

Author's responses to Reviewers Comments

Reviewer 1

Specific Comments to Authors:

Authors have tried their best to review the diabetic neuropathy with traditional way but for betterment and increment of weight of article, following changes should be required.

1. According to guideline of reporting a review, title should consist 'review article' with its type (i.e. systematic or meta-analysis or narrative or traditional).

Response: I apologize for the unclear title which affects the whole elaboration of the manuscript. Therefore, I amended the title and took into account the suggestion by the reviewer. The new title which better represent the review contents is "Issues and Challenges in Diabetic Neuropathy Management: A Narrative Review".

2. Titles and aim are confusing to readers.

Response: I apologize for the contradictions raised in titles and aim of the manuscript. It happened due to the mistakes I made during the initial preparation of the manuscript within limited period of time to prepare. To cut it short, the main idea is basically about diabetic neuropathy (DN) in general, not specifying on the painful diabetic neuropathy (PDN). Therefore, I amended the aim as described in the manuscript. The aim of this narrative review was to point out the issues and challenges in the management of DN in the current situation while understanding the molecular mechanisms leading to its progression, providing current and future direction in DN. In order to improve the quality of diabetic approaches, some suggested resolutions are also discussed.

3. According to authors, what is the difference between treatment and management? It should be cleared and introduce a small paragraph on the issues of current treatment and management which are missing.

Response: Thank you reviewer for alerting this simple mistake of us. We found no difference in those two terms and therefore, we have amended in the text as suggested.

4. The aim mentioned in abstract is confusing. The aim is to review only on painful diabetic neuropathy? If yes, title should be changed accordingly. Painful Diabetic neuropathy occurs generally in peripheral or proximal diabetic neuropathy. Hence, changes should be required in whole article according to your aim.

Response: We apologize for the confusion raised in this review. As we have previously mentioned in response #2, we currently focus on diabetic neuropathy in general and changes have been made in the manuscript focusing on general DN.

5. PDN was written in abstract without its full name. Abbreviations may use throughout the article only after the first citation in the manuscript with its full name.

Response: Thank you for reviewer for the comments. We have amended the use of abbreviations accordingly.

6. What is the meaning of PDN? Generally, PDN means Proximal Diabetic Neuropathy or Peripheral Diabetic Neuropathy. PDN is mentioned as Painful Diabetic Neuropathy

in introduction. Several reviews and literatures are available on diabetic neuropathy and peripheral diabetic neuropathy.

Response: PDN used in the text refers to 'painful diabetic neuropathy' as one of the variant of diabetic neuropathy.

7. What are the specific gaps and pitfalls in this available literature to undertake this review? These all must be mentioned in the introduction. How the gaps and pitfalls of previous reviews and presently available materials on diabetic neuropathy were fulfilled by this article? What is new in this manuscript? For highlighting the strength of article, this must be discussed at the end of article in details with final conclusive statement. Article is written only on the base of available materials. Discussion on each topic (containing the matters of reference literature) is missing. Though this is narrative or traditional review, discussion must be required to increase the knowledge or to add some new things which is not in present literature. Hence, detail discussion on prescribed matter must be included in the article. Matter must interpret or discuss with personal or expert opinion or practical approach or your own views and belief on it at the end of each heading. Or it may write as 'Discussion' - a separated heading in the article before conclusion. This essentiality is missing in article.

Response: Thank you reviewer for highlighting this important issue in this review. In fact, several reviews on DN highlighted recent scenarios and management linking to DN and majority of them seek to provide the molecular insight into the secondary complications to DN but not fully understand the molecular mechanism leading to its progression. These reviews have accidentally under looked the issues that possibly raised linking with diabetic management. In consequence, the prevalence of DN is escalating while management of DN remains challenging. This is the specific gaps and pitfalls in the previously published literature that we aimed to discuss and the new topic in this manuscript. We have also added "Discussion" section where we pointed out our view regarding the current diabetic management.

8. I found mismatching between quoted materials and its references at some places. See the comments in world file of manuscript. I have not checked each and every references of quoted material. Please check the references for quoted material in whole article.

Response: Thank you reviewer for the alert. We actually have read and studied the materials/references that we quoted in this manuscript. We believed we have appropriately cited the correct literature for this manuscript.

9. Narrative review generally includes algorithms which are totally missing in the article. Tables, graphs or algorithm (especially for causes, treatment or diagnostic assessment of the disease) make this article more valuable. Hence, try to make two or three tables and algorithms if possible. Check the whole article for linguistic correction. Some examples were mentioned in the comments in the beginning of the article (specially in introduction).

Response: We appreciate your suggestions regarding the algorithm that should be included in this manuscript for the value of this manuscript. We have added two tables summarising the diabetic management and therapeutic medications used to treat DN in this manuscript, and Figure 1 summarises the pathomechanisms leading

to DN. Moreover, as suggested by the reviewer, we have submitted this manuscript for proofreading for the improvement of manuscript quality. The certificate of proofreading is attached.

Reviewer #2:

Scientific Quality: Grade C (Good)

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

Conclusion: Major revision

Specific Comments to Authors: Diabetic neuropathy is a devastating disorder that turns into global epidemic, posing critical burden on individuals and community with huge implications on economy and output of a country. With the changes in lifestyle, the prevalence of diabetic neuropathy is unceasingly escalating. It is not an interesting manuscript. Authors cannot succeed to present their idea in a clear way adding information to the existing literature. What are the original findings of this manuscript?

Response: We appreciate the comments. This manuscript discussed some current issues and challenges faced by the patients, physicians and facilities in the management of DN. We added some discussion suggesting a number of recommendations that could be essential for the improvement of the available guidelines for DM or DN management.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes

3 Key Words. Do the key words reflect the focus of the manuscript? Yes

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? NA

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? NA

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes

8 Illustrations and tables. Are the figures, diagrams, and tables sufficient, good quality and appropriately illustrative, with labeling of figures using arrows, asterisks, etc, and

are the legends adequate and accurately reflective of the images/illustrations shown?
No figure, I recommend some figures can be drawn.

Response: We have added Figure 1 summarising the pathomechanism leading to DN development, and 2 tables for DN managements.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? NA

10 Units. Does the manuscript meet the requirements of use of SI units? Yes

11 References. Does the manuscript appropriately cite the latest, important and authoritative references in the Introduction and Discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Language use is very casual. Professional language editing is recommended.

Response: Thank you reviewer for the comment. We have submitted this manuscript for proofreading. The certificate of proofreading is attached together with this manuscript revision.

13 Research methods and reporting. Authors should have prepared their manuscripts according to BPG's standards for manuscript type and the appropriate topically-relevant category, as follows:

(1) CARE Checklist (2013) - Case report;

(2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial;

(3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis;

(4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and

(5) The ARRIVE Guidelines - Basic study.

For (6) Letters to the Editor, the author(s) should have prepared the manuscript according to the appropriate research methods and reporting. Letters to the Editor will be critically evaluated and only letters with new important original or complementary information should be considered for publication. A Letter to the Editor that only recapitulates information published in the article(s) and states that more studies are needed is not acceptable? NA

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? NA