WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 22, 669-677. Review Article ISSN 2277–7105

ATHEROSCLEROSIS: A REVIEW

Nilesh Kumar Pathak*[1] and Rohit Yadav[2]

[1]Ex. Assistant Professor, Royal Institute of Pharmacy and Advanced Studies, Ratlam, 457001, M.P.

[2]Assistant Professor, Institute of Pharmacy, Vikram university, Ujjain. 456001 M.P.

Article Received on
29 October 2023,

Revised on 19 Nov. 2023,
Accepted on 09 Dec. 2023

DOI: 10.20959/wjpr202322-30634

***Corresponding Author**
Nilesh Kumar Pathak
Ex. Assistant Professor,
Royal Institute of Pharmacy
and Advanced Studies,
Ratlam, 457001, M.P.

ABSTRACT

These review give a detail on causes of atherosclerosis, it's prevention, treatment, detection and some term related with atherosclerosis because atherosclerosis involving in the coronary heart disease which is the most common cause of death, accounting for one-third of all deaths, today The incidence of atheroma is widespread in developed countries why atheromatous plaques developed is not yet clearly understood but the predisposing factor appear to exert their effect over a long period. Atherosclerotic interference with blood supply to the body is the third most common cause of death after cancer.

KEYWORDS:

Arterial
Hyperlipidemia
Syndrom
Dietary
Plaques
Lipoproteins
Antioxidant
Niacin

INTRODUCTION

A disease of the arterial wall in which the layer thickens, causing narrowing of the channel and thus, impairing blood flow of the large and intermediate-sized arteries in which fatty lesion called atheromatus plaques develop on the inside surfaces of arterial walls called atherosclerosis.

Hyperlipidemia is a major cause of atherosclerosis and the atherosclerosis-associated conditions, such as coronary heart disease, ischemic cerebrovascular disease and peripheral vascular disease. This condition still accounts for the majority of morbidity and mortality among middle aged and older adults, the incidence and absolute number of annual events will increase over the next decade.

Dyslipidemia, including hyperlipidemia and hypercholesterolemia and low level of high density of lipoproteins cholesterol HDL are major cause of increased atherogenic risk; both genetic disorders and lifestyle diet high in calories, saturated fat, and cholesterol contribute to dyslipidemia seen in developed countries around the world. Severe hypertriglyceridemia requires therapy to prevent pancreatitis. Moderately elevated triglyceride level 150 to 400mg/dl also are concern because they often occur as part of the metabolic syndrome, which includes insulin resistance, obesity, hypertension, low HDL level and substantially increased CHD risk.[1-4]

Heredity - Family history, Gender - males are more susceptible than females until after the menopause. Increasing age, Hypertension, Diabetis mellitus, Smoking(active and passive) especially cigaretts, Excessive emotional stress in work or home enviorment, Diet, e.g. cholesterol and saturated fatty acids, Obesity, Lifestyle, e.g. Indisciplin and inactive, Excessive alcohol consumption, are basic cause of hyperlipidemia.[5] Cholesterol diet and passive smoking raise the lipid and cholesterol level with reducing the HDL level which causes hypercholesterolemia and hyperlipidemia existing heart disease such as heart attack, heart stroke etc in future.[6,7]

Lipids consist of a number of different chemicals: free fatty acids, triglycerides, sterols (cholesterol and cholesterol esters), and phospholipids (phosphoric acid a esters of lipids). Triglycerides exist in nature as solids (fats) or liquids (oils). This depends on room temperature, the length of the fatty acid chain, and the extent of their hydrogen ion saturation.

Types of Lipids in the Body

- **Fatty acids:** Used to synthesize triglycerides and phospholipids or catabolized to generate adenosine triphosphate (ATP). Fatty acids may be saturated, monounsaturated (monoenoic fatty acids), or polyunsaturated (polyenoic fatty acids).
- **Chylomicron** - largest of the plasma lipoprotein particles that transport **triacylglycerols** from the intestine to peripheral tissues.

- **Phospholipids:** Major lipid component of cell membranes.
- **Cholesterol:** Minor component of all animal cell membranes; precursor of bile salts, vitamin D, and steroid hormones.
- **Bile salts***:* Needed for digestion and absorption of dietary lipids.
- **Sex hormones***:* Stimulate reproductive functions and sexual characteristics.[8]

Lipoproteins: Transport lipids in the blood, carry triglycerides and cholesterol to tissues, and remove excess cholesterol from the blood.in simple way lipoprotein are classified in density form and according to volume and density relation density are inversely proportional to volume. It means higer density means low volume that's why HDL (high density lipoprotein) are known as good lipoprotein and LDL(low density lipoprotein) and VLDL(Very low density lipoprotein) means bad lipoprotein.

Low-Density Lipoproteins

An important factor in causing atherosclerosis is a high blood plasma concentration of cholesterol in the form of low-density lipoproteins. The plasma concentration of these highcholesterol low-density lipoproteins is increased by several factors, including eating highly saturated fat in the daily diet, obesity, and physical inactivity. To a lesser extent, eating excess cholesterol may also raise plasma levels of low-density lipoproteins.[9-10]

High-Density Lipoproteins

Much less is known about the function of high-density lipoproteins compared with that of low-density lipoproteins. It is believed that high-density lipoproteins can actually absorb cholesterol crystals that are beginning to be deposited in arterial walls. Whether this mechanism is true or not, high-density lipoproteins do help protect against the development of atherosclerosis. Consequently, when a person has a high *ratio* of high-density to low-density lipoproteins, the likelihood of developing atherosclerosis is greatly reduced.[11]

Triglycerides (TGL) & High cholesterol diet

Triglyceride means protection, insulation, energy storage. *(fats and oils)* The fat in the food eat is mostly in the form of triglycerides. High cholesterol diet leading to hyperlipidemia is regarded as an important factor in the development of ischemic heart disease,[5] and increasetriglycerides level. Triglycerides are a normal component of bloodstream. After you eat, our body digests the fats and repackages the fat as triglycerides, which are released into bloodstream. The blood carries the triglycerides throughout your body to give you energy or

to be stored as fat. Liver also produces triglycerides and changes some into cholesterol. Liver can change any source of excess calories into triglycerides.[12]

Obesity

Obesity can be considered as an abnormal state of lipid metabolism. The numbers of obese people are increasing in developed and even developing countries. Obesity could induce various live-threatening diseases, including type II diabetes, hypertension, coronary heart diseases stroke and certain cancers. The worldwide prevalence of obesity in adults is currently estimated to exceed 300 million.[13]

Optimum range

	Total CH (mg/dl)	Plasma lipid lavel (mg/dl) LDL-CH	TGs (mg/dl)
Optimal/desirable	<200	<100	<150
Borderline High	200-239	130-159	150-199
High	>240	160-189	200-499
High risk	-	>190	>500

Pathophysiology

it is a disease of the arterial wall in which the layer thickens, causing narrowing of the channel and thus, impairing blood flow of the large and intermediate-sized arteries in which fatty lesion called atheromatus plaques develop on the inside surfaces of arterial walls. In contrast, The narrowing is due to the formation of plaques (raised patches) in the inner lining of the arteries. These plaques consist of low-density lipoproteins, decaying muscle cells, fibrous tissue, clumps of blood platelets, cholesterol, Atherosclerosis also causes a great deal of serious illness by reducing the flow of blood in other major arteries.[14]

DIAGNOSIS OF ATHEROSCLOROSIS

You may have been diagnosed with atherosclerosis by your doctor in a number of ways:

- Clinical history: prior angioplasty, cardiac bypass surgery, carotid surgery
- Clinical presentation: heart attack, angina, or stroke
- Physical examination: bruit (noise heard over artery) or absent pulses
- Noninvasive test: ECG, stress test, ultrasound study
- Invasive test: angiogram showing narrowings or obstructions
- Blood test – Lipid Profile,

Detection and Monitoring of Atherosclerosis

Several invasive and noninvasive imaging techniques have been used to detect/diagnose atherosclerotic lesions, facilitate risk stratification, andmeasure atherosclerosis progression and lesionregression in response to lipid-lowering regimens. Some of these are coronary angiography, intravascular ultrasound (IVUS), IVUS-based palpography, angioscopy, intravascular thermography, optical coherence tomography, elastography, magnetic resonance imaging (MRI), computed tomography (CT), B-mode ultrasonography, electron-beam CT, immunoscintigraphy, and molecular imaging. A detailed discussion of these techniques, are mainly research-oriented.[15]

DRUG ARE USED FOR THE TREATMENT OF ATHEROSCLEROSIS

Classification

1. HMG-CoA reductase inhibitors(statins):

Lovastatin, Simvastatin, Pravastatin, Atorvastatin, Rosuvastatin

2. Bile acid sequestrants (Resin):

Cholestyramine, Colestipol

3. Activate lipoprotein lipase (Fibric acid derivatives):

Clofibrate, gemfibrozil, Bezafibrate, Fenofibrate.

4. Inhibit lipolysis and triglyceride synthesis:

Nicotinic acid.

5. Others:

Ezetimib, gugulipid.

6. B- bloker :

Propranolol, Metoprolol, Atenolol

7. Vasodilator:

Hydrlazine, Minoxidil

8. Anticoagulants:

Heparin, Lepirudin.[16]

Most of the cholesterol formed in the liver is converted into bile acids and secreted in this form into the duodenum then, more than 90% of these same bile acids is reabsorbed in the terminal ileum and used over and over again in the bile. Therefore, any agent that combines with the bile acids in the gastro intestinal tract and prevents their reabsorption into the circulation can decrease the total bile acid pool in the circulating blood. This causes far more

of the liver cholesterol to be converted into new bile acids. Thus, simply eating oat bran, which binds bile acids and is a constituent of many breakfast cereals, increases the proportion of liver cholesterol that forms new bile acids rather than forming new low-density lipoproteins and atherogenic plaques. Resin agents can also be used to bind bile acids in the gut and increase their fecal excretion, thereby reducing cholesterol synthesis by the liver. Another group of drugs called statins competitively inhibits hydroxymethylglutaryl-coenzyme A (HMGCoA) reductase, a rate-limiting enzyme in the synthesis of cholesterol. This inhibition decreases cholesterol synthesis and increases low-density lipoprotein receptors in the liver, usually causing a 25 to 50 per cent reduction in plasma levels of low-density lipoproteins.[17,18]

Importance of vitamin in hypolipidemic treatment: Niacin (Nicotinic acid) (vit B_3)

Niacin (but not niacinamide) has a broad lipid-lowering ability, it decrease VLDL and LDL levels, and Lp(a). It often increase HDL levels.[12] Niacin (NYN a sin), a water soluble vitamin, strongly inhibits lipolysis in adipose tissue. It inhibits VLDL secretion, in turn decreasing production of LDL. Increased clearance of VLDL and contributes to reduction of triglycerides. Niacin has no effect on bile acid production. Excretion of neural sterols in the stools in the stool is increased acutey as cholesterol is mobilized from tissue pools and a new steady state is reached. Niacin inhibits the intracellular lipase of adipose tissue via receptor-mediated signaling, possibly reducing VLDL production by decreasing the flux of free fatty acids to the liver.[19-20]

PREVENTION OF ATHEROSCLEROSIS

The most important measures to protect against the development of atherosclerosis and its progression to serious vascular disease are

- Maintaining a healthy weight, being physically active, and eating a diet that contains mainly unsaturated fat with low cholesterol content.
- Preventing hypertension by maintaining a healthy diet and being physically active, or effectively controlling blood pressure with antihypertensive drugs if hypertension does develop.
- Effectively controlling blood glucose with insulin treatment or other drugs if diabetes develops. Avoiding cigarette smoking. Several types of drugs that lower plasma lipids and cholesterol have proved to be valuable in preventing atherosclerosis.

- Avoid smoking Nicotine and other substances in a cigarette are harmful to the arterial wall. Smoking also causes the constriction of the coronary arteries resulting in further reduction of blood flow to the heart muscle.
- Have a medical checkup consult the doctor immediately if you have occasionally chest pain.
- Have enough sleep make a conscious effort to reduce the exposure to excessive stress at work. Meditate or listen to soft music or relaxation tapes.
- Patient Education patient and his or her family member or advocate should be instructed regarding the use of medications and monitoring of symptoms. The purpose, dose, and major side effects of each medication prescribed should be explained.[21]

CONCLUSION

Atherosclerosis is a diseases is caused by the increase the amount of LDL, VLDL in the artery. These disease caused by our indiscipline and inactivity but some time it is hereditary. Today drug are used in the treatment of atherosclerosis are given in huge quantity but Atherosclerosis cannot be properly cured but it can be prevented. It is clear that there are many things we can do to effectively prevent the disease, for example, exercise regularly, eat fat-free food together with fruits and vegetables and fibers food, and avoid smoking and alcohol. From times of year several studies have shown that dietary modifications such as high-fiber diets, low fat diets, diets rich in flavonoids and phenolic acids can reduce metabolic syndrome risk factors. Statins and synthetic antioxidants like probucol are modern anti-hyperlipidemic drugs which are widely used for atherosclerosis it has been focused on the natural products that have very few side effects.[4-6] We hope this information will help you change your life in a positive way to improve your heart's health and to live a fuller, longer and more satisfying life.

REFERENCES

1. Shatt A GF. A Review Article on Hyperlipidemia: Types, Treatments and New Drug Targets. Biomedical & Pharmacology Journal, 2014; 7: 399-409.
2. Verma N. Introduction to Hyperlipidemia and its Treatment: A Review. Int J Curr Pharm Res., 2017; 9: 6-14.
3. Nouh F, Omar M, Younis M. Risk Factors and Management of Hyperlipidemia (Review). Asian Journal of Cardiology Research, 2019; 2: 1-10.

4. Venkateshan S, Subramaniyan V, Chinnasamy V, Chandiran S. Anti-oxidant and Anti-Hyperlipidemic Activity of *Hemidesmus Indicus* in Rats Fed with High-Fat Diet. Avicenna J Phytomed, 2016; 6: 516–525.
5. Anatomy and physiology in health and illness. Ross and Wilson, Anne Waugh. Allison grant. Elsevier, 2006; 9: 112-113.
6. Jyoti S, Kumar PP, Kaur CD. Effect of *Quisqualis indica* Extract on Cholesterol Diet Induced Hyperlipidemia in Rats. Research J. Pharmacology and Pharmacodynamics, 2013; 5: 317-320.
7. Jyoti Sahu J, Patel PK, DubeyB. Effects of Methanolic Extracts of *Quisqualis indica* (Aerial Parts) on Passive Smoking Induced Hyperlipidemia in Rats. Asian J. Pharm. Tech., 2013; 3: 26-29.
8. Tortora Gerard J. and Derricksonbryar, Atextbook of Principles of Anatomy & Physiology, John wiley & sons, 2003; 12: 988-997.
9. Lankin VZ, Tikhaze AK, Kukharchuk VV, Konovalova GG, Pisarenko OI, Kaminnyi AI, et al. Antioxidants decreases the intensification of low density lipoprotein in vivo peroxidation during therapy with statins. Mol Cell Biochem, 2003; 249: 129-40.
10. Mamun MA, Hasan N, Shirin F, Belal MH, Khan MAJ, Tasnin MN, et al. Antihyperglycemic and Antihyperlipidemic Activity of Ethanol Extract of Garlic *(Allium sativum)* in Streptozotocin-induced Diabetic Mice. International Journal of Medical and Health Research, 2017; 3: 63-66.
11. Textbook of medical physiology, guyton Arthur c., & hall john e.elseviere publication, 2006; 12: 848.
12. Garvan c, kane md and James J., Lipskymd "drug Grape fruit Juice" Mayo clinic proceeding, 2000; 933-942.
13. Do ngoc lien, nguyenthuyquynh, nguyen, hoangquang, do van phuc and nguyen, anti obesityandbody weight reducing effect of fortunella japonica pell extract in experimentally obese mice" kkuscijournel, 2009; l: 37.
14. A textbook of principles of pharmacology Thepatho physiologic basic of drug therapy. Golan david E., Tasjiananman H., Armstrong Ehrin J., wolter Kluwer, 2008; 2: 418-423.
15. Nicholls S.J, chhatriwalla A.K., Lundman P., Impact of statins on atherosclerosis plaque, future cardiol, 2007; 3: 157-164.
16. Tripathi K.D., A text book of essential of medical pharmacology, Jaypee medical publishers, 2008; 613-619.

17. Crouse J.R., Grobbee D.E., O'leary D.H., Measuring effect on intima media thickness: evaluation of resuvastatin in subclinical atherosclerosis, Journal of cardiovasc drugs ther, 2004; 18: 231-238.
18. Taylor A, Shaw L.J., Fayd Z., Tracking atherosclerosis regression: A clinical tool in prevention cardioatherosclerosis, 2005; 115: 459-467.
19. Katzung G., A textbook of Basic and clinical Pharmacology, Published by McGraw hill Lange publication, 2007; 10: 568-570.
20. Finkel Richard, Clask Michell A., Luigi X, Cubeddu, A textbook of Pharmacology, Luppincott'swolterskluwer, 2006; 4: 256-258.
21. *Ucla Champ* Ucla Cardiovascular Hospitalization Atherosclerosis Management Program: Champ, January 2001.