Author’s response to reviews

Title: Intravitreal dexamethasone implant for central retinal vein occlusion without macular edema

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Author’s response to reviews:

Response to Review Comments

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We very much appreciate the editor and the reviewers for their deep and thorough review of our manuscript. We have revised the paper in line with their suggestions. We hope this revised paper now meets your level of satisfaction. Below are our answers to the reviewers’ comments.

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General Comments

Thank you for amending your manuscript according to our requests. However, there are a few minor revisions that are necessary before we can accept the manuscript for publication:

Comment 1: We note that you describe this study as a retrospective study, however, we also note that you have described a study intervention and a control group in the Methods section. In light of this, please can you clarify the following:

- Please can provide more details of the control and test group included in your study in the Methods section of your manuscript.

- Please can you also clarify whether the treatments and follow up procedures the patients included in your study were part of standard care or if they were assigned these treatments and follow up procedures to meet the aims of your study?
If these treatments and procedures were assigned to the patients to meet the aims of your study, your study will then fall within the International Committee of Medical Journal Editors (ICMJE)’ definition of a clinical trial: any research study that prospectively assigns human subjects to one or more health related interventions to evaluate the effects on health or biological outcomes. As such, Biomed Central requires that a Trial Registration Number is provided in order for the manuscript to be published.

Although a TRN is usually required prior to the start of the peer-review process, the BMC-series journals does accept retrospectively registered trials. If you have not registered the trial, we therefore request that you do so as soon as possible so that your study can be accepted for publication. All trials must be registered with an ICMJE approved registry, as listed in the ICMJE guide: http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/

Once you know your trial registration number, please submit a revised version of your manuscript with the number and date of registration included in the abstract. The last section of the abstract should be Trial Registration: listing the trial registry and the unique identifying number, e.g. Trial registration: Current Controlled Trials ISRCTN73824458, as well as the date of registration. Please note that there should be no space between the letters and numbers of the trial registration number. If registration took place after the first participant was enrolled, please state also “Retrospectively registered” at the end of this section.

- If the treatments and procedures carried out on the patients were assigned to them to fit in with your research aims, please clarify whether you obtained written or verbal consent from the participants in your study. If verbal, please state the reason and whether the ethics committee approved this procedure.

Response to 1: We retrospectively analyzed the efficacy of IVD treatment by setting the untreated observed CRVO eye as a control. But, as the reviewer indicated, the description on “study intervention” and “control group” could cause confusion in explaining our study design. Therefore, we have removed the term “intervention” from the Method section and referred to the comparative group as “observation group” instead of “control group”. The descriptions of the study design have been revised to “cohort study”. IVD treatments were performed as a part of standard care in our clinic and not assigned to the patients for our study. CRVO indication for IVD implant treatment were added in 2011 in South Korea, where the study was conducted, and it was actually applied in 2013 by our institution. IVD implant therapy was administered to all CRVO without ME patients who agreed to treatment since January 2013, except for two patients who refused treatment. Before that time, CRVO eyes with no ME were usually observed without any treatment. There were no additionally required conditions or judgment involved in deciding whether to treat. Study subjects were collected through a review of the medical records from February 2012, not from February 2014. We have clarified the study design and added a detailed explanation in the Method section (p. 5 line 90 - p. 6 line 111). In addition, as we mentioned in the Method section, we did not obtain patient consent, since data were analyzed anonymously (line 95, page 5).
Comment 2: In the Abstract, please change the heading "Objective" so that it reads as "Background"

Response to 2: We have changed the heading "Objective" to "Background" in the Abstract.

Comment 3: In the main manuscript, please change the heading "Introduction" so that it reads as "Background"

Response to 3: We have changed the heading "Introduction" to "Background" in the main manuscript.

Comment 4: The Availability of data and materials section refers to the raw data used in your study and presenting tables and figures is not sufficient to state that all data is contained within the manuscript and additional files. Please only use this statement if you have indeed provided all raw data on which your study is based. We strongly encourage all authors to share their raw data, either by providing it in a supplementary file or depositing it in a public repository and providing the details on how to access it in this section. If you do not wish to share your data, please clearly state this in this section along with a justification. Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].

Please note that if you do wish to share your raw data and do not have consent from all patients to publish this data it will need to be de-identified.

Please also note that if you include your raw data as a supplementary file you will need to provide, after the References, a section titled “Additional files” where you list the following information about each of your supplementary files: * File name (e.g. Additional file 1), * Title of data, * Description of data. All additional files will also need to have been cited in the main manuscript.

Response to 4: We agree with your comment. We have modified the Availability of data and materials section as “The datasets used and analyzed during the current study are available from the corresponding author on reasonable request”.
Comment 5: Please add a “Conclusions” section after the “Discussion” section. This should state clearly the main conclusions of the research article and give a clear explanation of their importance and relevance.

Response to 5: We have added the Discussion section after the Conclusion section as follows:

“This retrospective cohort study firstly revealed that IVD implant for the treatment of CRVO without ME was significantly effective in improving venous engorgement, retinal hemorrhage, RNFL swelling, and visual symptoms by presumed alleviation of venous outflow. In two cases treated with IVD implants, a complete resolution of cilioretinal artery occlusion associated with CRVO was observed. Therefore, we concluded that IVD implant may be an effective treatment option in CRVO with no ME and further studies are warranted to verify this.”

Comment 6: Please provide a list of all the abbreviations used in the manuscript. This list should be placed just before the Declarations section. All abbreviations should still be defined in the text at first use.

Response to 6: We have added a list of abbreviations used in the text before the Declarations section.

Comment 7: We note that the email for the corresponding author on the title page is different from the email listed for the corresponding author on the submission system. Please ensure that the emails listed on both the title page and the submission system are consistent.

Response to 7: Both e-mail addresses belong the corresponding author. However, to avoid confusion, we have changed the e-mail address on the title page to a registered one on the submission system.

Comment 8: At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Response to 8: All the authors again greatly appreciate this review. The manuscript has been rechecked and the necessary changes have been made in accordance with the editor’s suggestions and comments. We have made some additional edits to clarify the meaning and to correct grammatical errors. Please see the above responses and the revised clean version manuscript.

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