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Review Article

Unclogging the heart: the potential of statins to reverse coronary artery blockage

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ABSTRACT

Acute coronary syndrome (ACS) comprises three life-threatening cardiovascular conditions-unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI)-all characterized by reduced myocardial blood flow leading to ischemia and potential cardiac tissue damage. Established risk factors for ACS include age over 50, smoking, obesity, diabetes mellitus, and hypertension. Statins, a cornerstone in cardiovascular disease management, function by inhibiting HMG-CoA reductase, a key enzyme in hepatic cholesterol synthesis. Beyond lipid-lowering, emerging evidence supports their role in stabilizing and regressing atherosclerotic plaques. This narrative review explores the impact of statin therapy on arterial blockages associated with ACS. Data from multiple clinical trials and studies indicate that statins significantly reduce both morbidity and mortality in ACS patients. Notably, intensive statin regimens, particularly with rosuvastatin, have demonstrated greater efficacy in inducing plaque regression and improving plaque stability compared to standard therapy. In summary, statins are integral to the acute and long-term management of ACS, offering both anti-inflammatory and plaque-stabilizing effects. Their ability to reverse atherosclerosis, especially with high-intensity therapy, underscores their essential role in reducing adverse cardiovascular outcomes. The robust evidence supporting their use highlights the necessity of early initiation and sustained administration in ACS patients to improve prognosis and survival.

Keywords: Acute coronary syndrome, Statins, Myocardial infarction, Unstable angina, Stable angina, Cholesterol

INTRODUCTION

Acute coronary syndrome (ACS) is a critical medical emergency marked by the abrupt blockage of the heart's blood flow, leading to a lack of essential nutrients and oxygen reaching the heart muscle. This blockage is often due to plaque buildup known as atherosclerosis in the coronary arteries, resulting in heart muscle ischemia or possibly a blood clot forming. Atherosclerosis is a progressive disease characterized by the accumulation of fatty deposits, cholesterol, calcium, and other substances on inner walls of arteries. Pathogenesis of atherosclerotic plaque formation is a complex and multifaceted process that involves dysfunction of endothelium, lipid accumulation, inflammation and smooth muscle cell proliferation.[1-3] Prompt intervention and targeted therapies to combat these processes are essential for preventing and treating atherosclerosis causing damage to heart. ACS encompasses various conditions, including STEMI, unstable angina, and NSTEMI.[4]

Chest discomfort or pain is the most frequent indication of ACS, possibly spreading to the neck, jaw, shoulder, or arm. Additional symptoms may involve shortness of breath, nausea, sweating, and dizziness. Risk factors for ACS include smoking, high blood pressure, high

cholesterol, diabetes, obesity, and a sedentary lifestyle. Additionally, a family history of heart disease, as well as factors such as race, age, sex, and ethnicity, can further elevate the risk of developing ACS.[5]

Diagnosing ACS requires a comprehensive evaluation of patient's medical history, thorough physical examination, blood tests to measure troponin levels, and imaging procedures such as an electrocardiogram or angiography.[6]

Treatment for ACS typically consists of a combination of medications to prevent blood clotting, lower blood pressure, manage cholesterol, alleviate pain, and optimize oxygen levels. In specific circumstances, invasive procedures like PCI or CABG may be required to enhance myocardial perfusion and alleviate ischemia within the coronary arteries.[7-9]

Furthermore, it is crucial to emphasize lifestyle modifications to prevent further episodes of ACS. A healthy diet, incorporating relaxation techniques, and regular exercise are critical components of a comprehensive plan for long-term heart health.[10] Timely identification and management of ACS can significantly enhance patient outcomes and mitigate the likelihood of adverse outcomes.[11]

MECHANISM OF ACTION OF STATINS

Statins exert their pharmacological effects by reducing cholesterol biosynthesis, primarily in the liver.[12] Statins are inhibitors of hydroxymethylglutaryl-CoA (HMG-CoA) reductase enzyme and thus help in reducing cholesterol in the body.[13] Cholesterol synthesis starts with the conversion of HMG-CoA to mevalonic acid. The enzyme responsible for this conversion is HMG-CoA reductase. Mevalonic acid is then converted to cholesterol via a series of intermediate reactions. Cholesterol is packed in VLDL particles and released from cells. Statins being HMG-CoA reductase inhibitors, competitively inhibit the HMG-CoA reductase enzyme thus inhibiting de novo cholesterol synthesis leading to a decrease in the intracellular supply of cholesterol and a decrease in VLDL secretion. Depletion of intracellular cholesterol levels enhances gene expression and synthesis of LDL receptors which leads to an increased uptake of LDL cholesterol by the cell and a decrease in plasma LDL levels. By reducing plasma LDL levels, statins positively help in preventing the buildup of plaque in arteries. The inhibition of HMG-CoA reductase also has beneficial pleiotropic effects. These effects include controlling cell growth and differentiation, which are essential processes in maintaining overall health.[11] Some of the commonly used statins include atorvastatin, rosuvastatin, simvastatin, lovastatin, and pravastatin.

STATIN AND REVERSAL OF CORONARY ARTERY BLOCKAGE

This paper focuses on the efficacy of rosuvastatin and atorvastatin on the regression of coronary artery plaque. The database of PubMed, EMBASE, and Cochrane was used and 5910 pts with CHD were identified. Regression of CAP may occur from intensively lowering LDL-C (mean rosuvastatin 33 mg/dL and mean atorvastatin 60 mg/dL) during a period of >17 months. LDL-C level reduction should be greater than 40% or reach a goal level of <78 mg/dl for regressing CAP.[14]

One of the studies focused on RCT on 60 pts with rosuvastatin for 1 year. Plaques were followed up by MRI. Both thoracic and abdominal plaques were followed up. In summary, the trial showed that, in comparison to standard therapy, intense lipid-lowering with rosuvastatin resulted in additive plaque regression with thoracic plaques showing more regression.[15] As a result, rosuvastatin's anti-inflammatory and LDL-C lowering properties may offer long-term benefits to people at elevated risk.

The research, which was conducted as a subset of the COSMOS study, aimed to examine the effects of rosuvastatin on lipid levels, drug tolerance, and the influence of prior lipid-lowering therapy in Japanese CAD patients.

Key discoveries include: Rosuvastatin treatment resulted in notable enhancements in lipid parameters such as increased HDL-C, reduced LDL-C, and better LDL-C/HDL-C ratio. Patients with lower initial HDL-C levels experienced greater increases in HDL-C levels. Overall, these findings suggest that rosuvastatin effectively improves lipid profiles and contributes to plaque regression in Japanese CAD patients.[16]

One of the studies on statin use in STEMI patients. IVUS and RF IVUS were performed on two noninfarct-related epicardial arteries for 103 patients after successful PCI. Treated with 40 mg/day of rosuvastatin for 13 months. In summary for individuals with STEMI, high-intensity rosuvastatin medication administered over 13 months is linked to the regression of coronary atherosclerosis in arteries unrelated to infarcts, without affecting the RF-IVUS-defined necrotic core or plaque profile.[17]

Endothelial dysfunction leads to atherosclerosis. The research focused on the effect of long-term rosuvastatin therapy on endothelial function in inflammatory joint disease patients and atherosclerosis. Eighty-five statin naive pts with a carotid plaque were given rosuvastatin for 18 months and a linear regression model was used for correlation. Long-term rosuvastatin-assisted lipid lowering enhanced endothelial function in IJD patients with established atherosclerotic disease. The improvement in endothelial function was longitudinally linked with decreased arterial stiffness and CP regression.[18]

The challenger trial assessed the effects of rosuvastatin on carotid plaque and volume using high-resolution MRI. A prospective open-label blinded endpoint trial was performed on 52 patients after administrating rosuvastatin 5 mg/day. The data was available for 38 patients after 24

months. No change in plaque volume by MRI, but a significant regression of lipid-rich plaque was observed with rosuvastatin treatment. Moreover, the percentage decrease in LRNC volume was positively correlated with the reduction in LDL-C. These results demonstrate that statin therapy's decrease of LDL-C has a positive impact on the composition of plaque as measured by MRI.[16]

One of the studies focused on the effect of 10 mg rosuvastatin vs 20 mg atorvastatin in lowering lipid levels, elevating ABI index and carotid artery IMT.6 months of treatment showed that rosuvastatin was more effective than atorvastatin. The outcomes demonstrate that statin medication can cure atherosclerotic plaques and improve peripheral atherosclerosis.

One of the studies focused on the carotid plaque height in patients with inflammatory joint diseases. Rosuvastatin was used for eighteen months. Carotid plaque height was evaluated by B-mode ultrasound. There was no correlation between LDL exposure and carotid plaque height. Conclusions: In individuals with IJD, intensive lipid lowering with rosuvastatin led to CP height regression and a significant reduction in LDL-C. The degree of CP height decrease was unaffected by the LDL-c objective being met, changes in LDL-c, or exposure to LDL-c levels during the study period.[19]

One of the nonrandomized studies involved 48 patients and 51 atherosclerotic sites. For a year patients were treated with either simvastatin (20 mg daily n=24) or rosuvastatin (10 mg daily, n=24) for the same period. There was a decrease in fibrous and fibro fatty volumes of plaque. Rosuvastatin halted necrotic core progression.[20]

A prospective study in which 36 patients with ACS are enrolled. Effect of statin on plaque composition by IVUS after six months of ACS is seen. Plaques were of two types: thin cap fibro atheroma (TCFA, n=20) and no thin cap fibro atheroma (n=26). Reduction of lipid core percentage was seen in TCFA but not in non-TCFA.[21]

One of the studies compared 43 males and 5 females between 39 and 81 years of age. Six patients in the statin group and 8 patients in the other group didn't use statin. The study showed that statin use reduces aortic shear stress and stabilizes the plaque.[22]

Patients with acute MI are at risk of recurrent coronary events due to unstable coronary plaque. Initiating statins in the early period helps stabilize vulnerable plaque due to their pleiotropic effects.

The impact of statins on plaque morphology is assessed by OCT (optical coherence tomography) in DM patients of combine trial. The 391 patients were taken, and 82 had no statin at baseline. OCT was performed in 463 lesions of which 96 lesions were assessed in the statin naïve and 367 lesions in the statin-treated group. The study concluded that without statin treatment showed more vulnerable and unstable plaque features like thinner fibrotic cap, wider lipid arc, and higher prevalence of lipid-rich plaque, TCFA (Thin cap fibro atheroma), and higher prevalence of plaque rupture. So, statins help in stabilizing atherosclerotic lesions.[23] Statins along with reducing LDL-cholesterol can stabilize atherosclerotic plaque too.[3]

Twenty-nine hypercholesterolemic patients with coronary heart disease were treated with atorvastatin (10-20 mg/day) for eighty weeks. There were two groups high-grade yellow coronary plaques and low-grade yellow plaques. IVUS was used for measuring. Both plaque stabilizing and regression were seen but the plaque stabilizing effect of atorvastatin was stronger for more vulnerable high-colour grade plaque.[2]

The Saturn employed serial IVUS in 1039 patients treated daily for a year with rosuvastatin 40 mg or atorvastatin 80 mg. The study provided that high-intensity statin treatment is associated with regression and stabilizing of ELP (Echolucent plaque) and AP (attenuated plaque).[1]

CONCLUSION

After reviewing various articles, we came to the conclusion that in fifty-four percent statins reverse the blockage while in thirty percent statins stabilize the plaque and in fifteen percent both stabilizing and reversal of plaque were seen. Statins, a lipid-lowering agent, is a powerful drug that can be used in the treatment of patients with ACS aiming for the reversal of coronary blockage. Statin, HMG Co-A reductase inhibitor works by reducing LDL-C, and VLDL, increasing HDL-C and thereby maintaining LDL-C/HDL-C ratio. This mechanism not only shows significant breakdown of plaque but also inhibits de novo cholesterol synthesis which prevents further formation of plaques. Furthermore, Statins having limited adverse effects show excellent prognostic outcomes in the management of ACS patients of all age groups regardless of sex and race. Thus, Statin treatment overall impacts lowering all-cause mortality caused by cardiovascular disease. Future research should be engaged in large-scale clinical trials of statins for ACS with better prospects of safety, efficacy, and optimal dosage.

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