, and CHD documentation should be considered while designing pharmacological treatment in addition to TLC. Currently available lipid-lowering medications include plant sterols, ezetimibe, niacin, fibric acid derivatives, bile acid sequestrants or bile binding resins, statins, and niacin. If dietary changes don't work, a doctor may prescribe medication made specifically to decrease blood cholesterol levels [22].

Fibric acid derivatives (Fibrates)

Fibrates, a family of commonly used antihyperlipidemic medications that result in a large reduction in plasma triglycerides and a minor reduction in LDL sterols, include clofibrate, gemfibrozil, fenofibrate, and bezafibrate. Moderate increases are seen in HDL cholesterol levels. According to the results of angiographic experiments, fibrates are primarily responsible for delaying the onset of coronary artery disease and coronary atherosclerosis.

New Potential Targets and Treatments

Recently, many clinical trials revealed new potential agents with promising antihyperlipidemic activity.

Acyl-CoA cholesterol acyl transferase inhibitors (ACAT)

The enzyme that catalyses the conversion of intracellular cholesterol into cholesteryl esters is called acyl-CoA cholesterol acyl transferase, or ACAT. There are two isomers of ACAT, known as ACAT1 and ACAT2.

Microsomal triglyceride transfer protein (MTP) inhibitors

Microsomal triglyceride transfer protein (MTP) is involved in the manufacture of CD1, antigen- presenting molecules, the control of cholesterol ester biosynthesis, and the transfer of neutral lipids between membrane vesicles.

Cholesteryl ester transfer protein (CETP)inhibitors

The liver's CETP makes it easier for cholesteryl esters to transfer from proatherogenic apo lipoprotein B- containing lipoproteins, such as VLDLs and LDLs, to anti-atherogenic HDLs.

Moreover, the majority of research supported the notion that CETP inhibition inhibits the development of atherosclerosis and provided evidence that CETP may participate in reverse cholesterol transfer, which may have a proatherogenic effect [23].

Squalene synthase inhibitors

Farnesyl pyrophosphate is catalysed by Squalene Synthase (SqS) to produce squalene. This is the initial step in the synthesis of sterols, of which cholesterol is one [24].

Lanosterol synthase inhibitors

The first sterol intermediate in the cholesterol synthesis pathway, lanosterol, is produced by the cyclization of (S)-[25]. oxidosqualene by lanosterol synthase (LSS).

Conclusion

According to the aforementioned study, hyperlipidemia poses a significant risk for heart disease. Treatment options for hyperlipidemia include modern medications, diet plans, traditional treatments, and consistent exercise. Maintaining a healthy diet and maintaining physical fitness can lower the risk of hyperlipidemia, CVD, and many other diseases.

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