STATINS ARE PROTECTIVE AGAINST DEMENTIA
Gökhan Erkol
Turkey

Vascular changes are evident in the brains of patients with different types of dementias. Even in the first neuropathological investigation of Aguste D.'s brain, Alois Alzheimer described vascular changes besides neuritic plaques and neurofibrillary tangles (1). The importance of vascular changes in the development of dementia is well established after the NUN study. Plaques and tangles are necessary but sometimes they are not sufficient to cause a demening illness (2). Vascular changes are not limited to atherosclerosis; blood brain barrier changes, cerebral amyloid angiopathy, and micro bleeds may also cause dementia. These vascular changes usually develop as a result of long time exposure to the vascular risk factors. Strokes, atherosclerosis, hypertension, diabetes mellitus, heart disease, dyslipidemia are thought to be causes for neurodegeneration, vascular dementia and Alzheimer's disease (3). Several longitudinal population studies revealed that the existence of the midlife vascular risk factors usually resulted in a cognitive impairment, sometimes dementia (4, 5).

Statins are cholesterol lowering drugs that inhibit hydroxyl methyl glutaryl coenzyme A and cause a reduction in blood cholesterol levels, especially in LDL-C levels. They also show a pleotropic effect via isoprenoid reduction; regulate nitric oxide metabolism, have antinflammatory effect (inhibit the production of adhesion molecules and proinflammatory cytokines), inhibit angioneogenesis in some chronic disease (ie. macular degeneration and some cancers) but promote angioneogenesis in cardiovascular disease. They also have anti platelet and antithrombotic action. Recently; with the better understanding of amyloid beta metabolism in the brain; the role of cholesterol has become evident in the amiloidogenic pathway of the beta amyloid precursor protein cleavage (6).

Evidence for the effectiveness of statins in dementia protection, mostly comes from observational studies. In a recent meta-analysis, Wong et al. reported a slight benefit for the prevention of AD and all types of dementia with statin use. A subgroup analysis of gingko evaluation of memory study showed protective effects of statins in healthy individuals, but not in patients with mild cognitive impairment and dementia. Lipophilic statins tended to reduce dementia risk more than the hydrophilic ones (7, 8, 9).

Numerous studies using statins for prevention or treatment of dementia revealed negative results (10, 11, 12,13, 14). The factors underlying the failure of transferring the success of epidemiological studies to the prevention studies may be as follows:

Nearly all patients recruited for the studies were in late old age (15).

Patients enrolled to the studies were mostly cognitively impaired in some degree.

Most of the studies excluded hypercholesterolemic patients which were the main target of the statin treatment.

We all are aware of the fact that, Alzheimer’s disease’s and most of the other dementias’ pathologic process begins long before the disease becomes evident. Statin treatment must be initialized in midlife (for the patients with hypercholesterolemia) and continued for a prolonged follow up period to achieve a possible success.

And finally we have to find a way to follow the effect of statins on the disease process such as structural and functional biomarkers (16, 17).

References:


