Reviewer’s report

Title: Repeated intravitreal injections of antivascular endothelial growth factor in patients with neovascular age-related macular degeneration may increase the risk of ischemic optic neuropathy

Version: 0 Date: 26 Aug 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS:
I read and reviewed the manuscript entitled "Repeated intravitreal injections of antivascular endothelial growth factor in patients with neovascular age-related macular degeneration may increase the risk of ischemic optic neuropathy". The topic is interest and the work is well done.

I have some suggestions on the present study as below.
REQUESTED REVISIONS:

First, the lack of ocular demographics such as visual acuity, intraocular pressure values may strengthen the study. If these can not be done, it should be mentioned in the limitations of the study.

Secondly, the association of the metabolic vascular disease particularly hypertension and diabetes mellitus affect the ION incidence. Although authors mentioned this association, I suggest to add a few discussion about this issue. Besides, also they mentioned that group III had higher incidence of ION, older patients (even reported no difference between groups) tend to have more morbidities including DM, HT, ischemic cardiac disease etc that may exist with ION.

thirdly, I agree with the authors that mentioned a potential mechanism may be the transient IOP elevation after intravitreal injection of anti-VEGF. Moreover, I think that the mechanism of the Anti-VEGFs needed to be evaluate with respect to their prevention of new vessels as well as collateral vessels as in heart. One may think that to prevent the new vessel formation in the retina or choroid, it may result with inadvertent regression of the collateral vessels of the optic nerve head. This may cause an increased risk of ischemic optic neuropathy particularly in patients who received multiple doses of AntiVEGFs.

Fourthly, The Anti-VEGFs used in their study was not mentioned. An off-label drug, bevacizumab and other licensed drugs such as aflibercept, ranibizumab, etc. If possible to compare their effect on ION, what are the difference? this may be strengthen their study.

Finally the question is " Do we observe higher incidence of ION in patients receive higher number of intravitreal injections? or The patients need is higher in these patient population who tend to develop ION?" These may be discussed.

The lack of control subjects with similar demographics may be discussed at least in the limitations paragraph.

*A minor comment: "Neovascular age-related macular degeneration (AMD) is characterized by the proliferation of abnormal blood vessels (neovascularatures) in the choroid and can cause severe vision loss."

"in the choroid" or "from the choroid"???

ADDITIONAL REQUESTS/SUGGESTIONS:

See comments above
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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