

Peer Review File

Article information: <http://dx.doi.org/10.21037/aes-21-20>.

Reviewer 1

Comments:

Good manuscript evaluating the use of statins for age-related macular degeneration. The study is well presented, the authors have completed the Narrative Review reporting checklist.

I would like to remark some issues.

Comment 1: First, although the information that statins can affect the progression of cataracts is very interesting, it is not relevant for the present study.

Reply 1: The relationship between cataract and age-related macular degeneration (AMD) has been studied for over a century [e.g., Mainster MA, Ajlan RS. 2020. Clinical Photoc Retinopathy. Albert and Jakobiec's Principles and Practice of Ophthalmology, 4th ed. Springer Nature]. Statins potentially affect both disorders. As reviewer 1 stated: “the information that statins can affect the progression of cataracts is very interesting”.

Changes to text 1: none required

Comment 2: Second, besides the methodology of research selection is not mandatory on the Narrative Review, I would like to know more about the criteria used to select the articles included in the narrative.

Reply 2: We used numerous of mechanism-based PubMed searches to prepare our report and assure its scientific accuracy and timeliness. A partial list of search terms used in conjunction with “statins” or “age-related macular degeneration” includes: oxidative stress, cytokines, inflammation, vascular endothelial growth factor, lupus erythematosus, TNF-alpha, protein isoprenylation, endothelial cell function, reactive oxygen species, free radicals, complement factor H, etc.

Changes to text 2: none required

Comment 3: Finally, on the conclusion, I definitely agree that it is needed more studies evaluating this issue, my point is not only large studies is needed, but also studies in several different populations once genetics factors can influence in the results. Therefore, if in on hand the ideal study to correlate statin with AMD is difficult to execute because of growing prevalence of statin use, on the other hand, the high prevalence of statin use increases the importance of the future studies.

Reply 3: We thank reviewer 1 for this thoughtful suggestion. We incorporated it into our

manuscript.

Changes to text 3: We attached the following phrase on lines sentence on page 9, lines 181-2 “that take into account the genetics and ethnicity of subjects”.

Reviewer 2

Comments:

In the article titled "Narrative Review of Statins for Age Related Macular Degeneration: Promising but Unproven", the authors have made a brief review of the particularities of statinas in AMD. This topic is of special interest because of the similarities between coronary heart disease and AMD. The idea of the article is good, the topic is interesting and current.

Comment 1: However, in order to obtain greater visibility, the article should investigate more in the ways of action of the statinas as well as add figures that illustrate these ways.

Reply 1: The goal of our manuscript is to present a concise, problem-focused analysis that a busy clinician might find useful, not to obtain “greater visibility” for our work, which has had excellent “visibility” (e.g., one of us has publications cited to date in ~7000 scientific reports).

Changes to text 1: none required.

Comment 2: Likewise, the bibliographic citations are not very abundant or very recent to be a review.

Reply 2: Our literature review and citations are currently up-to-date. A third of our 43 references were published in the past 5 years, 7 in the past 2 years. Reviewer 2 feels our references are not sufficiently “abundant.” We could have referenced all 127 articles we retrieved and analyzed for this manuscript but chose to cite those most useful for readers.

Changes to text 2: none required

Comment 3. It is missed that the section on the analysis of clinical trials with statins as well as the meta-analysis does not further explain the conditions of each study as well as the most characteristic results.

Reply 1: This comment’s English translation is unintelligible.

Changes to text 1: none required

Comment 4: In short, it is too light a review for a topic of interest where a multitude of studies and clinical trials are being carried out to test its validity.

Reply 4: none required.

Changes to text 4: none required.

Summary of responses to reviewers and editorial office

We incorporated reviewer 1's thoughtful suggestion into our manuscript, couldn't find anything useful in Reviewer 2's remarks and completed the checklist requested by your editorial office.

***Please note:** our manuscript's title was changed following your editorial office suggestion to include the words "Narrative Review of". However, after discussing it, we restored the original title since it appeared to us the use of such words was unnecessary and we felt more comfortable with our original title.*