Reviewer's report

Title: Impact of insufficient drug efficacy of antiparkinson agents on patient's quality of life: A cross-sectional study

Version: 4
Date: 26 December 2014

Reviewer: Seyed-Mohammad Fereshtehnejad

Reviewer's report:

Date: 26 December 2014

To: The Editor-in-chief of the BMC Neurology journal;

Regarding the reviewing process of the manuscript titled “Impact of insufficient drug efficacy of antiparkinson agents on patient’s quality of life: A cross-sectional study”, I must note that this article has been reviewed. This is a cross-sectional survey using mailed questionnaires to gather data on how common is insufficient drug efficacy among the Japanese Parkinson’s disease patients and how it affects their quality of life. Although the manuscript addresses an important issue in PD, there are some major concerns and issues regarding sampling methodology and data validity, which must be taken into account. My comments and queries are as follows:

# ABSTRACT

1. A brief definition of the insufficient drug efficacy should be mentioned in the “Methods” section of the abstract.
2. The “Results” section of the abstract needs to be improved by using the effect sizes for the mentioned correlations/associations.
3. The final “Conclusion” presented in the abstract is not in line with the main aim of this study to answer the question how insufficient drug efficacy might affect quality of life. It needs to be revised.

# INTRODUCTION

4. The first sentence of the “Introduction” section should be revised since Parkinson’s disease is the second commonest neurodegenerative disease among the elderly and not the entire population. This needs to be clarified.
5. The following statements need to be cited to their relevant references:
   “… as the Japanese population continues to rapidly age”
   “Inappropriate pharmacotherapy or insufficient management of wearing-off can lead to insufficient drug efficacy”
6. I recommend providing more explanations about the concept of “insufficient drug efficacy” and what exactly do the authors mean by this term.

# METHODS

7. Page 4, line 1: the first age category should be probably written as <3 years.
Please check it again.

8. The most important concern about this project is the validity of information since all data were gathered as self-reported by the patients without even checking with their medical records. How could authors deal with this issue? How valid are patients’ answers on their Hoehn and Yahr staging? How valid are the answers given by patients on their complete list of medication?

9. As the questionnaire was mailed to participants, I wonder how the authors managed the problem of cognitive deficit in study population. Nowadays, there are growing evidence to show that at least some degrees of mild cognitive impairment is present even in the early stages of Parkinson’s disease in many of them.

10. Another major issue is the sampling method that has been used in this study. While authors mentioned that finding “the frequency of insufficient drug efficacy” is one part of their aims, the mailing questionnaire method without any random sampling method could not be able to provide frequency information. Patients who have experienced insufficient drug efficacy were more likely to participate in this survey and sent back their filled questionnaires. As a result, the study population is not representative of the general Parkinson’s disease individuals. How have the authors dealt with this problem?

11. Please clarify if the Japanese-translated and validated version of the PDQ-8 has been used in this study. Also please provide a reference for that.

12. It seems helpful to give more information about the PDQ-8 questionnaire including its scale and direction of the scores. How was the PDQ-8-SI calculated?

13. Have the authors used a standard definition for “insufficient drug efficacy”? What is the reference for that? If not, how could the authors be sure that these four questions could lead to valid answers to assess the “insufficient drug efficacy”?

# RESULTS

14. Unlike general PD populations, there is a female preponderance in this study population that has made it non-representative sample.

15. Moreover and as previously mentioned, there are just few patients in the mild stage of disease due to the fact that these patients were not probably eager enough to participate in the survey. Thus, it is not possible to judge about the frequency of insufficient drug efficacy in a PD population based on the findings of this study.

16. Please provide statistical details such as the test’s name and the appropriate effect size while assessing the relationship between self-reported severity of PD and frequency of insufficient drug efficacy.

17. It could be of interest to perform multivariate analysis to check if the insufficient drug efficacy could still have an independent effect on quality of life score after adjustment for Hoehn and Yahr score and/or disease duration adjusted for the baseline characteristics such as age and sex. I recommend using multivariate linear regression model for this purpose.
# DISCUSSION

18. Page 8, line 5: If “no previous reports investigated Japanese subjects” using the PDQ-8, then it becomes necessary to provide statistical data on the reliability and validity of the Japanese version of the questionnaire prior to interpreting any findings from that.

19. As previously mentioned, it is really difficult to extrapolate the findings of this study since the sampling method was inappropriate and the validity of the answers and variables has not been assessed. Therefore, many parts of the discussions should be mentioned cautiously.

20. This study has totally ignored the non-motor features of Parkinson’s disease, which are in fact very important determinants of quality of life in these patients. Non-motor symptoms could also accompany insufficient efficacy of the medication and also worsen quality of life as a confounder factor or even a mediating variable. How could the authors discuss the issues?

It seems that this manuscript does not have good quality and I recommend rejection.

Seyed-Mohammad Fereshtehnejad MD. MPH.
Department of Neurobiology, Care Sciences & Society, Karolinska Institutet, Stockholm, Sweden

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.