Title: Statins and dementia: effect of statins beyond the treatment of dyslipidemia

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Statins have been one of the mostly prescribed medications for the primary and secondary prevention of cardiovascular disease (CVD) in the recent decade.\(^1\) Potential role of statins in lipid lowering and CVD prevention are undeniable, and accumulated evidence suggest that statins are one of the most essential components of standard treatment of CVD.\(^2\) Their most favorable actions in addition to lipid lowering, are that they have a number of effects by improvement of endothelial function, reducing inflammation consequently stabilization and even small percentage of regression of the atherosclerotic plaques.\(^3\) Hence, they are cornerstone of pharmacotherapy for management of patients with CVD.

There is still debate concerning the influence of statins on the cognitive function especially for those who has dementia and Alzheimer’s disease. Lately, observational data have been accumulating in regard with improvement of cognitive function as part of pleiotropic effects in those who had been taking statins for a long period. However, some randomized trials investigating the statins’ pleiotropic effects have failed to demonstrate any additional positive effects on cognitive function in patients with dementia and Alzheimer’s disease.\(^4\)

In this issue of European Journal of Preventive Cardiology, Olmastroni et al carried out an updated systematic review and meta-analysis of all observational studies in terms of the risk of Alzheimer’s disease and dementia in those who received statins.\(^5\) The meta-analysis is published timely because authors focused on possible influence of long term statin treatment in cognitive function, particularly for the risk of dementia and/or AD which in turn eliminates the concerns with the using of this lipid lowering medication with regard to possible effects on the cognitive function up to now raised by stakeholders. Authors have followed all requirements of guidelines using PRISMA and MOOSE to conduct the study. Pubmed, EMBASE databases and Cochrane Library were used to search for the literature including dementia, Alzheimer and statin words only in English from inception to 2021. And they had included the studies met the following criteria: (i) observational case or case-control studies; (ii) adults; (iii) statins users compared to non-users; (iv) adjusted estimate and 95% CI for outcomes for the AD or dementia risk. Primary outcome were AD and dementia diagnosed with international guidelines criteria. Overall, 46 observational studies were included in the meta-analysis by Olmastroni et al. Among, 38 out of them cohorts and 8 case-control studies with the sample size from 123 to 2004692 patients which had been published between 2000 and 2021. Totally, 25 studies for dementia risk, 10 for AD risk and while 11 reporting adjusted estimates for both the outcomes. The meta-analysis found that statin takers tended to have reduced risk of dementia (OR 0.80; CI 0.75 to 0.85) and AD than non-users (OR 0.68; CI, 0.56 to 0.81). In addition, subgroup analysis of orderly patients (≥75) revealed that statin-associated risk reduction for dementia was 18% and for AD was 27%. As far as the gender

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deference is concerned, there had been no difference between men and women with regard to reduction either in the risk of dementia (both OR 0.86; CI 0.81 to 0.92) or AD (OR 0.71; CI 0.47 to 1.06 for men and OR 0.85; CI 0.48 to 1.49 for women). Regarding the lipophilic and hydrophilic statins, there were similar reduction in the risk of dementia (OR 0.83; CI 0.76 to 0.90 and OR 0.59; CI 0.43 to 0.82), respectively. Even though the high potency and low potency statins showed a similar reduction in the risk of dementia (OR 0.80; CI 0.72 to 0.88 and OR 0.84; CI 0.79 to 0.90, respectively), high potency statins tended to have greater efficacy in reducing the risk of dementia (P=0.05).

The meta-analysis results are in line with the findings by Song et al with regard to the possible positive effects of statins on cognitive function where relative risk of dementia for the use of statins was 0.62 (95% confidence interval 0.43-0.81). However, Song et al failed to reveal causality of the cases and the findings were only stratified by follow-up and number of dementia cases.6 In another meta-analysis conducted by Wong et al7 demonstrated that statins might reduce the risk of AD and dementia which in turn agrees with the results of this meta-analysis by Olmestorini et al.

Even though, the meta-analysis has several limitations, such as heterogeneity of diagnostic criteria for dementia, the diagnosis were not fully supported by standardized tests, and included studies’ estimation methods for statin usage were different, it shows up-to-date, comprehensive knowledge with respect to the neurocognitive risk associated with statin treatment as well as provides extensive knowledge on possible cognitive influence by statin potency. Main strengths of this meta-analysis are: (i) provides comprehensive overview of statin use on AD and/or dementia risk from 46 studies; (ii) included 5 738 737 participants with high number of AD and/or dementia patients; (iii) analyzed in great detail as authors stratified by age, sex, type of study design, statin solubility and statin potency. Indeed, Olmestorini et al specifically categorized the statin types, analyzing two subgroups of patients with a lipophilic and hydrophilic statins, showing no significant difference for dementia and AD.

The meta-analysis was also normally positive in the context, demonstrating trends towards positive influence of long term statin treatment on neurocognitive function, which in turn agrees with the findings of Poly et al who have recently conducted a similar study.8 Furthermore, two more other latest meta-analysis showed that dementia risk had been lower on those with long term statin treatment.9,10 Indeed, the findings is of great interest and require further clarification of mechanisms in detail and meticulous clinical validation.

In summary, the meta-analysis of Olmastroni et al. is momentous, because it encourages the scientific community to focus on statins’ not only primary lipid lowering efficacy but also long term beneficial pleotropic effects on neurocognitive functions. Given the insufficiency of data regarding the statins' possible cognitive influence in elderly, the authors highlighted the need of specifically designed randomized trials focused on standardized methods for the diagnosis of dementia with large number of participants and expensive follow-ups in this field. Statins’ positive neurocognitive action in long-term period would give us further insight in the field.

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References


