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STATIN MEDICATIONS: THEIR MULTIFACETED ROLE IN VARIOUS DISEASE CONDITIONS

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ABSTRACT

Statin, which inhibits HMG-CoA reductase, statins are type of medication to decrease cholesterol, that are frequently used to treat atherosclerotic cardiovascular disease. Given that statins can be accustomed to treat a variety of disorders. One family of drugs called statins is mostly used to reduce blood cholesterol levels. They function by preventing the synthesis of cholesterol by an enzyme. It will be helpful in such types of diseases as cardiovascular disease, hypercholesterolemia, atherosclerosis, familial hypercholesteromia, diabetes, stroke prevention, peripheral artery disease, chronic kidney disease, inflammation, and Alzheimer's disease. In this review, we can understand the recent statin therapy that is more commonly and widely used in different diseases and that is generally useful for further study and research purpose.

Keywords: HMG-CoA reductase inhibitor, statins, roles, diseases

INTRODUCTION:

A class of medications known mostly for their ability to decrease cholesterol, statins have shown promise as adaptable therapeutic agents that play a critical role in the treatment of a number of disorders other than hypercholesterolemia. Because they are effective in treating a variety of medical disorders, these drugs, which block the enzyme that produces cholesterol, have completely changed the face of modern

medicine. An overview of the changing function of statins in various diseases is given in this introduction, which also highlights the wide range of applications and possible advantages they may have for various health issues. The main purpose of statin prescriptions, which include popular names like Atorvastatin (Lipitor), Rosuvastatin (Crestor), and Simvastatin (Zocor), is to lower LDL (low-density lipoprotein) cholesterol levels. Among the primary risk factors for cardiovascular illnesses, such as heart attacks and strokes, is elevated low-density lipoprotein (LDL). Statins contribute to lowering low-density lipoprotein cholesterol or, consequently, the risk of atherosclerosis, atherosclerotic cardiovascular disease, and its aftereffects by blocking the synthesis of cholesterol. Additionally, statins must lower blood levels of bad cholesterol and have a reducing effect on the body. They also have a moderate effect on elevating high-density lipoprotein cholesterol, or good cholesterol. Statins must enhance heart health overall and provide a preventative strategy for this kind of illness. Statin which are more generally prescribed because of their less side effect and cost effective to the diseases patients **[1, 2]**.

Statin Mechanisms of Action

The following mechanisms are involved in the current purpose of statin therapy. HMGCR in hepatocytes is inhibited by statins.3-hydroxy3-methylglutaryl-coenzyme A (HMG-CoA) is converted to melvalonic acid, which is an initiator in the synthesis of new cholesterol biosynthesis route, by HMGCR the enzyme that sets the pace for the hepatic cholesterol synthesis pathway. Statins additionally the endogenous substrate engage in reversible competition.

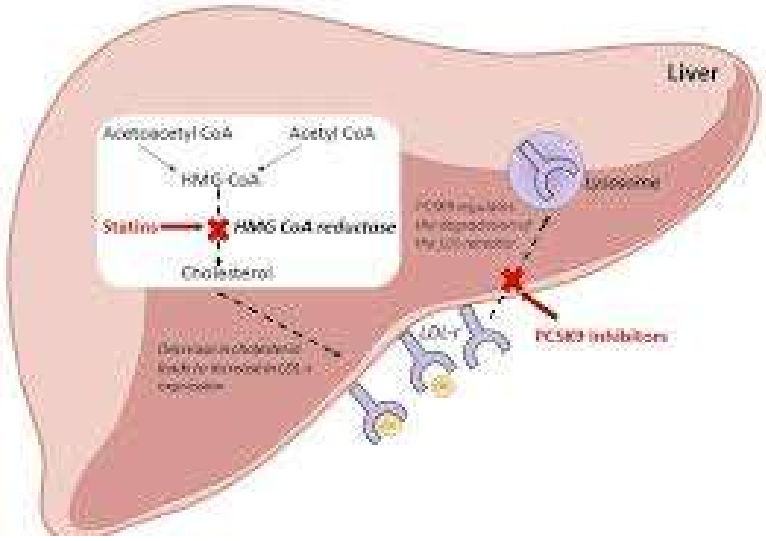

Figure 1: Mechanism of action of Statins

HMG-Coenzyme A, for the reductase's operative site. The function of the enzyme is attenuated when the statin binds to an enzyme's active site, the enzyme's structure changes. Higher-affinity statins function as competitive antagonists by attaching to enzyme's active site as well as blocking the binding of HMG-CoA, a lower-affinity endogenous substrate. Hepatocytes produce less cholesterol and have fewer intracellular cholesterol reserves as a result of the ensuing conformational shift and inhibition of HMGCR. A protease is activated in the endoplasmic reticulum to try to maintain homeostasis and counteract this drop in intracellular cholesterol by cleaving the sterol regulatory element-binding protein (SREBP) from its protein precursor.Following unbinding, the SREBP is moved to the nucleus. The component that controls sterols (SRE) found in the gene's promoter regions which producing low-density lipoprotein receptor is bound by SREBP in the nucleus. Increased synthesis of low-density lipoprotein receptor protein and increased expression of low-density lipoprotein receptor mRNA are the results of improved translation of the low-density lipoprotein receptor gene. The hepatic low-density lipoprotien receptor protein develops and has constitutive exocytosis in response to hepatocyte surfaces. After low-density lipoprotein cholesterol is endocytose and broken down by lysosomes in the hepatocyte, free low-density lipoprotein cholesterol binds to newly synthesised LDL-R. Intracellular cholesterol levels rise as a result of low-density lipoprotein cholesterol internalisation, which also encourages low-density lipoprotein cholesterolto return to homeostatic values. This sequence of events culminates in a decrease in circulating low-density lipoprotein cholesterollevels, which is primarily caused by an increase in the surface density of hepatic low-density lipoprotein receptor cells **[1, 8, 10]**.

Table 1: Statin and Cholesterol-Reduction Medicines [10]

Generic name	Brand name	Typical dose	Dosage form
Statins			
Atorvastatin	**Lipitor**	**10 mg** **20 mg**	**Tablet**
Fluvastatin	**Lescol** **Lescol XL**	**40 mg** **80 mg**	**Capsule** **ER tablet**
Lovastatin	**Altoprev**	**40 mg**	**Tablet**
Pravastin	**Pravachol**	**40 mg** **80 mg**	**Tablet**
Rovustatin	**Crestor**	**5 mg/10 mg**	**Tablet**
Ezetimibe	**Zetia**	**10 mg**	**Tablets**
Alirocumab	**Praluent**	**75 mg/ml every 2 weeks**	**Injection**
Evolocumab	**Repatha**	**140 mg/ml every 2 weeks**	**Injection**

Goals of Statin Therapy

Preclinical research and clinical studies support the use of statins to either cure the beginning of ASCVD or delay its progression. Here, it was clearly demonstrated how elevated levels of LDL-C, or low-density lipoprotein cholesterol are linked towards the creation of ASCVD and how effective statin medications are at improving patient results by decreasing LDL-C levels and the frequency and occurrence of deaths linked to ASCVD. overall. The use of statins as a primary preventive therapy enables high-risk patients to keep their LDL-C levels within normal limits. Statins are used as secondary prophylaxis in individuals with ASCVD because they effectively lower LDL-C levels and lower the chance of a catastrophic cardiac occurrence.

Statin Therapy in Coronary Artery Disease [1, 2, 7, 15]

Statin has been demonstrated that statins dramatically lower cardiovascular clinical events in a range of patients. Moreover, compared to standard therapy, intense statin therapy has a greater clinical benefit. 80 mg of atorvastatin, taken between 24 and 96 hours after hospital admission decreased the risk of death, myocardial infarction, cardiac arrest, and recurrent ischemia.CAD patients may be prescribed high-dose statins, like rosuvastatin or atorvastatin which reduce plaque buildup in the arteries. Lovastatin typically has fewer comorbidities. However, no trend towards prescribing a specific statin to patients who were healthier or sicker was found. With respect to the distribution of daily dosages. In the majority of cases, smaller statin doses (10–20 mg) were prescribed, which are roughly similar in terms of reducing LDL-C levels. Very few patients received the maximum dosage of any statin.

The treatment of neurodegenerative diseases with statins [3].

Statins are being used to treat a variety of neurological conditions, such as Parkinson's and Alzheimer's illnesses Alpha-synuclein (α-S), a presynaptic neuronal protein that normally binds to plasma membranes, aggregates and that is implicated in the aetiology of Parkinson's disease. Further more, elevated cholesterol levels are linked to the advancement of the disease, and statins can lessen α-S aggregation and neuropathology in Parkinson's disease animal models. Parkinson's disease incidence may be decreased by statin use.That is, lower the effect of Parkinson in disease patients.

Elevated cholesterol levels are linked to the advancement of the disease and the development of plaques, which are a fundamental feature of Alzheimer's disease.

There is no difference in cognitive deterioration between patients receiving statin medication (pravastatin and/or simvastatin) for at least 12 months.

Statins can be used to prevent strokes [1, 4, 12, 13]

Strokes happen when there is a reduction in blood flow to the brain, which kills off neurons. Affected brain regions frequently cause symptomatic dysfunction in body parts under their control as a result of this cell death. There are two primary types of strokes: ischemic (more common) and hemorrhagic.The former is caused by a blood flow obstruction, while the latter is brought on by harmful pressure that results from the brain's arterial blood vessels rupturing. Moreover, embolic stroke and thrombotic stroke are the two additional causative subtypes of ischemic stroke. Thrombotic stroke is brought via the creation of a thrombus in an arterial supplying the brain, and it is frequently linked to hypercholesterolemia and atherosclerosis. To prevent the incidence and severity of stroke, statin-induced lowering of cholesterol concentrations has been demonstrated to reduce the risk of stroke. The relative risk of stroke decreased by in LDL cholesterol. The choice of statin can vary depending on specific characteristics. Statins are frequently administered to lower the risk of stroke. The two statins that are currently on the market that are frequently used to prevent stroke are rosuvastatin (brand name Crestor) and atorvastatin (brand name Lipitor). These two statins have demonstrated effectiveness in lowering cholesterol and offering cardiovascular advantages, which can help reduce the risk of stroke in cases where elevated cholesterol is a significant cause. Depending on the patient's health, cholesterol levels, and medical history, an exact decision between atorvastatin and rosuvastatin as well as the dosage will be madeand different types of dosage tablets are available in Market.

Statins are effective in treating bacterial infections [1, 9]

The ability of statins to control immune responses and inflammation may help avoid the onset of a number of illnesses, such as bacterial infections of the host, sepsis, TB, and listeriosis. In respect to bacterial infections, statins appear to control the expression of extracellular receptors involved in the adhesion and absorption of particular bacteria. Statins can reduce the secretion of proinflammatory cytokines and hinder bacterial movement and biofilm formation.Statins inhibited the ability of Mycobacterium TB, the causative agent of tuberculosis in the majority of cases, to impair

immune cell development. Likewise, the administration of statins prior to Listeria monocytogenes infection reduced the bacteria's capacity to evade the immune response by preventing them from escaping phagosomes.These items show how statins may be used to treat and prevent bacterial infections.Advanced Pharmaceutical Industries kindly donated rosuvastatin, atorvastatin, and simvastatin. The DMSO was used to dissolve the drugs (rosuvastatin, atorvastatin, and simvastatin) to a 1 mg/ml stock concentration. for minimum inhibitory concentration analysis. Every medication was a raw material. To aid in the drug's dissolution, DMSO was employed. DMSO without statin was used as a negative control since DMSO is known to have no inherent antibacterial activity.

Statins are used in familial hypercholesterolemia [11, 18]

A crucial enzyme in the liver's production of cholesterol, hydroxyl-methylglutaryl coenzyme A reductase, is specifically inhibited by statins. Subsequently, the protein that binds to sterol regulatory elements 2 is activated, a transcription factor that in turn increases the production of LDL receptors. Triglyceride-rich lipoproteins and other apoB-containing lipoproteins, such as low-density lipoprotien, are taken up from the circulation more frequently as a result of this upregulation.

The statins lovastatin, simvastatin, fluvastatin, atorvastatin, rosuvastatin, and pitavastatin are now available on the market. Depending on the type and dosage of statin, the LDL cholesterol-lowering effects range from 30% to 60% . LDL cholesterol can be lowered by 50–60% with high-intensity statin therapy (e.g., atorvastatin 40–80 mg/day or rosuvastatin 20–40 mg/day), whereas moderate-intensity statin therapy (e.g., atorvastatin 10–20 mg/day or pravastatin 40–80 mg/day) can produce 30–40% less cholesterol. Pitavastatin, the newest statin on the market, lowers low-density lipoprotein (LDL) cholesterol by 30–45% at daily doses of 1–4 mg.

Statin is used in chronic kidney disease [16, 17]

The progressive, long-term decline of kidney function over time is the hallmark of chronic kidney disease (CKD). The kidneys are essential for controlling blood pressure, preserving electrolyte balance, and filtering waste and extra fluid from the blood. In its early stages, CKD frequently goes undiagnosed and usually progresses slowly. High blood pressure, certain hereditary factors, and diabetes are the most typical reasons of persistent kidney disease.

Complications comprise fluid retention, electrolyte imbalances, anaemia, and an elevated risk of cardiovascular disease that might arise as the disease advances. When chronic kidney disease (CKD) worsens, it can progress to end-stage renal disease (ESRD), which is characterized by profoundly reduced kidney function and the need for dialysis or kidney transplantation.

In individuals with chronic kidney disease (CKD), statin therapy is widely used to manage excessive cholesterol and reduce the risk of cardiovascular events. The following statins are frequently used, while the selection of a statin.

1. Atorvastatin (Lipitor): To lower loe-density lipoprotien cholesterol levels and lower the risk of cardiovascular events, CKD patients frequently take atorvastatin.
2. Rosuvastatin (Crestor): Due to its efficiency in decreasing cholesterol, rosuvastatin is another statin that is commonly used in patients with CKD. Based on renal function, cholesterol levels, and other medical factors, a customised statin dosage and choice should be made.

CONCLUSION:

The review provides a thought-provoking analysis of various chemical agents and their effectiveness. Researchers are able to assess prospective treatment strategies and get a deeper comprehension of the pathogenesis of diseases by using statin therapy.These medications' drawbacks have also been explored, which can direct further study and drug development.Overall, this analysis advances our knowledge and comprehension of disease. It is emphasized how crucial it is to use in different diseases because it enables scientists to evaluate particular components of the illness and perhaps even discover novel treatments that could be used in clinical settings.

This review paper, in my opinion, is highly beneficial for anyone looking to learn more about statin therapy in different diseases. It provides valuable information about the use of different statins in different diseases.This can open the door for more improvements in the comprehension and treatment of this disorder.In the end, having this knowledge may result in better patient outcomes and a higher standard of living.

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