



A Study of the Role of Statins in the Treatment of Coronary Heart Disease

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Abstract: Statins, as hydroxymethylglutaryl coenzyme A reductase inhibitors, have a significant effect on lowering cholesterol, and are widely used in the clinical treatment of cardiovascular and cerebrovascular diseases, and are potent drugs for the prevention and treatment of coronary heart disease. Recent studies have shown that statins also have other effects, such as lowering blood pressure, lowering blood glucose, stabilizing atherosclerotic plaques, slowing down the proliferation and migration of smooth muscle cells, anti-inflammatory and antihypertensive, etc., which are very significant. This paper addresses the physicochemical properties, pharmacological effects, adverse effects, and therapeutic applications of statins in the treatment of cardiovascular diseases (coronary heart disease).

Keywords: statins, coronary heart disease treatment, review

1. Statins

In the history of medicine, penicillin has played a pivotal role in saving countless lives, and is therefore known as the "miracle of modern medicine". The Japanese chemist Endo Sho admired Fleming, the inventor of penicillin, and was very interested in the study of bacterial metabolism. He speculated that some microorganisms might produce HMG-CoA reductase inhibitors, which could inhibit cholesterol synthesis. After countless arduous experiments, Chapter Endo finally discovered mevastatin derived from *Penicillium citrinum*, a compound that can competitively inhibit the blocking of cholesterol synthesis and achieve cholesterol-lowering effects. In the 1950s, American physiologist Ancel Benjamin Keys pointed out that blood cholesterol level is one of the main culprits of coronary atherosclerosis in heart disease through long-term cardiovascular disease epidemiological research in many countries. According to the World Health Statistics Report 2017 released by the World Health Organization (WHO), 56 million people died worldwide in 2015, of which 17.7 million died of cardiovascular disease, which is known as the "number one killer" of human mortality. Statins are the most common clinical drugs used in the treatment of these diseases, such as atorvastatin and simvastatin, which play an important role in the treatment of coronary heart disease and other cardiovascular diseases.

1.1 Molecular formula, physical and chemical properties

The chemical structure of statins, i.e., 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, is roughly divided into three parts: first, the 3,5-dihydroxyheptanoic acid structural fragment similar to that of the natural substrate, HMG-CoA, and the 3-hydroxypentolactone ring, which is able to be converted into an effective hydroxy acid by opening up the ring after administration of a statin in vivo. The second is the hydrophobic ring structure covalently attached to 3,5-dihydroxyheptanoic acid, which plays an important role in the binding of the drug to reductase; the third is the substituent group on the ring, which determines the solubility and pharmacokinetic properties of the drug. Most statins have strong lipid solubility, and most of the commercially available statins are either sodium or calcium salts; those that are sodium salts are soluble in water, while those that are calcium salts have lower solubility in water.

1.2 Pharmacological effects

The first is a significant hypolipidemic effect. Hydroxymethylglutaryl coenzyme A reductase is an essential enzyme in cholesterol synthesis, and statins are able to inhibit the specific competition for this enzyme, which can reduce cholesterol synthesis, lowering the level of selected LDL-C (low-density lipoprotein cholesterol) and TC (total cholesterol). At the same time, these drugs enhance receptor expression for LDL (low-density lipoprotein) on surface cells, facilitating the clearance of LDL and VLDL (very low-density lipoprotein) residues. Therefore, statins are mainly used in the clinical treatment of hypercholesterolemia and other diseases, and have a very significant lipid-regulating effect. Secondly, they have a significant blood pressure lowering effect. Numerous experimental studies have shown that compared to the use of other drugs, statins provide better control of blood pressure, keeping it around 140/90 mmHg. In addition, statins have several effects such as improving skin cell function, promoting smooth muscle cells, proliferation maintaining atherosclerotic plaque stabilization.

1.3 Adverse Reactions

Because statins have all the above pharmacological effects, they are widely used in the treatment of stroke, coronary heart disease, hypertension, tumors and other diseases. In a large number of clinical treatment practices, statins have been found to be highly tolerable and safe, but they can also produce adverse reactions, such as constipation, rash, abdominal pain, indigestion, influenza-like symptoms, etc. However, this will not affect the overall therapeutic effect, and can be recovered on its own after stopping the drug. In a very small number of patients, liver function abnormalities or myopathy may occur after taking statins. If these conditions occur, it is necessary to stop taking the drug immediately and check the serum creatine kinase of the person taking the drug, so as to replenish the coenzymes in time and quickly relieve the clinical symptoms. If the patient himself has abnormal thyroid function or abnormal liver and kidney function, especially in elderly and severe infectious patients, the risk of myopathy will be significantly increased after taking statins. In addition to this, in the case of patients with sepsis, seizures and major surgery, we do not recommend statins to continue treatment.

2. Coronary heart disease

2.1 Overview of coronary heart disease

Coronary heart disease, known as coronary atherosclerotic heart disease, or sometimes called ischemic heart disease, is the Coronary artery Atherosclerosis causes myocardial ischemia and hypoxia caused by heart disease The coronary arteries are the only supply of blood to the heart. The coronary arteries are the only arteries that supply the heart blood The coronary arteries are the only blood vessels that supply blood to the heart. blood vessels They are called coronary arteries because of their crown-like shape. coronary arteries Coronary arteries are called coronary arteries because of their coronary-like shape. This blood vessel also hardens along with the blood vessels throughout the body, showing atherosclerotic changes that cause the blood supplying the heart to Blood circulation This causes atherosclerotic changes in the blood supply to the heart, resulting in blood circulation obstacles, causing myocardial ischemia and hypoxia, that is, coronary heart disease. Coronary heart disease is a common disease and It is a common disease among middle-aged and elderly people It seriously jeopardizes human life. Most people usually do not have any Symptoms and work, study and live as usual, but often have signs of myocardial ischemia, such as if they feel pre-cardiac discomfort or Weakness If you feel discomfort or fatigue in the front of the heart, you should have an Electrocardiogram (ECG) If you feel pre-cardiac discomfort or fatigue, you should have an ECG in time to prevent it as early as possible.

2.2 The role of statins in the treatment of coronary heart disease

Coronary artery disease is usually treated in three ways, depending on the severity of the disease: medication, surgery and external counterpulsation. The most common of these is drug therapy. It is found that during the development of coronary heart disease, patients may experience symptoms such as myocardial ischemia and hypoxia, and the clinical manifestations of the treatment process are chest tightness and shortness of breath, palpitations and panic attacks, angina pectoris, etc., and statins have the effects of anti-angina, anti-arrhythmia, and anti-heart failure. In addition, coronary heart disease is caused by coronary atherosclerosis, and statins can effectively reduce the lipid content of atherosclerotic plaques, reduce the content of protein hydrolyzing enzymes to maintain the stability of atherosclerotic plaques. At the same time, statins have a significant role in lowering blood lipids, blood pressure, blood sugar, and patients with coronary heart disease are often accompanied by high blood pressure, high blood lipids and high blood sugar. Statins are also hydroxymethylglutaryl coenzyme A reductase, which can effectively reduce cholesterol synthesis and alleviate the patient's condition. In summary, statins have an important role in the treatment of coronary heart disease.

2.2.1 Lowering lipid indices in patients with coronary heart disease

Abnormal blood lipid index refers to the total cholesterol, triglyceride, LDL cholesterol exceeding the normal range or HDL cholesterol lower than the normal level in the blood, which is the main cause of coronary heart disease. For the treatment of patients with hyperlipidemia, clinics generally use Betaine and Niacin, etc., but their efficacy varies and they are not able to provide comprehensive treatment. The latest research shows that statins have a very good therapeutic effect on patients with coronary heart disease who have abnormal blood lipid indexes. In the experiment, researchers found that statins can slow down the smooth muscle cell proliferation and migration, but also by controlling platelet damage to blood vessels to regulate. Most critically, in the treatment of patients with hyperlipidemia, statins can inhibit the rate-limiting enzyme of cholesterol synthase - HMG-CoA reductase, thus reducing the synthesis of cholesterol in the liver, and then reduce the free cholesterol content in the cells, which is favorable for the increase of LDL cholesterol receptors in the cells, and promote its activity to enhance the blood circulation of LDL cholesterol. Statins can accelerate the clearance of LDL cholesterol from

the circulation and ultimately lowering plasma triglyceride and LDL cholesterol levels. Therefore, statins are proved to be the most ideal lipid-lowering drugs.

2.2.2 Reducing blood pressure indicators in patients with coronary heart disease

At this stage, the prevalence of coronary heart disease combined with hypertension is increasing year by year in China, which has a very close relationship with people's poor living habits and dietary structure. Coronary heart disease combined with hypertension is one of the very serious cardiovascular diseases, which seriously affects the quality of life of patients and jeopardizes their life safety. Currently commonly used drugs for the treatment of hypertension are diuretics, β -receptor antagonists, calcium channel antagonists, etc. Clinicians often combine statins and antihypertensive drugs, and through comparative experiments, it can be concluded that statins have a good efficacy in lowering the blood pressure index of patients with coronary heart disease - treatment of hypertension, set up group A as the conventional therapy Group B was given Rosuvastatin on the basis of 1 time/d, 20 mg/time, and after 4 weeks of comparison, group B's blood pressure decreased greatly, and the improvement was more obvious than that of group A, confirming the exact efficacy of Rosuvastatin.

2.2.3 Anti-inflammatory effects

Atherosclerosis is a chronic inflammatory response in which inflammatory cells allow inflammation to seep out by traversing or adhering to vascular endothelial cells, exerting vascular endothelial cell adhesion molecules and leukocytes gradually interacting with each other. In one study, when atorvastatin was applied to treat patients with chronic heart failure and blood cholesterol >22 mg/L, serum levels of inflammatory factors such as Svcam-I and interleukin-6 were reduced. In the treatment of acute coronary syndrome (ACS), atorvastatin, when administered in high doses, exerts a strong anti-inflammatory effect, and plasma MMP-9 and hs-CRP levels are significantly reduced, suggesting that in addition to being effective in lipid regulation, it also has a strong anti-inflammatory effect, which results in a significant reduction in the chances of adverse cardiovascular events. In the study, the difference of various inflammatory indexes between the two groups of patients before treatment was not obvious; while the C-reactive protein (CRP), low-density lipoprotein (LDL-C), serum total cholesterol (TC), triacylglycerol (TG) levels of the patients in the observation group after treatment showed a significant downward trend compared with those before treatment; high-density lipoprotein cholesterol (HDL-C), nitric oxide (NO) levels of the patients after treatment compared with those before treatment HDL-C and nitric oxide (NO) levels increased significantly after treatment compared with before treatment, and the difference was statistically significant ($P < 0.05$). In the control group, there was no statistically significant difference in the levels of the above indicators after treatment compared with those before treatment, with $P > 0.05$, which was not statistically significant. This study suggests that atorvastatin has better anti-inflammatory effects in the treatment of coronary artery disease than conventional internal medicine treatments.

2.2.4 Stabilization of atherosclerotic plaques

During atherosclerotic plaque formation, peroxidation, lipid accumulation, and chronic inflammatory stimuli, contribute to it, and plaque rupture induces platelet aggregation and causes thrombosis, leading to acute coronary syndrome (ACS). Application of statins increases TGF-B synthesis within VSMCs, upregulates TGF-B receptor II levels, strengthens the TGF-B/smad pathway, enhances the susceptibility of VSMCs to TGF-B-mediated apoptosis, and facilitates TGF-B-mediated extracellular matrix accumulation, resulting in atherosclerotic plaques that tend to stabilize.

3. Summary and outlook

In summary, statins are widely used in the treatment of cardiovascular diseases with satisfactory efficacy by virtue of their effective anti-inflammatory, stabilizing atherosclerotic plaque, improving vascular endothelial function, preventing thrombosis, and lowering blood pressure, blood lipids, and blood glucose. Statins are well tolerated and the discontinuation rate due to adverse reactions is low. However, it is still necessary to do a good job of close observation during the medication period, consulting patients for muscle symptoms, and being alert to the side effects of medication, to promote the safety and effectiveness of medication, and to ensure the efficacy of the treatment. Due to its more varieties of drugs, there are still subtle differences in the pharmacological effects and strength of each drug, leading to some problems in its clinical application. Therefore, when applying statins, it is important to make a reasonable assessment of the patient's condition, control the dosage and type of medication, not to ignore the adverse phenomena that may be caused by the drug, continuously monitor the patient's condition and deal with the anomalies immediately when they are detected, so as not to jeopardize the patient's health and safety. In order to safely promote statins, we need to continue to deepen our research and explore their potential value, thus laying a solid foundation for clinical treatment.

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