Reviewer's report

Title: Psychosis in Parkinson disease: implications of patient-side factors and medications

Version: 2 Date: 30 January 2013

Reviewer: Ramit Ravona-Springer

Reviewer's report:

Review for manuscript: "Psychosis in Parkinson disease: implications of patient-side factors and medications"

This manuscript addresses an important clinical question. Since psychosis in PD subjects is prevalent and given the risk associated with antipsychotic treatment, it is important to identify patient and treatment related factors associated with increased risk for psychosis, some of which may be modifiable. Additionally, the clinician's knowledge about patient populations that are at increased risk for psychosis, will enable a more integrative approach that takes into consideration the risks and potential advantages of treatments thus potentially decreasing the risk for treatment induced psychosis.

Thus, the rationale for the study is understood, however, I do have several remarks regarding the methodology and the writing of the study:

1. The title of the manuscript is misleading. The authors did not look at psychosis in PD, but rather, at psychosis which was severe enough to justify antipsychotic treatment.

2. Were there clear criteria as to what type of psychosis is severe enough to justify antipsychotic treatment? In this matter there is substantial variability among clinicians.

3. The definition of hazard period is not clear. What was the basis for decision that hazard period starts 1 day before initiation psychosis. Since the authors defined psychosis as psychotic symptoms severe enough to justify antipsychotic treatment, it may very well be that patients were psychotic for a substantial period of time before that time.

4. Looking at the MMSE and acknowledging the fact that some patients had a very low MMSE score and some were treated with cholinesterase inhibitors, it is clear that some subjects were frankly demented. Yet, the authors did not acknowledge this fact in description of patients included in the study or in the discussion.

5. The authors mentioned that subjects who underwent surgery were excluded from the study since in these subjects, psychosis may be part of delirium, yet,
this patient population is prone for other medical conditions associated with delirium (UTI, pneumonia, etc). The authors did not refer to this issue in description of subjects, as a factor contributing to results or in the discussion. It is important to state if and how was delirium excluded

6. The authors state that hospitalized patients were included. Elderly subjects suffering from a neurodegenerative disease that are hospitalized are prone for delirium- either due to the medical condition due to which they were hospitalized, the hospitalization itself or the treatments received. This issue did not receive attention in the manuscript.

7. The primary outcome of the study was serious psychosis, i.e. psychosis requiring prescription of antipsychotic drugs in the presence of psychotic symptoms (illusions, false sense of presence, hallucinations, delusions). What about antipsychotics prescribed for agitation, aggression?

8. The description of record review process is not clear. What does it mean "...records were retrospectively reviewed in two years"?

9. The authors state that "Modified Hoehn–Yahr (mH–Y) stage and the score of Mini–Mental State Examination (MMSE) of the patients were thought to be stable in the study period and were collected at the enrollment. In contrast prescription was collected consecutively because it was changeable weekly or monthly". Wht did the authors assume that mH-Y and MMSE would remain stable? In PD both motor and cognitive progression of disease are seen over time.

10. Discussion: in general, in the discussion section of this manuscript, significant effort is devoted to discuss mechanisms (which were not assessed in the current study) rather than to discuss the results, their importance and potential implications.

11. The first sentence of the discussion refers the reader to another study that deals with different patient population the current (population based study vs clinic based). The first sentences of a discussion should summarize the main findings and stress their importance.

12. The authors claim that incidence of psychosis in the current study is high relative to other reports due to recurrence of psychosis- this statement is not clear.

13. Then, the authors refer to mild psychosis, which was even more prevalent in previous studies, yet was not at all assessed in the current study.

14. In page 10, 2nd paragraph, the authors cite previous studies which address sleep disorders as risk factors for psychosis in PD, yet sleep disorders were not assessed in the current study and mechanisms associating psychosis to sleep disorders are not relevant.

15. The role of anticholinergic medications and their association with cognitive decline and delirium is not discussed.
16. When discussing results regarding cholinesterase inhibitors, the authors should discuss the indication, which is Parkinson's disease dementia and the implication of this on the results.

17. In the middle paragraph on page 10, the authors write that there was a significant interaction between PD duration and use of anticholinergics because anticholinergics are old drugs and prescribed for patients with longer duration. The rationale behind this claim is not at all clear. If anything, clinicians should and do avoid these medications in the elderly.

General issues (by review guidelines):
1. Is the question posed by the authors well defined?
The question studied is of great importance. There is problem with the definition—the authors claim in the title to assess psychosis in PD, whereas, de facto there are assessing psychosis severe enough to require antipsychotic medications.

2. Are the methods appropriate and well described?
No. Detailed specifications in the remarks above.

3. Are the data sound?
No. please see remarks above regarding problems with methodology of the study (definition of patient population, data collected. These affect the quality of data.)

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
See above

5. Are the discussion and conclusions well balanced and adequately supported by the data?
In general, in the discussion section of this manuscript, significant effort is devoted to discuss mechanisms (which were not assessed in the current study) rather than to discuss the results, their importance and potential implications. Specific comments are in remarks 11-17 above.

6. Are limitations of the work clearly stated?
No. please see answer to (5).

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
The authors acknowledge previous works, many of which are not relevant for the current report.

8. Do the title and abstract accurately convey what has been found?
No. The title is misleading.

9. Is the writing acceptable?
As detailed above, there are several unclear sentences and paragraphs.