Author’s response to reviews

Title: Effect of Oral Colchicine on Peripapillary Retinal Nerve Fiber Layer Thickness in Patients with Familial Mediterranean Fever

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Effect of Oral Colchicine on Peripapillary Retinal Nerve Fiber Layer Thickness in Patients with Familial Mediterranean Fever

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BMC Ophthalmology

Dear Mr. Tanyıldız,

Your manuscript "Effect of Oral Colchicine on Peripapillary Retinal Nerve Fiber Layer Thickness in Patients with Familial Mediterranean Fever" (BOPH-D-17-00445R2) has been assessed by our reviewers. They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Ophthalmology.
Their reports, together with any other comments, are below. Please also take a moment to check our website at http://boph.edmgr.com/ for any additional comments that were saved as attachments.

If you are able to fully address these points, we would encourage you to submit a revised manuscript to BMC Ophthalmology.

Once you have made the necessary corrections, please submit online at:

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Please include a cover letter with a point-by-point response to the comments, describing any additional experiments that were carried out and including a detailed rebuttal of any criticisms or requested revisions that you disagreed with. Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes.

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A decision will be made once we have received your revised manuscript, which we expect by 03 Jan 2018.

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I look forward to receiving your revised manuscript and please do not hesitate to contact us if you have any questions.

Best wishes,

Gerhard Garhofer
BMC Ophthalmology
https://bmcophthalmol.biomedcentral.com/
Editor Comments:

The manuscript has been reviewed by two experts in the field. While the merits of your work are appreciated, the comments of the reviewers clearly indicate the need for substantial revisions. I especially agree with reviewer 2 who has raised important suggestions regarding the data analysis and the presentation of the data.

Reviewer reports:

Koen Willekens (Reviewer 1): Dear,

congratulations with this excellent original research article on the pRNFL thickness in FMF patients with and without colchicine treatment. To further improve the quality of the manuscript please consider the following:

- background: add here the explaining sentences that are currently in the discussion as of why colchicine could have an effect on the pRNFL thickness.

- methods: you specify to have only done the 3 consecutive circular line scans in these patients. Was this not combined with a more profound analysis of the optic disc rim and cup or the macular ganglion cell layer? If these data are available, please incorporate them in the manuscript

- results: the first sentence states that 66 FMF patients were enrolled, the second states that 10 were excluded and the third is again talking about 25+41=66 patients. This is confusing; please adapt

please add a representative figure of the OCT scan (scanned image + software analysis and pRNFL thickness measurements)

- discussion:

"We didn't found..."); convert to writing language "we did not find..."

"hypopion uveitis" is a somewhat vague description of a typical(?) Behcet uveitis (bilateral nongranulomatous panuveitis and retinal vasculitis with a typical mobile hypopion)

Please address if the OCT images were assessed for any signs of intraretinal edema, disc swelling, hemorrhages, etc.

Please address possible confounding factors regarding pRNFL measurements: status of the vitreous (PVD stage/vitreopapillary traction / epiretinal membrane /etc.) To exclude for instance glaucoma, did you perform a visual field test in all patients? (if so, please report the MD values)
Doreen Schmidl (Reviewer 2): This is an interesting and well written manuscript investigating a potential effect of oral colchicine treatment on peripapillary retinal nerve fiber layer thickness in patients with familial Mediterranean fever. Although the authors are addressing an important issue, there are several points that need to be clarified.

1. Most importantly, as the study did not reveal a significant difference, the authors need to comment on the power of the study to detect differences. What was the minimum detectable difference in the selected sample size? This is crucial to convince the reader that the study was not underpowered. This is also important because one of the measured parameters almost reached level of significance.

2. The authors state that this was a prospective study. In my point of view, this was a cross sectional design with an untreated control group. Please clarify.

3. The authors have included 2 control groups, consisting of untreated patients as well as healthy subjects. It is not clear in the results section what is referred to as „control group“. Please separate more clearly the three different groups throughout the whole manuscript, in particular in the results section. In addition, when the authors report on the subgroup analysis, it gets even more confusing. Please revise the results section to make it more easy for the readers to distinguish between the treated patient group, the untreated patient group and the healthy group.

4. In the results section it is stated that no difference was observed between the three groups in any of the quadrants. However, based on the 4 p-values, it is not clear which tests were performed between which groups. Please revise.

5. In the subgroup analysis it is not clear what is the N for each subgroup. Is the sample size of the subgroup large enough to allow conclusions?

6. In the subgroup analysis the authors report mean thickness and thickness values for all quadrants. However, for the whole group, no mean thickness values are reported. Please comment.

7. "None of our patients had a severe score" This phrase is unclear to me. Please reconsider.

8. As no difference as found in respect to the different severities, I don't feel that this additional subgroup analysis adds much information and can maybe omitted, also in respect to the small sample size in this subgroups.

9. The language still requires revision. There are several grammatical error and misspellings in the manuscript, i.e. „We didn’t found a statistical significant difference…"

10. Did the authors take blood samples of TNF-alpha and/or IL-1ß? This would be interesting to correlate to the results.

11. The authors may want to add a figure showing the main results of the study.
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- Ethics approval and consent to participate
- Consent to publish
- Availability of data and materials
- Competing interests
- Funding
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