Author's response to reviews

Title: Topical insulin-like growth factor-1 treatment using gelatin hydrogels for glucocorticoid-resistant sudden sensorineural hearing loss: a prospective clinical trial

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Author's response to reviews:

Dear Editor and Reviewers,

We appreciate your review of our manuscript entitled “Topical insulin-like growth factor-1 treatment using gelatin hydrogels for glucocorticoid-resistant sudden sensorineural hearing loss: a prospective clinical trial” (Manuscript ID MS: 5722664624366101). The comments of the reviewers have been helpful in allowing us to revise our manuscript.

Reviewer: S.R.

Minor essential revision
There appears to be a typographical error in the first paragraph of the Introduction in which the authors state that there are 4000 new cases of SSNHL annually in the USA. Since the annual incidence of SSNHL is noted to be 5-30/100,000 population, the USA incidence should probably 40,000 annual cases.

Response: We have corrected as 4,000 to 40,000 in Page 5, Line 8 in the
revised version.

Reviewer: D.L.

1. The primary outcome measure is the measure of the hearing improvement. The endpoint is defined as change in a 5-frequency threshold average in one place, but in other place it is defined as mean hearing level (Page 10). It would help the reader if the same term was used to describe the endpoint throughout the paper (threshold improvement or mean hearing level improvement). (Minor Essential Revision)

Response: In the original version, we stated the mean hearing level at 12 or 24 weeks after the test treatment as just for information. As pointed out by the reviewer, this statement could make readers complicated. We thus eliminated this statement from the revised version.

2. On p. 9, the description of the sample size calculation could be clarified. First, the null hypothesis is considered an equivalence test; the methods should state that clearly. Second, the conceptual null hypothesis sentence should be stated prior to the sentence describing the conditions under which the sample size was calculated (e.g., the sentence about the binomial distribution). Finally, please clarify how many patients represent the 10% excluded. (Minor Essential Revision)

Response: According to the comment, we have stated the null hypothesis prior to the statement for calculation of the sample size, and revised as ‘The null hypothesis was that the proportion of patients with hearing improvement at 12 or 24 weeks after the test treatment would be equivalent to the proportion of patients with hearing improvement reported in a historical control administered hyperbaric oxygen therapy.’ in Page 9, Line 1-4.. The 10% excluded is 3 samples, which is described in the revised version (Page 9, Line 6).

3. Some of the symptoms of presumed drug-induced adverse effect such as tinnitus, floating sensation also could be the disease related. For example, it would help the authors to identify cases for few adverse events if we knew which subjects entered the study with a "floating sensation" and which subjects developed a "floating sensation" after the gel treatment. For subjects entering the study with the symptom, experiencing the symptom after treatment may not be associated with the treatment. For subjects without the symptom, experiencing the symptom after treatment may be associated with the gel. (Major Compulsary Revision)
Response: This is a helpful comment to clarify causes of adverse events. In all patients with dizziness, the dizziness appeared after the test treatment, suggesting association with the test treatment, which described in Page 10, Line 21-22. Exacerbation of tinnitus was found in two patients. However, it appeared on day 29 or 33 after the test treatment. We thus consider that exacerbation of tinnitus may not be associated with the test treatment. This issue is stated in Page 10, Line 25-Page 11, Line 1.

4. What is the “floating sensation”? Please define clearly. Do you mean a light-headedness or dizziness? (Minor Essential Revision)

Response: We have used dizziness instead of floating sensation in the revised version.

5. The term “no response” was used while the “recovery” was used for hearing improvement. I suggest to use the term “no recovery” to be consistent. (Minor Essential Revision)

Response: We have substituted “no response” with “no recovery” in the text and table 1 according to the suggestion.

6. In reference 15 under References, the year of publication is missing. (Minor Essential Revision)

Response: We have described the year of publication, which is 2008.

We appreciate your review of this work.

Sincerely yours,

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