ATORVASTATIN IN ACUTE STROKE: A STEPPING STONE TO THE SERENDIPITY

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ABSTRACT

BACKGROUND

Stroke is a vascular dismay that has led to several deaths and deformities. Despite this unwarranted picture it is largely preventable and treatable. The statins have been the flagship molecules for the purpose.

METHODS

We studied 150 patients admitted in Jawaharlal Nehru Medical College, Hospital, presenting with acute ischemic stroke, and evaluated the effect of high intensity atorvastatin on the temperament of carotid plaque.

RESULTS

80% of our study patients who were administered high intensity atorvastatin, displayed a carotid Doppler picture of plaque regression.

CONCLUSIONS

High dose atorvastatin shows a definite improvement in the size of atheromatous plaque, which is a major prognosticator of ischemic stroke, hence should be advocated in such patients.

KEYWORDS

Stroke, Plaques in Carotid, High Dose of Atorvastatin, Remodeling & Vascularisation of Thrombus.

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BACKGROUND

Stroke: A Vascular Race Against Time

A stroke is a vascular race against time, a race, which is lost more often than not, resulting in death or disability. This monster engulfs 15 million people every year. Being the 2nd most faithful killer, it has overburdened the healthcare delivery system. The disability associated with stroke is incapacitating and is less amenable to treatment. The lifetime risk of a silent covert stroke reaches almost cent percent elderly population. Despite this bigger picture, stroke is many a times preventable and at times treatable. A Complex Web for the Clogged Arteries Atherosclerosis is systemic disease with multifactorial web of causation. An atherosclerotic plaque involving a major arterial system is a major cause of ischemic stroke. The arteries are predisposed to this fatty transformation by the elevated plasma cholesterol levels,[1,2] making the plasma lipid picture an important prognosticator and foreteller of atherosclerosis.[3,4,5,6,7] Increasing evidences advocate the role of inflammation in pushing forward the cart of acute stroke. This has been speculated that the atherosclerosis involves an intricate cross-talk between the circulating blood cells and the cells of the arterial wall leading to the narrowing of the vascular channels.[8] The story of atherosclerosis begins with endothelial disharmony and this further progresses to inflammatory processes that seeds the beginning of plaque formation by the trigger of cytokines and leukocyte reqruitment.[9,10] The studies in the past have tried to decipher the pathobiology of the thrombosis-atherosclerosis by counting on the levels of various plasma markers and urine.[11] The thrombosis and pro-inflammatory conditions are the mainstay for the genesis of large artery atherosclerosis.[12] The thrombogenic machinery is stipulated by the elevated levels of fibrinogen and D-dimer. A stumbled fibrinogen versus D-Dimer ratio denotes that an individual is highly predisposed towards generation of cardioembolic stroke. The inflammatory states is earmarked by an higher levels of C-reactive protein, fibrinogen and an unwarranted erythrocyte sedimentation rate, all which push the individual towards the atherothrombotic states. Few other non-specific mechanisms are known to exist which can cause the strokes of other patterns, like the lacunar stroke.

A Statin in Time Saves Nine

The 3-hydroxy-3-methyl glutaryl coenzyme-A (HMG-CoA) reductase inhibitors, the statins are a member of a well settled family of drugs that improve the lipid profile and ameliorate vascular channels which are clogged with atherosclerotic plaques.[13,14,15,16,17] Trials have come to the conclusion that these HMG-CoA reductase inhibitors have the propensity to reduce the jeopardy of the 1st or a recurrent stroke among the patients with known heart disease giving it the crown for being the therapy for the secondary prevention of an abrupt vascular phenomenon alongside the anti-platelet and antihypertensive

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agents.[18,19,20] The HMG-CoA inhibition reduces the intrinsic cholesterol biosynthesis, further it increases the expression of low density lipoprotein (LDL) responsible for the uptake and the clearance of LDL cholesterol. This forms one of the many mechanisms of statins involved rectifying the arterial clutter. Several other pleotropic effects are also said to be working in coherence for this purpose. The statins re-establish the endothelial function, culminates the plaque stability, derides the inflammation and prevents the clustering of platelets hence prevents the thrombus formation. The exact neuroprotective principle of the statins has not been fully denuded but, the animal models suggest the augmentation of the blood supply of the brain tissue by the virtue of an increased amount of nitric oxide production. This, along with the fall in glutamate toxicity and a well replenished neurogenesis and angiogenesis has been found to be the reason behind the neuroprotective mechanism of statins.[20-25] Cortellaro et al came to the conclusion that atorvastatin can possibly reduce the inflammatory and thrombotic demeanour of carotid plaque.[26]

Happy Arteries-Happier Brain

The chemokines of the endocytic pathway, involved in the inflammation is targeted by the atorvastatin thus benefiting the endothelial function.[27] The statin therapy invariably reduces the size of the infarct, more so in the patients with ischemic infarct, whatever may be the basic aetiology responsible.[28] The outcomes were held at a better scenario when a higher dose of statin was used in place of low doses.[29] Another study failed to agree with this fact, they advocated the use of high dose statins only in the patients with atherosclerotic stroke.[30] But either of these agreed that a blend of various effects of statins are imperative specially in the first week of the episode of stroke.[31]

Carotid Bullet to Brain Target

Presence and persistence of a plaque, particularly with surface irregularities, when assessed by B-mode ultrasonography, may be of great assistance in catching the intermediate-to high-risk folks in addition to the vascular risk estimated and calculated by the presence of time-honoured risk attributes. In addition, the degree of carotid stenosis, along with other dimensions of the carotid artery plaque, such as the etiquettes of the plaque surface and anatomy of the same may be commanding credential of stroke risk. There is no Indian study specially those involving the people of eastern Bihar, which could compare the effect of high and low dose statins on acute stroke. We carried out a study in the population of eastern Bihar to uncover the consequence of high dose Atorvastatin on the plasma lipid levels, the effect on the morphology of the carotid plaque(Figure 1) and its size and also the circumferential improvement of the patients with ischemic stroke over a period of 11 months our study.

Aims and Objectives

To see the effect of atorvastatin on the size of atheromatous carotid plaque in the patients with acute ischemic stroke.

METHODS

This prospective cohort study was performed from June 2018 to April 2019. A total of 150 patients with acute cerebral infarction who were admitted to the medicine departments of Jawahar Lal Nehru Medical College and hospitals, were studied. All the patients with acute cerebral infarction were established by computerized tomography or magnetic resonance imaging and all of the preferred subjects were of acute ischemic/embolic stroke**.** They received no any other lipid, anti-oxidant drugs during atorvastatin treatment. All the patients at the time of admission were subjected to CAROTID DOPPLER and Plaque thickness in the carotids were measured. 100 patients who had plaque in the carotids were given high dose of atorvastatin 40 mg/d for a period of 6 weeks. All the patients were again subjected to CAROTID DOPPLER to see the Plaque slump after 6 weeks (Figure 2).

Inclusion Criteria

1) CT/MRI proven cases of acute ischemic stroke were included in the study.
2) Normal Liver and Kidney function.

Exclusion Criteria

1) No prior history of statin based, or any other lipid lowering therapy.
2) No history of any other anti-oxidant agents.
3) Women of child bearing age.

RESULTS

In our study it was observed that 80% of the patients showed plaque disappearance or recession of size on Carotid Doppler.

DISCUSSION

High-dose atorvastatin can better reduce plaque thickness and volume - In order to know the changes of plaque after treatment with atorvastatin, plaque thickness and volume were detected. The results indicated that atorvastatin could significantly decrease plaque thickness and volume at the dose of 40 mg/d. Our study was in coherence with ACC/AHA guidelines which suggest that, high dose atorvastatin is an effective medication for the prevention and treatment of acute ischemic stroke.

CONCLUSIONS

The authorities have picked the hands of acute stroke in the muddled spillway against time, but it is never too late to intervene before the thunderstorm of stroke jumps in. Atorvastatin is an important arm in the armamentarium when used in appropriate doses against the acute ischemic stroke. The study carried out in our college has filled up the lacunae of studies carried out in Gangetic planes of eastern Bihar and it further strengthened the role of statins in Acute Ischemic Stroke.

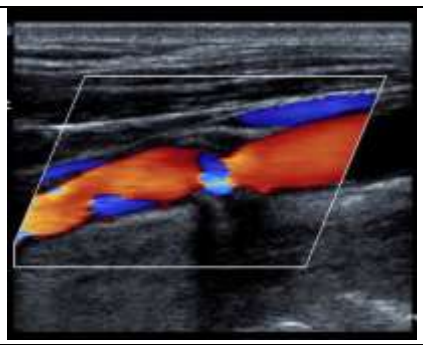

Figure 1. Right Carotid Doppler Before Treatment

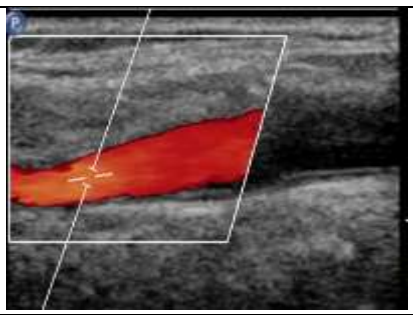

Figure 2. Right Carotid Doppler After Treatment

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