Reviewer's report

Title: Relapse according to antipsychotic treatment in schizophrenic patients: a propensity-adjusted analysis

Version: 1 Date: 1 December 2010

Reviewer: Leslie Citrome

Reviewer's report:

This is a novel report of antipsychotic polypharmacy versus monotherapy in the maintenance treatment of schizophrenia. The dataset is rich in terms of ratings of psychopathology, social and occupational functioning, quality of life, and extrapyramidal tolerability. Propensity-adjusted analysis permits a more precise view of potential differences in outcomes between groups in non-randomized study designs. The report itself is concise and focused.

Major Compulsory Revisions

1. The data was collected about a decade ago. Please clarify if this was a pre-planned analysis of data collected prospectively or whether this was a retrospective post-hoc analysis of a dataset collected for other purposes.

2. Please provide any references/citations to reports that have already been presented/published regarding this dataset.

3. In the abstract, "Patients with polypharmacy also presented a higher general psychopathology PANSS score (p=0.04)" ought to be changed to "Patients with polypharmacy also presented a higher general psychopathology PANSS subscore (p=0.04) (but no statistically significant differences in the PANSS total score or the PANSS positive or negative subscales)." Corresponding changes in the text should also be made. In the text, some commentary should be made regarding the similarity in general of the PANSS scores between the two groups.


5. Please clarify the language contained in section 2.3, Study outcome. Specifically, "(2) a re-emerge of florid psychotic symptoms such as delusions, hallucinations, bizarre behaviour," and "(3) thought disorder lasting 7 days or more." imply that these cannot exist at baseline. Many patients in treatment have baseline psychotic symptoms and/or a baseline thought disorder that is chronic and persisting, yet are considered "stable." Do the authors mean a worsening from baseline? If so, what were the operational criteria, if any, used in this study?

6. In section 3.1 of the results, please clarify what "Role-Emotional limitations" is, as many readers will be unfamiliar with this.

7. In section 4 (discussion), suggest deleting the sentence "This finding is in contrast to the generally upheld notion that there is no support for combining 2
antipsychotics."
8. In section 4, delete the word "negative" from the heading "Several hypotheses can be proposed to explain our negative result."
9. The discussion should include some additional text regarding dosing of antipsychotic when used as monotherapy and when used in combination treatment. Is this information available in the dataset? It would be of interest to see if combination antipsychotic patients received low doses of each antipsychotic, low doses of one and high doses of the other, or high doses of both.
10. Additional methodological comments:
   a. One assumption is that combination antipsychotic therapy usually consists of 2 medications. Was this usually the case in this study? How many patients received 3 or more antipsychotics simultaneously?
   b. How was a depot medication handled? Does receiving a depot plus the corresponding oral count as polypharmacy?
   c. What amount of prescribing overlap was required before declaring that the patient belonged in the combination antipsychotic group? One day? One week? One month?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

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