Reviewer's report

Title: Anti-depressive effectiveness of olanzapine, quetiapine, risperidone, and ziprasidone: a pragmatic, randomized trial

Version: 1 Date: 26 April 2011

Reviewer: Nienke Vulink

Reviewer's report:

The paper is interesting and elaborates data about the anti-depressive effects of atypical antipsychotics in patients with psychotic disorders. The original paper has been published before in BMC Psychiatry (2010) which already described effectiveness and general anti-depressive effects of atypical antipsychotics in psychotic patients. Up till now, at least 10 papers already described the anti-depressive effects of atypical antipsychotics. However, most studies were short term and sponsored by the pharmaceutical industry.

This is the first long term, naturalistic study examining anti-depressive effects of different atypical antipsychotics. One of the major limitations is the missing placebo condition. Another limitation is the high dropout. In total 226 patients were randomized, 109 patients were screened after 6 weeks, while only 52 patients were assessed at 3 months. In addition, only 15 patients completed the 24 months of the trial. Did patients drop out because of increase of depressive symptoms? Therefore, no final conclusions can be drawn from long term follow-up.

- Major Compulsory Revisions

Methods patients
1. Regarding the aim, it is not clear why patients with major depressive disorder with psychotic features were assessed together with patients with primary psychotic disorders.
2. How many patients were diagnosed with a comorbid major depressive disorder?

Results
1. As described above, in total 226 patients were randomized, 109 patients were screened after 6 weeks, while only 52 patients were assessed at 3 months. In addition, only 15 patients completed the 24 months of the trial. Did patients drop out because of increase of depressive symptoms? Reasons for dropout were only shortly described in Figure 1.

- Minor Essential Revisions

Methods
3. Adjust the following sentences:
a. “the diagnoses were determined by experienced clinicians”
b. “were suffering from an episode of manic psychosis”

4. What is meant by experienced clinicians? Are they psychiatrists?
5. It was no clear if the authors used a structured clinical interview to diagnose major and comorbid diagnoses.
6. It is not clear what is meant by the following exclusion criterion: “unable to use atypical antipsychotics” (intolerance? side effects?). Were patients with a bipolar disorder excluded? It is also unclear what is meant by “unable to cooperate reliably during investigation”.
7. How did the authors discriminate which patients were candidates for electroconvulsive therapy? Moreover, ECT is the main treatment option for patients with major depressive disorder.

Treatments
1. Rewrite: “A reason for discarding drugs was sought”.

Statistical procedures
2. Repeating sentence: “For multiple comparisons, Benjamini-Hochberg adjustments were applied.

Results
3. Improve English writing
4. Explain: “Eighty (74.1%), The corresponding figures were 1 (3.4%) for olanzapine, 0 for quetiapine, and 5% (18.5%) for ziprazidone-treated FCGs.

Discussion
1. Some English improvement: for example: “The mean CDSS sum score in the BPP at baseline was 6.5, and 42.7% of the sample had CDSS sumcore >6” and (End of second paragraph) “compared to in our study”.

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