May 22, 2022

Dear Dr. Wang:

Thank you for considering our manuscript (Manuscript ID: 76360, Case report) entitled, "**Effects of intravascular photobiomodulation on motor deficits and brain perfusion images in intractable myasthenia gravis: a case report**" for publication in World Journal of Clinical Cases. We appreciate the time and effort you and each of the reviewers have dedicated to providing insightful feedback on ways to strengthen our paper. We have carefully studied the reviewers' questions and comments and responded to them point-to-point (shown below this letter). We have also incorporated changes that reflect the detailed suggestions you have graciously provided. The manuscript has been revised accordingly. Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries. We hope you will find the revised version acceptable for publication.

Best regards.

Yours sincerely,

Shin-Tsu Chang

Department of Physical Medicine and Rehabilitation, Kaohsiung Veterans General Hospital

E-mail: ccdivlaser1959@gmail.com

Tel: 886-7-3422121

May 22, 2022

PEER-REVIEW REPORT

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: In this manuscript, the author reported a case of myasthenia gravis that received intravascular laser irradiation of blood (ILIB) interventions (a potentially novel therapy,) and regained muscle power and better life quality. Some concerns and suggestions are listed as below: Why the patient was advised to receive ILIB? Why three courses of ILIB were used? Can the helium-neon laser with a wavelength of 632.8 nm reach deep CNS tissues? Several years of conventional treatments, including acetylcholinesterase inhibitors and immunosuppressive drugs, should be provided in details. Why did not you try the second line therapy, such as RTX? Long-term effects of ILIB intervention is not clear. I wonder if MG patients still need acetylcholinesterase inhibitors and immunosuppressive drugs following ILIB. When the benefical effect of ILIB was noted (hours, days or months)? Antibody status of this patient was not mentioned.

Response to the reviewer's comments: We appreciate the comments and suggestions by the reviewer and respond below to each point.

1. Why was the patient advised to receive ILIB?

   The patient's symptoms were not ameliorated with conventional treatments such as medication and traditional rehabilitation. In addition,

due to the remarkable curative effect of ILIB in our hospital, the patient came to see a doctor specially, and was willing to try this new treatment.

2. Why three courses of ILIB were used?

Previously, one course of ILIB did not provide significant effects. Also, the results of next-generation sequencing (NGS) analysis were inconsistent. After three courses of ILIB, the NGS results tended to be stable and consistent (Unpublished data). Therefore, we currently administer three courses of treatment as multiples of three (6 times, 9 times, etc.), which has resulted in significant improvements in neurological disorders (although case numbers are low and it is also personal experience, such as REF). The patient continues to receive ILIB and is confident in the treatment effects. The patient is still receiving ILIB and is confident in ILIB.

REF.

Jui-Hsiang Sung, **Shin-Tsu Chang**. Reversal of impaired blood flow of the basal ganglion from the prior focal perfusion defect in a case of ischemic infarction: observation during the two stages of administration of Intravenous laser irradiation of blood. **HSOA Journal of Medicine: Study & Research 2019; 2(1): 011. DOI: 10.24966/MSR-5657/100011**

3. Can the helium-neon laser with a wavelength of 632.8 nm reach deep CNS tissues?

Yes. ILIB does not directly irradiate the head with laser light, but rather directs the laser light to the veins of the upper arms. The irradiated red blood cells will circulate throughout the body. Within 1 hour, the whole body circulates about 6–7 times, including deep CNS tissues. We believe that the following two mechanisms allow oxygen delivery to the ischemic site through narrowed capillaries: 1) the increased oxygen-carrying capacity of the irradiated RBCs can enhance oxygen supply to brain tissue, and 2) the RBCs have better deformability. Moreover, the irradiated RBCs supply the ischemia site with oxygen and nutrients. Thus, through these mechanisms, the helium-neon laser with a wavelength of 632.8 nm may affect deep CNS tissues.

4. Several years of conventional treatments, including acetylcholinesterase inhibitors and immunosuppressive drugs, should be provided in detail.

Thank you for these reminders. The patient was prescribed acetylcholinesterase inhibitor, pyridostigmine (oral: 60 mg/tab, 2 tabs three times daily), for 1 year. Later, he was administered immunosuppressive drugs; namely, rituximab (IV: 375 mg/m^2, once weekly for 4 weeks), and also received six courses of IVIG to improve his conditions. However, his symptoms did not improve as anticipated. We have revised the "***History of past illness***" of the "**CASE PRESENTATION**".

5. Why did not you try the second line therapy, such as RTX?

The patient had previously tried rituximab (page 6, line 18 of first manuscript) without change in his symptoms of MG. Thus, the patient was advised to try ILIB. ILIB may be an alternative therapy for refractory disease. In addition, as the patient experienced refractory MG, we have modified the title to include the word "**intractable**".

6. Long-term effects of ILIB intervention are not clear.

Indeed, the long-term effects of ILIB cannot currently be answered. We have a case receiving nine courses of ILIB, with excellent effects, as described in *REF*. After receiving ILIB therapy, the patient with MG had maintained a good quality of life. We continue to follow up on the long-term effects in this patient with MG.

REF.

Jui-Hsiang Sung, **Shin-Tsu Chang**. Reversal of impaired blood flow of the basal ganglion from the prior focal perfusion defect in a case of ischemic infarction: observation during the two stages of administration of Intravenous laser irradiation of blood. **HSOA Journal of Medicine: Study & Research 2019; 2(1): 011. DOI: 10.24966/MSR-5657/100011**

7. I wonder if MG patients still need acetylcholinesterase inhibitors and immunosuppressive drugs following ILIB.

The patient no longer needs to take acetylcholinesterase inhibitors and immunosuppressive drugs. Instead, he receives ILIB regularly, followed by appropriate self-care and simple exercise therapy at home.

8. When the beneficial effect of ILIB was noted (hours, days or months)?

During monthly outpatient visit, we assess the patient's clinical condition. We observed distinct changes in the 4–5th sessions (i.e., days 4–5) of the patient's first course of ILIB; however, the differences in scale scores were significant after 30 sessions (third round) of ILIB.

9. Antibody status of this patient was not mentioned.

On Page 7 line 1 of first manuscript, we mentioned that "Laboratory evaluation revealed a positive acetylcholine receptor antibody." However, the value (5.97 nmol/L) was not reported. Thank you for this reminder; we have added this value to the revised manuscript. The same measurements were also checked after three courses of ILIB; however, the values have not been reported due to external testing.

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: This is a good case . And if it is true , there

are more cases to study. It is very valuable. The myasthenia gravis is a refractory autoimmune disease. The patients can develop muscle weakness crises, even life-threatening.

Response to the reviewer's comments: We appreciate the encouraging comment by the reviewer.

EDITORIAL OFFICE'S COMMENTS

(1) Science editor :

Reviewer's comments: Why the patient was advised to receive ILIB? Why three courses of ILIB were used? Can the helium-neon laser with a wavelength of 632.8 nm reach deep CNS tissues? Several years of conventional treatments, including acetylcholinesterase inhibitors and immunosuppressive drugs, should be provided in details. Why did not you try the second line therapy, such as RTX? Long-term effects of ILIB intervention is not clear. I wonder if MG patients still need acetylcholinesterase inhibitors and immunosuppressive drugs following ILIB. When the benefical effect of ILIB was noted (hours, days or months)? Antibody status of this patient was not mentioned.

Language Quality: Grade C (A great deal of language polishing)

Scientific Quality: Grade C (Good)

Response: We have answered the questions above.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de

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Response to the Company editor-in-chief's comments: We appreciate it very much for suggestions, and we have done it according to your advice.

1. The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240

   We are sorry for low quality of the English language. The revised manuscript and the letter of answering reviewers' have been edited and proofread by a professional English language editing company, hoping that the quality of the English language could meet the requirements of the journal.

2. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

   Thanks for your instructions, we have completed this work.

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   Thanks for your reminders, we have completed this work.

4. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table

should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Thanks for your instructions, we have completed this work.