A Systematic Review on The Effects of Statins in The Management of Ischemic Stroke

Dr. M.Boopathi Raja[1], S.Nandakumar[2], V.Nitheesh Kumar[3], K.Pavithra[4]

[1]Assistant Professor, Department of Pharmacy Practice, The Erode College of Pharmacy, Tamil Nadu.

[2,3,4]Interns, Doctor of Pharmacy, The Erode College of Pharmacy, Tamil Nadu.

ABSTRACT

Stroke is considered to be the fourth leading cause of death and became the fifth leading cause of disability. The global stroke fact sheet released in 2022 reveals that the risk of stroke has increased by 50% over the last 17 years and at present 1 in 4 people is estimated to have a stroke in their lifetime. According to the centre for disease control and prevention, over 2.7 million people die from Ischemic stroke globally. High cholesterol may increase the risk of stroke by boosting the risk of vascular disease, which is a risk factor of stroke. The relationship between the lipids and stroke is complex, on investigation, the total cholesterol level, LDL-C, the total cholesterol to HDL-C ratio and non HDL-C are significantly associated with the increased risk of ischemic stroke. Statins are effective in preventing the vascular diseases and are widely recommended for the secondary prevention and management of ischemic stroke by significantly decreasing the cardiovascular risk and improving functional performance to improve clinical outcome in preventing the recurrence of ischemic stroke.

Keywords: Ischemic stroke, Cardiovascular disease, Cholesterol, Statins.

INTRODUCTION

The World Health Organization(WHO) defined stroke as rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hrs or leading to death with no apparent cause other than of vascular origin[1]. By 2022, the burden of stroke is increasing in India. At present, stroke is considered to be the fourth leading cause of death and became the fifth leading cause of disability; with incidence of stroke ranges between 105 and 152 per 100000 people per year, in India[2]. Stroke can be classified into two main categories namely, Ischemic Stroke and Hemorrhagic Stroke[3]. The global stroke fact sheet released in 2022 reveals that the risk of stroke has increased by 50% over the last 17 years and now 1 in 4 people is estimated to have a stroke in their lifetime[4].

ETIOLOGY:

Ischemic stroke- (85% of all strokes)

It is caused by atherosclerotic disease, cardioembolic and others such as cervical artery dissertion, endocardities, vascularities, hypercoagulable state, herniation.

Haemorrhagic stroke- (15% of all strokes)

It occurs due to Intracerebral Haemorrhage(ICH), Subarachnoid Haemorrhage(SAH)[5].

ISCHEMIC STROKE

Ischemic stroke occurs when the blocked blood vessels limits the blood supply to the brain[6]. According to the centre for disease control and prevention, Ischemic stroke occurs when the blood clot or blood vessels of the brain got interrupted or reduced. Recent studies suggest that among stroke about 80% are ischemic stroke and 12% are Hemorrhagic stroke in nature. Moreover, over 2.7 million people die from Ischemic stroke globally[4].

Ischemic stroke can be classified based on duration of onset if symptoms and causative agent. The major classification system of Ischemic stroke TOAST, CCS, Sparkle Classification of Stroke[7].

The signs and symptoms of stroke may include sudden onset numbness or weakness in an arm or leg, facial drooping, difficulty in speaking or understanding speech, confusion, trouble with balance or coordination and loss of vision. Sometimes Acute ischemic stroke is proceeded by a transient ischemic attack(TIA), which can be charecterised by temporary episodes of brain dysfunction due to decreased or intrrupted blood flow[8].

The recent study suggest that the ischemic stroke in younger adults is increasing over older adults with an increased risk factors of hypertension, dyslipidemia, diabetes mellitus, tobacco use and obesity[9].

In the subacute phase of stroke management, the treatment should focus on preventing the potential complications of stroke such as, DVT, Pulmonary Embolism, and aspiration pneumonia, where pneumonia is a serious complication, that accounts for 15-25% of deaths associated with stroke, generally occurs in the 48-72 hours after the stroke. Pulmonary Embolism occurs more frequently and accounts for a substantial number of death after ischemic stroke[10].

PATHOPHYSIOLOGY OF ISCHEMIC STROKE:

Generally stroke is an abrupt neurological outburst caused by impaired perfusion through the blood vessels to the brain. The ischemic occlusion contribute to around 85% of casualities among stroke patients, that generates thrombolic and embolic conditions in the brain. In thrombosis condition, the blood flow is affected by narrowing of blood vessels due to arthrosclerosis, thus the buildup of plaque constricts the vascular chamber and forms clot, causing thrombotic stroke. In case of embolic stroke, decreased blood flow to the regions of circle of willis, causes an embolism causing severe stress and necrosis of brain blood cells[11].

LIPID LEVELS AND THE RISK OF ISCHEMIC STROKE:

High cholesterol may increase the risk of stroke by boosting the risk of vascular disease, which is a risk factor of stroke. When there is a plaque or fatty deposit buildup in the arteries due to high cholesterol, the blood flow to the brain can be blocked, reducing the amount of oxygen reaching the brain cells[12].

As a risk factor, hyperlipidemia history increases the incidence of stroke, where the great portion of progress of atherosclerosis is asymptamatic. It would be symptomatic only if an obstruction in the cerebral flow arises to develop functional damage to the brain by accelerating damage to certain cerebral artery[13].

The relationship between the lipids and stroke is complex, where there exist a direct relationship between cholesterol levels and ischemic stroke. The high level of total cholesterol is associated with higher risk of ischemic stroke, whereas lower level of total cholestrol are generally associated with increased risk of brain hemorrhage[14]. On investigation, the total cholesterol level, LDL-C, the total

cholesterol to HDL-C ratio and non HDL-C are significantly associated with the increased risk of ischemic stroke[15].

STATINS IN THE MANAGEMENT OF STROKE:

Statins are effective in preventing the vascular diseases and are widely recommended and are used for the secondary prevention and management of ischemic stroke. American Heart Association(AHA) and American Stroke Association(ASA) recommends that the statin therapy should reduce the risk of cardiovascular and cerebrovascular events among people with a previous history of stroke and Transient Ischemic Stroke(TIA)[16].
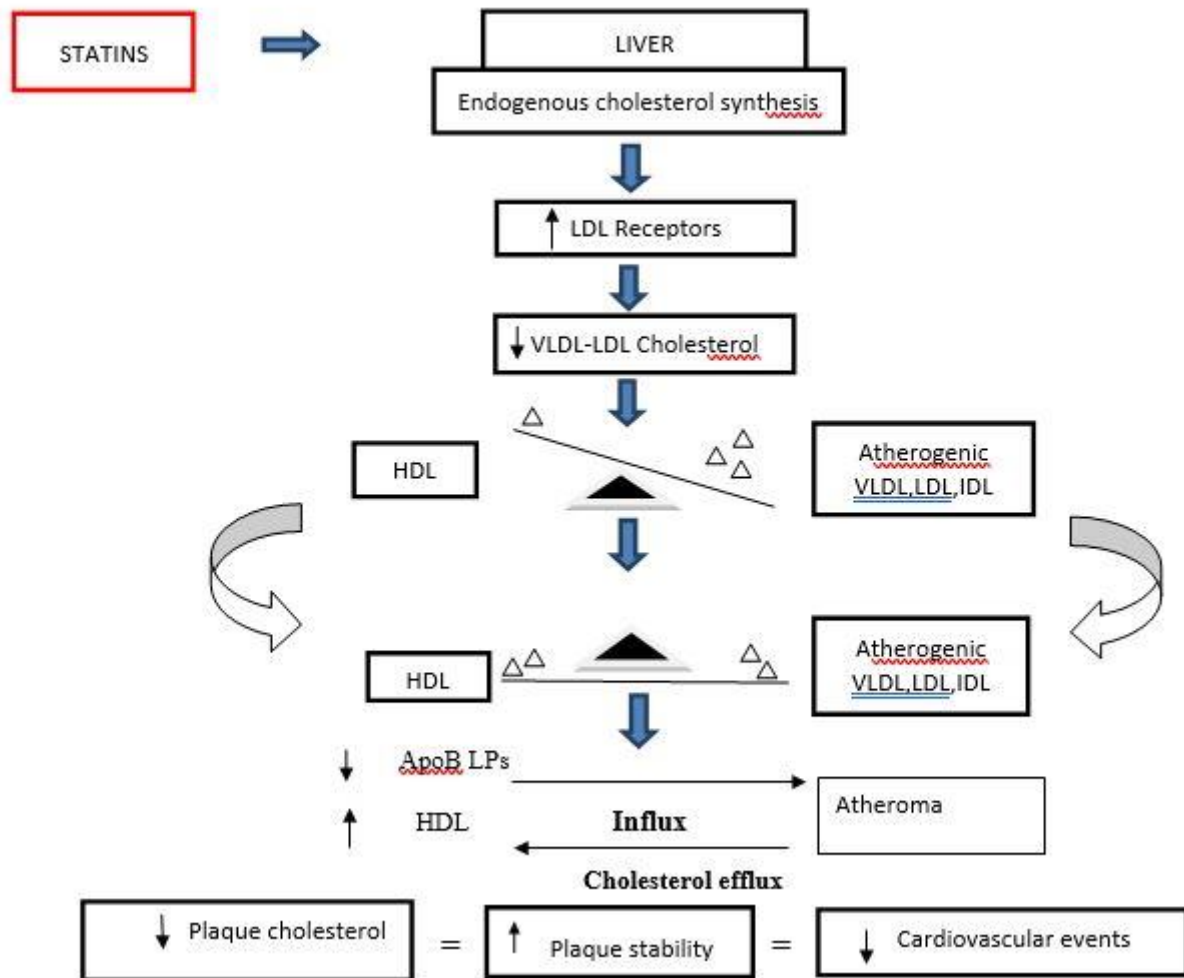

Figure 1: Mechanism of Statin therapy

Statins work by inhibiting HMG COA reductase, ultimately leading to reduction not only the level of cholesterol but also bad to the non-lipid dependent, pleiotropic effect on ischemic stroke. There is a growing evidence suggesting that the statins interrupt the isopranoids biosynthesis. Statins also found to increase the production and bioavailability of endothelium derived nitric oxide(NO) and by activating endothelial RAS which is associated with cellular proliferation and leads to pro-angiogenic effects. Statins protects vascular endothelium agonist compliment mediated injury through decay accelerating factor(DAE) upregulation. Thrombosis plays an important role during ischemic stroke, in such cases

statins reduce the production of Thromboxane A2(TXA2) in platelets and erythrocyte membrane, resulting in decrease in thrombogenic potential of there cells[17].

CLINICAL PREVENTIVE EFFECTS OF STATINS IN ISCHEMIC STROKE:

Statins have emerged as guideline therapy for primary and secondary stroke prevention associated with the reduced risk of incident and recurrent stroke. In patients with recent stroke or TIA and without known coronary heart disease, 80 mg of atorvastatin per day reduced the overall incidence of ischemic stroke, despite the small incidence of hemorrhagic stroke[18].

Recommended doses of statins in prevention of ischemic stroke,

Atorvastatin	Trail of ASCOTLLA-10mg/day[19] GREACE Study-10-80mg/day[20] SPARCL-80mg/day[21]
Pravastatin	Care Study-40mg/day[22] Lipid Study-40mg/day[23]
Simvastatin	Scandinavian Simvastatin Study (4S)-40mg/day[24] Heart Protection Study-40mg/day[25]
Rosuvastatin	JUPITER Trail-40mg/day[26]

According to the AHA and ASA guidelines, statin therapy is useful for stroke secondary prevention, especially for stroke survivors with high LDL levels, by reducing their risk by at least 50%. Although statin use has been established for preventing recurrent stroke, whether patients have good adherence to statin therapy is still unclear, resulting in worst outcomes[27].

SAFETY AND EFFICACY OF STATIN THERAPY IN ISCHEMIC STROKE:

Statin therapy appear to be safe for use in vast majority of patients. However, patients with multiple medical co-morbidities are at increased risk of adverse effects from long-term statin use. Statin can safely be used in patients with CKD, although clinicians should be cautious in using high dose statins and combining therapy with fibrates/ezetimibe. Myalgia and rhabdomyolysis are the common side effects from statin use. Overall statin drugs appears to be safe in the vast majority of patients and the protective benefits of statin therapy for outweigh the potential risk[28].

CONCLUSION

Statin therapy play an important role in the management of ischemic stroke, among patients with established vascular disease and high burden of vascular risk factors. It also significantly decrease the cardiovascular risk and improving functional performance and to improve clinical outcome in preventing the recurrence of ischemic stroke.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no compeing interests exist.

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