Hyperlipidemia

Hyperlipidemia is a medical condition characterized by an elevation of any or all lipid profile and/or lipoproteins in the blood. It is also called hypercholesterolemia/hyperlipo proteinemia . Although elevated low density lipoprotein cholesterol (LDL) is thought to be the best indicator of atherosclerosis risk, dyslipidemia (abnormal amount of lipids in the blood) can also describe elevated total cholesterol (TC) or triglycerides (TG), or low levels of high density lipoprotein cholesterol (HDL).
Lipids are fats in the blood stream, commonly divided into cholesterol and triglycerides; Cholesterol (VLDL + HDL) circulates in the bloods stream and is involved in the structure and function of cells. Triglycerides (TG) are best viewed as energy that is either used immediately or stored in fat cells. TG is manufactured in the liver from the foods or by being absorbed from the intestine. Arteries are normally smooth and unobstructed on the inside, but in case of increased lipid level, a sticky substance called plaque is formed inside the walls of arteries. This leads to reduced blood flow, leading to stiffening and narrowing of the arteries. It has been proved that elevated plasma levels of cholesterol and of LDL are responsible for atherosclerosis in man, and epidemiological data suggests that elevated plasma levels of HDL have a protective effect . This medical condition or problem is divided into two subtypes: primary hyperlipidemia and secondary hyperlipidemia.

Causes of Hyperlipidemia:

The main cause of hyperlipidemia includes :
-changes in lifestyle habits in which risk factor is mainly poor diet i.e. with a fat intake greater than 40 percent of total calories, saturated fat intake greater than 10 percent of total calories; and cholesterol intake greater than 300 milligrams per day or treatable medical conditions.
-Result of an unhealthy lifestyle including taking high-fat diet being overweight, smoking heavy alcohol use and lack of exercise.
- Other factors include diabetes, kidney disease, pregnancy, and an underactive thyroid gland. polycystic ovarian 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.

1-primary hyperlipidemia:

as a result of genetic problems i.e., mutation within receptor protein, which may be due to single (monogonic) gene defect or multiple (polygenic) gene defect. And may result of change in dietary and lack of proper physical activities.

The various classes of primary hyperlipidemia.

VLDL (very low density lipoprotein).

TYPE	DISORDER	CAUSE	OCCURANCE	ELEVATED PLASMA LIPOPROTEIN
I.	Familial lipoprotein lipase deficiency	Genetic	Very rare	Chylomicrons
IIa	Familial hypercholesterolemia	Genetic	Less common	LDL
IIb	Polygenic hypercholesterolemia	Multifactorial	Commonest	LDL
III	Familial dysbetalipoproteinemia	Genetic	Rare	IDL, Chylomicrons Remnants
IV	Hypertriglyceridemia	Multifactorial Genetic	Common	VLDL
V	Familial combined hyperlipidemia	Genetic	Less common	VLDL,LDL

1-Familial hypercholesterolemia (FH) :

a disorder of defective LDL-C clearance , caused by a genetic mutation resulting in a defective or absent LDL receptor .FH patients may exhibit excess cholesterol deposition in the iris ,clinically manifested as arcus senilis, also in tendons (tendon xanthomas) if untreated may have chance of myocardial infarction.

2-polygenic hypercholesterolemia:

the most primary disorder causing an increase in cholesterol, caused by combination of environmental and multiple genetic factors.
high in saturated fatty acids can reduce LDL receptor activity thus reducing the clearance of LDL particles from the systemic circulation .

3-Atherogenic dyslipidemia (hypertriglyceridemia):

characterized by moderate elevation of TG(Triglyceride)(150-500mg),indicative of elevated VLDL.
Patients have increased in visceral adiposity (abdominal fat) and are

hypertensive and insulin resistance .

Secondary hyperlipidemia:
This arises as a result of other underlining diseases like diabetes, myxoedema, nephritic syndrome, chronic alcoholism, with use of drugs like corticosteroids, oral contraceptives, Beta blockers.

Pharmacological Agent

1- 3 -Hydroxy -3-Methyle-Glutaryl Coenzyme A Inhibitor (HMG-COA) (Statins):

Prodrugus : (Lovastatin,Simvastatin)

reductase, interrupting the conversion of HMG-CoA to mevalonate, the rate-limiting step in de novo cholesterol biosynthesis. Reduced synthesis of LDL and enhanced catabolism of LDL mediated through LDL receptors appear to be the principal mechanisms for lipid- lowering effects. When used as monotherapy, statins are the most potent total and LDL cholesterol- lowering agents and among the best tolerated, Eliminated primarily by the liver .

Side Effects:

-muscle pain , weakness (myalegia) ,headache , GI symptoms .
-Constipation, dyspepsia, flatus, abdominal pain,.
-skin rash.
Elevated serum aminotransferase levels (primarily alanine aminotransferase), elevated creatine kinase levels, and rarely rhabdomyolysis .
-can be threatening with acute renal failure ,arrest,cardiac arrest due to electrolyte imbalance .
-diabetes .

2- cholesterol absorption inhibitor

Ezetimibe:

interfere with the active absorption of cholesterol and plant sterol from the intestinal lumin into the enterocyte by binding to and inhibiting this transporter.
About less than 50% of cholesterol is transported from the intestine to the liver by chylomicrons .
Causes upregulation of the hepatic LDL receptors and increased clearance of circulation VLDL,LDL particles.

side effects:

Ezetimibe is well tolerated; approximately 4% of patients experience gastro intestinal upset: diarrhea, abdominal pain ,back pain .

3-Fibric acids (gemfibrozil, fenofibrate, clofibrate)

Fibrate activate peroxisome prliferator-activated receptors (PPAR) are located in the nucleus of the cell and are ligand-dependent transcription factors that regulate target gene expression, reducing the synthesis of TGs in the liver, reducing the TGs content of the secreted VLDL particles.

Gemfibrozil

reduces the synthesis of VLDL and, to a lesser extent, apolipoprotein B with a concurrent increase in the rate of removal of triglyceride-rich lipoproteins from plasma.

Fenofibrate

is primarily metabolized by conjugation with peak plasma concentration , it is highly bound to plasma protein with an 1/2 20 hr , excreted through urine**.**

Side effects:

Nausea ,vomiting , dyspepsia , diarrhea , abdominal pain , flatulence and constipation .
this agents are indicated in the reduction of the TG levels in patients with hypertriglyceridemia.

4-Bile acid resins (cholestyramine, colestipol, colesevelam)

bind bile acids in the intestinal lumen, by disrupting the normal enterohepatic circulation of bile acids from the intestine lumen to the liver , the liver is stimulated to convert hepatocellular cholesterol into bile acid. Result in reduction in the concentration of the cholesterol in the hepatocyte, insoluble in water.

Side effects:

-constipation , abdominal bloating ,epigastric fullness ,nausea, vomiting , steatorrhea ,flatulence .

5-Niacin

Niacin (nicotinic acid) reduces the hepatic synthesis of VLDL, which in turn leads to a reduction in the synthesis of LDL. Niacin also increases HDL by reducing its catabolism.

Side effects

Cutaneous flushing and itching appear to be prostaglandin mediated, Gastrointestinal intolerance is also a common problem, elevated liver function tests, and hyperglycemia.

6-Fish oil supplementation :

Diets high in omega-3 polyunsaturated fatty acids (from fish oil) , reduce cholesterol, triglycerides, LDL, and VLDL and may elevate HDL cholesterol.

Side effects

thrombocytopenia and bleeding disorders have been noted, especially with high doses (15 to 30 g/day).