Reviewer's report

Title: Early onset of treatment effects with oral risperidone

Version: 1 Date: 25 November 2006

Reviewer: Stefan Leucht

Reviewer's report:

General
The paper addresses a very important general question in the pharmacological treatment of schizophrenia - the onset of action of antipsychotic drugs. What the paper adds to this debate is a measurement after 1 and 3 days after initiation of treatment, and a more naturalistic sample. Usually studies do not examine patients before 1 week of treatment. Limitations are a lack of placebo control and the high drop-out rate, but the latter problem is not significant at the crucial time points 1 and 3 days.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Please add some patient characteristics. Probably you have those in the other manuscript, but it is too difficult for the reader to go back there.
Here you could also stress that these were quite severely ill patients (PANSS total score 100, locked ward) taken from routine care - in contrast to the patients in meta-analyses which were all taken from randomised registrational studies with all their problems.
2. You should describe the 3 days results in the text. According to table 1 the numerical change after 1 day was small, but it was quite substantial at day 3. If positive symptoms had significantly changed at day 3 this would be important. Furthermore, the drop-out rate at the important day 3 was still small, so that this concern is not a problem here.
3. Were other medications than benzodiazepines also allowed? If yes, please give some specification.
4. Could it be that the change of positive symptoms was more pronounced, because these acutely ill patients on a locked ward had low levels of negative symptoms - leading to a floor effect? Looking at the PANSS subscores this was not necessarily the case, but it may deserve a discussion.
5. I think the lack of a placebo group needs to be discussed, although I think it is not essential, because the doctors in clinical practice who thought that there is a delay of onset did also not subtract a placebo effect.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
A personal thought: Yes, there may be non-pharmacological factors, but antipsychotics have never been examined in humans without non-pharmacological factors. I think that there is simply hardly any evidence to support the delay of onset hypothesis. In old and new studies antipsychotics separate from placebo usually not after 1 week of treatment. It is surprising that this had been overlooked for years.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No
Declaration of competing interests:

My conflict of interest could be that our group found a similar result in a meta-analysis and that I was glad to see it confirmed.