Reviewer’s report

Title: Clozapine and desmethylclozapine: correlation with neutrophils and leucocytes counting in Mexican patients with schizophrenia

Version: 0  Date: 30 Mar 2019

Reviewer: Emilio Fernández-Egea

Reviewer’s report:

Dear Editor in chief of BMC

Many thanks for asking me to review this manuscript. I apology for the delay. This work is a cross-sectional analysis of 41 clozapine treated patients. They found an significant correlation between clozapine (and norclozapine) plasma levels and the white cells counts. Author suggest that this could help preventing episodes of fatal agranulocytosis. I think the study has few major issues to address before considering this conclusions as firm.

Issues:

1- It is unclear the goal of the study. If the goal is to help detecting agranulocytosis, perhaps is simpler to check white cells rather than checking clozapine plasma levels as risk factor? If author are suggesting high plasma levels could predict future agranulocytosis, then a longitudinal study is needed.

2- Poor control of potential confounders:

   a. Patients are at different stages of the clozapine treatment (some within first month of treatment, other after three years). For instance, it is know a decrease in white cells counts after 8 weeks on treatment.

   b. There is no information regarding other medications. This is relevant as might influence plasma levels and white cells counts.

3- Intro: I found it perhaps excessively long and not really focused on the study goals. I would benefit of greater concision, use of better terms (extrapyramidal disorder or symptoms?) and precision (TRS is considered after one or two antipsychotic resistance?)

4- Discussion:

   a. The limitation section should be extended.

   b. Clozapine metabolism is mainly through 1A2
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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Needs some language corrections before being published

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