Author’s response to reviews

Title: Safety and efficacy of wiping lid margins with lid hygiene shampoo using the “Eye Brush”, a novel lid hygiene item, in healthy subjects: A pilot study

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Author’s response to reviews:

Dear Dr. Deepa Nath,

Thank you so much for your consideration.

I have finished writing an author response letter and revising the manuscript in response to the reviewers’ comments.

Additionally, American Journal Experts editors have made some changes to our manuscript based on grammatical issues. We have updated Table 1 based on the information obtained by MediProduct Co., Ltd., Tokyo, Japan.

Today, I will submit these revised documents to BMC Ophthalmology.

Again, I greatly appreciate your decision on our study report.

Best regards,

Hirotaka
Authors' Responses to the Reviewers:

Response to Melanie Eberle, MD, MaHM (Reviewer 1)

Comments to the Author

Very nice pilot study and a very nice treatment concept. Due to the limited number of patients, the conclusion is unfortunately also limited. A larger study is necessary to confirm the results. Although the delivered results are limited, it is worthwhile to publish this work due to the original approach.

Our response to this comment

Thank you very much for your review. We sincerely appreciate your comments regarding our research article.

Response to David Goldblum, MD (Reviewer 2)

Comments to the Author
Interesting initial pilot small numbers asks for larger study

Our response to this comment

Thank you very much for your review. We sincerely appreciate your comments regarding our research article.

Response to Research Square (Reviewer 3)

Comments to the Author

The authors evaluate a novel eyebrush to improve lid hygiene and show that a combination of the eye brush with eye shampoo yielded the best results. I have certain reservations about the study.

Our response to this comment

Thank you very much for your review. We sincerely appreciate your comments regarding our research article.

Comments to the Author

REQUESTED REVISIONS:

Abstract: The methods section is a bit unclear. Were all 12 eyes (of 6 patients) given all 4 of the interventions, or were the interventions equally divided amongst the eyes?

Our response to this comment

All 12 eyes (of 6 patients) were given all 4 of the interventions. We have changed “Twelve eyes of 6 subjects were evaluated” to “Twelve eyes of 6 subjects were all evaluated.”
Comments to the Author

Also, the term “Eye brush” is new and gives the impression that it is a device to apply something such as eye shampoo or perhaps, another solution. Hence, it is confusing that there is one group of only eye brush. Was this not combined with anything to apply?

Our response to this comment

One group was treated with only the eye brush, which was not combined with anything other than tap water. Although we clearly present the detailed procedure in the “Procedure details” in the Methods, we have changed “tap water” to “tap water alone” in the Methods of the Abstract.

Comments to the Author

The results section does not make much sense in this context. Since these were healthy subjects, how did eyestrain and discharge decrease? Are these not asymptomatic to begin with?

Our response to this comment

We have changed “healthy subjects” to “subjects with normal meibomian glands” throughout the manuscript.

Comments to the Author

The authors should also clarify in the abstract itself how a washout rate of 0.3% Tarivid ophthalmic ointment (a surrogate for wiping efficacy) was actually measured.

Our response to this comment

We have changed “Wiping efficacy was determined based on washout rates of 0.3% Tarivid ophthalmic ointment applied to eyelids and lid margins” to “Wiping efficacy was determined by post-wiping scores for the remaining fluorescein-stained 0.3% Tarivid ointment fully applied to
eyelids and lid margins under microscopic view illuminated by blue light just after performing each of the four lid hygiene methods described above”.

Comments to the Author

Main manuscript body:

The sample size is exceedingly small to draw meaningful conclusions.

It appears that the same eyes were subjected to all the groups with change over every week into the next protocol. What is the rationale of using the same eyes for all interventions? It may have been better to recruit more subjects and give one group to one set of subjects.

Our response to this comment

Using the same eyes for all interventions rather than recruiting more subjects and using one procedure for one set of subjects is reasonable in that the different eyes could respond to the same procedure in a different way due to their own innate characteristics.

We have added “Finally, due to the limited number of patients, the conclusion is also limited. However, using the same eyes for all interventions in this study rather than recruiting more subjects and using one procedure for one set of subjects could be reasonable in that the different eyes could respond to the same procedure in a different way due to their own innate characteristics. In any case, a larger study is necessary to support the results” to the Discussion.

Comments to the Author

When was the evaluation done for the tap water, eye brush and eye shampoo groups?

Our response to this comment

The evaluation for the tap water, eye brush and eye shampoo groups was performed just after the procedure. We have changed “Each procedure was performed during a different week” to “Each procedure was performed during a different week, and the evaluation was performed just after the procedure” in the Methods.
Comments to the Author

What is the chemical content of Tarivid ointment? Please clearly specify whether it is Ofloxacin ointment or not.

Our response to this comment

We have changed “Tarivid ophthalmic ointment” to “Tarivid ophthalmic ointment (Ofloxacin ointment)” in the Methods.

Comments to the Author

All the scoring systems appear subjective and are not standardized, which is open to individual interpretation. This requires more than one investigator to see the eye and grade the various tests.

Our response to this comment

We have changed “Second, in our studies, no subject or investigator masking was employed. This lack of masking might cause placebo effects on the results” into “Second, in our studies, no subject or investigator masking was employed. This lack of masking might cause placebo effects on the results. Furthermore, avoiding subjective scoring without individual interpretation requires more than one investigator to see the eye and grade the various tests” in the Discussion.

Comments to the Author

Was there any masking in the study protocol? If we assume that the Tarivid ointment was applied on the first day of every protocol and not daily, then at the 7th day, a masked grader who is unaware of the exact treatment used, should have graded the outcomes and scored the tests. The absence of masking is a major limitation of the study, though the authors acknowledge this.
Our response to this comment

As you noted, we included the absence of masking as a major limitation of the study. Indeed, the evaluation of the post-wiping scores was determined just after the procedure on the same day.

We have changed “Post-wiping scores were determined for the ointment remaining on the eyelids under microscopic view illuminated by blue light (graded 0-6 based on Table 2, Figure 2C1, C2) after performing each of the four lid hygiene methods described above” to “Post-wiping scores were determined for the ointment remaining on the eyelids under microscopic view illuminated by blue light (graded 0-6 based on Table 2, Figure 2C1, C2) just after performing each of the four lid hygiene methods described above” in the Methods.

Comments to the Author

The details of Bonferroni correction and p value cut offs should be part of the statistical analysis section.

Our response to this comment

We have moved the details of Bonferroni correction and p value cutoffs to the statistical analysis section.

Comments to the Author

Since there are 4 tests for each group and each test has a separate score, did the authors combine the scores from all tests to arrive at one composite score (wiping efficacy) and calculate statistical differences? Please specify this in the methods section, i.e., how were scores from different investigative modalities combined? The results can be held credible only when this point is clarified by the authors. The authors should also mention the one month outcomes of the combined group.
Our response to this comment

We did not combine the scores from all tests to arrive at one composite score (wiping efficacy) and calculate significant differences. Scores from different investigative modalities were not combined in this study. We have added “We did not combine the scores from all tests to arrive at one composite score and calculate significant differences. Scores from different investigative modalities were not combined in this study” to the statistical analysis section in the Methods. We already mentioned the one month outcomes of the combined group shown in Figure 7 and Additional file 4 for Supplementary Table for Figure 6, 7 in the Results. We have revised “There was no significant deterioration in TBUT, corneal and conjunctival staining scores, lid-margin staining scores or DR-1 scores after any method (Figures 3-7, Additional files 1-4 for Supplementary Tables for Figures 3-6)” to “There was no significant deterioration in TBUT, corneal and conjunctival staining scores, lid-margin staining scores or DR-1 scores after any method (Figures 3-7, Additional files 1-4 for Supplementary Tables for Figures 3-7)” in the Results.

Comments to the Author

ADDITIONAL REQUESTS/SUGGESTIONS:

The authors should include the small sample size as a limitation for the study.

Our response to this comment

We have added “Finally, due to the limited number of patients, the conclusion is also limited. However, using the same eyes for all interventions like in this study rather than recruiting more subjects and giving one procedure to one set of subjects could be reasonable in that the different eyes could respond to the same procedure in a different way due to their own innate characteristics. In any case, a larger study is necessary to support the results” to the Discussion.

Again, thank you very much for your valuable comments on our manuscript.

We sincerely appreciate your time and effort in reviewing our study.