

Editor in Chief
World Journal of Stem Cells

Dear Editor

Thank you very much for the decision on our manuscript submitted to the World Journal of Stem Cells (Manuscript ID: 65171), entitled “**Stem Cell Therapy and Diabetic Erectile Dysfunction: A Critical Review**”.

In response to your invitation to revise the paper, we would like to submit a revised version of this manuscript, which address all comments raised by the reviewer and the scientific editor. Please also see the point by point response to reviewer’s comments below.

We would also like to inform that we have added 3 new co-authors in the revised manuscript.

If you need further information regarding this submission please do not hesitate to contact me.

Yours sincerely

Delvac Oceandy

Response to Reviewer's Comments (MS#65171)

Reviewer #1: This manuscript mainly describes the latest studies of stem cells for the treatment of diabetic ED, including the pathogenesis of diabetic ED, the diagnostic criteria of ED, and the treatment of diabetic ED. It focuses on the progress of stem cell therapy for the treatment of ED in diabetes. The advantage over other therapies is to treat ED from the root of tissue damage. However, Most studies are limited to experimental animals, only 4 studies on human because “the research on stem cell therapy for ED in humans remains to be limited”. The work of this manuscript is logical.

We thank the Reviewer for the very positive comments.

1) However, there are some points to be further improved as well: There is a little insufficient in explanting of the mechanism for using stem cells as a therapy for ED.

To address this comment we have added text in the revised manuscript to further explain the mechanism underlying the therapeutic effects of stem cells for diabetic ED. (Page 13, last paragraph to page 14, first and second paragraphs)

Possible Mechanisms of Stem Cell Therapy for Diabetic ED

There are at least two possible mechanisms underlying the therapeutic effects of stem cell implantation for diabetic ED. First, stem cells may differentiate to specific cells and hence, regenerate the damaged tissue. In diabetic ED, the implanted stem cells may differentiate to myogenic cell precursor that subsequently in the presence of growth factors such as FGF and TGF-Beta can differentiate to myoblasts^[40,63]. The myoblastic cells are known to have the capability to differentiate to vascular smooth muscle cells. The new smooth muscle cells may repair and improve damaged vascular tissues and hence improve the erectile function^[64,65]. Second possible mechanism may involve the capability of stem cells to secrete beneficial paracrine factors. Stem cells are known to secrete angiogenic factors such as vascular epithelial growth factor (VEGF), basis Fibroblast Growth Factor (bFGF) and SDF-1. These factors are potent inducers of angiogenesis and neovascularization^[66,67]. Stem cells can also produce factors such as Wnt4 and Wnt7b, which are able to promote the differentiation of myoblasts to smooth muscle cells^[63]. Together, the ability of stem cells to differentiate to smooth muscle cells and to produce beneficial paracrine factors that induce angiogenesis and neo-vascularization may be the underlying mechanisms of the therapeutic effects for diabetic ED.

2) In the paragraphs of the research progress of stem cell treatment of diabetes ED, the tense is confused.

This has been amended. All of the text in the sub-section “Current Progress in Stem Cell Therapy for Diabetic ED” (page 11-12) have been checked and proofread.

3) In main text, Bahk et al.(ref. 61) and Protegerou et al.(ref. 62) the cell numbers needs to be expressed in exponential power format.

This has been corrected according to Reviewer's suggestion (page 13).

4) In addition, the list of references is not the style of the journal, the reference numbers should be superscripted in square brackets at the end of the sentence.

We have amended list of references and the style of journal citations according to the guideline.

Response to Comments from Science editor:

1 Scientific quality: The manuscript describes a minireview of the stem cell therapy and diabetic erectile dysfunction. The topic is within the scope of the WJSC.

(1) Classification: Grade B;

(2) Summary of the Peer-Review Report: This manuscript mainly describes the latest studies of stem cells for the treatment of diabetic ED, including the pathogenesis of diabetic ED, the diagnostic criteria of ED, and the treatment of diabetic ED. It focuses on the progress of stem cell therapy for the treatment of ED in diabetes. The advantage over other therapies is to treat ED from the root of tissue damage.

The questions raised by the reviewers should be answered

We have addressed all of the comments and issues raised by Reviewer 1, please see point by point response to Reviewer 1 comments above.

(3) Format: There are 2 tables and 1 figure;

(4) References: A total of 68 references are cited, including 20 references published in the last 3 years;

(5) Self-cited references: There is no self-cited reference; and

(6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade A. A language editing certificate issued by Enago was provided. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJSC. 5

We have added financial support (Mandate Research Grant from Universitas Airlangga, grant number 1408/UN3/2019) in the revised manuscript. Please see page 2 of the revised manuscript.

Issues raised: (1) The authors did not provide original pictures. 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;

We have now provided original figure file in Powerpoint format in the resubmission.

(2) If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

We do not present any copy-righted figure(s) in this manuscript.

6 Recommendation: Conditional acceptance.