Reviewer’s report

Title: Non-adherence to antipsychotic medication, relapse and rehospitalisation in recent-onset schizophrenia.

Version: 2 Date: 12 September 2007

Reviewer: Wolfgang Gaebel

Reviewer's report:

General

In 2006 the authors published a random-controlled study, which demonstrated that an integrated biomedical and psychosocial treatment proved superior to standard treatment in reducing negative symptoms, minor psychotic episodes and in stabilising positive symptoms, but not in reducing hospital admissions or major psychotic recurrences. The primary outcome measures were evidence of full and stable recovery from all clinical features of schizophrenic disorders.

A second article was published by the authors in 2007 about the same study, examining the impact of medication adherence. No difference in adherence was found between the integrated treatment group and the standard group.

In the new article the authors focus on non-adherence again, which was associated with relapse, hospital admission and having persistent psychotic symptoms.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) The randomised design with two different clinical conditions and the development of the research question resulting from the earlier articles are not made clear and transparent enough in this publication. The results of the previous publication demonstrating that the two interventions "seemed to be equal in effects on adherence to medication" should be pointed out explicitly. It should also be emphasized that the proportions of patients that were adherent to medication throughout the study were much the same in the IT and the ST groups.

2) A limiting factor of the analysis is that it does not differentiate between first-generation and second-generation antipsychotics (excluding clozapine) and clozapine regarding the effect on drug adherence. Problems with efficacy or tolerability of antipsychotics may decrease a patient’s volitional adherence and affect clinical state.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

3) The authors conclude that one of the limitations of the study is the exclusion of patients with major substance abuse. Here it should be mentioned that substance abuse is a robust predictor of antipsychotic non-adherence and treatment discontinuation, revealing the sample bias of the study.

4) Another limitation according to the authors is that the adherence to medication was not systematically evaluated biologically. As one of the assessments, the authors earlier mention plasma assays. It remains unclear if the information on adherence gathered from plasma assays has been assessed on a regular basis and analysed. It would be interesting to compare drug adherence based on patient interviews to adherence based on plasma assays.

5) A study by Velligan et al. (2005) examined the agreement among objective and subjective measures of adherence to oral antipsychotic medications and suggests that neither patients nor physicians were able to accurately identify adherence. Therefore the reliability of patient interviews as a basis for measuring adherence requires further discussion.

6) Methodically, a comparison of adherence to oral antipsychotics with non-adherence patients combined with depot users is problematic. The authors hypothesize that de-pot users are always associated with non-adherence with oral antipsychotics.

7) The small numbers of participants, especially of those using depot-antipsychotics should be discussed as a limitation of the study.

Discretionary Revisions (which the author can choose to ignore)

8) A new article by Cooper et al. (2007) fails to be discussed. According to Cooper, studies examining adherence to antipsychotic treatment suffer from a lack of differentiation between persistence and compliance as two separate components of adherence. Patients still undergoing treatment with any atypical antipsychotic drug 1 year after their first prescription were considered persistent. Of these patients, those with a supply of drugs for at least 80% of the days were deemed compliant. Persistence with the initial antipsychotic may indicate optimal pharmacotherapy and be a precursor to longer-term effectiveness and other positive outcomes. The authors of the present study do not differentiate between these two separate components of adherence.

What next?: Accept after discretionary revisions

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:
I declare that I have no competing interests.