

Dear Editor,

Journal title: World Journal of Psychiatry

Manuscript NO: 61646

Title: Chronic Serotonin Syndrome: A Retrospective study

Thank you for the reviewers' comments concerning our manuscript. We have made modifications to the original manuscript based on the comments and suggestions. All of the changes made to the manuscript are highlighted. I hope you'll find it satisfactory.

Reviewer Comments

Authors studied the serotonin syndrome (SS), an adverse drug reaction that is a consequence of excessive activation of central and peripheral serotonergic receptors by the clinical use of several serotonergic drugs. It is characterized by altered mental activity, neuromuscular hyperactivity, and autonomic disturbances, and sometimes it can lead to death. Diagnosis of SS is purely clinical and primary care physicians are not familiar with this syndrome. Thus, misdiagnosis for mild SS is common in clinical practice and studies on SS are focused on acute and severe cases. Then, in this retrospective study, authors evaluate clinical aspects of the mild chronic SS through the study of patients having symptoms that met the Hunter criteria for SS for more than 6 weeks. They hypothesize that patients receiving serotonergic drugs for a long period could be suffering from a mild and chronic SS that is not diagnosed as such, and in some of them SS may progress rapidly to death. Thus, authors suggest that these patients should be thoroughly physically examined to detect symptoms of chronic SS. This is an interesting and well written paper that may helps to unmask mild cases of SS

in patients under chronic serotonergic treatment that present non-specific clinical symptoms. I only have minor concerns.

Reply: Thanks for the comments

The name of the hospital where data are obtained is not given in the Methods section.

Reply: We have acknowledged the suggestions

In the Discussion, authors stated "... cyproheptadine (a 5-HT_{2A} antagonist) ...". It is the main drug used in cases of SS, thus I suggest to specify that cyproheptadine is a 5-HT antagonist the first time that it appears in the abstract as well as in the main text (second paragraph of Results). I suggest using only the abbreviated form "SS" instead "serotonin syndrome" throughout the text. The terms "5-hydroxytryptamine" and "5-HT" are included in text at the end of the Discussion section. I suggest to introduce these terms as synonymous of serotonin at the beginning of the Introduction and to use only one of them: "serotonin" throughout the text

Reply: We have modified as suggested. All of the changes made to the manuscript are highlighted.

Science Editor Comments

1 Scientific quality: The manuscript describes a retrospective study of the chronic serotonin syndrome. The topic is within the scope of the WJP. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: This is an interesting and well written paper that may help to unmask mild cases of SS in patients under chronic serotonergic treatment that present non-specific clinical symptoms. The questions raised by the reviewers should be answered; and (3) Format: There are 2 tables. A total of 14 references are cited, including 1 reference published in the last 3 years. There are 2 self-citations.

Reply: We included two self-citations as we considered that both are related to the topics and are necessary.

2 Language evaluation: Classification: Grade A. No language editing certificate was provided.

Reply: We have tried our best to meet the requirements of the quality of the journal. We have also taken the help of a native speaker of English.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form, and the written informed consent. No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJP.

5 Issues raised: (1) The “Author Contributions” section is missing. Please provide the author contributions. 6 Recommendation: Conditional acceptance.

Reply: We have already provided author Contributions. You can find it here.

Contributors:

Prakash S was involved in the conceptualization of the project, data collection, statistical analysis, supervision of the project, and writing original draft.

Rathore C was involved in analysis and Interpretation of data, and writing original draft.

Rana K was involved in analysis and Interpretation of data, and revising the manuscript for Intellectual Content

Diptangshu Roychowdhury was involved data collection and revising the manuscript for Intellectual.

Deepali Lodha was involved data collection and revising the manuscript for Intellectual.

All authors approved the final manuscript.