

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 61517

**Title:** The possible effect of blonanserine on gambling disorder: A clinical study protocol and a case report

**Reviewer's code:** 05426634

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Director

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2020-12-14

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-12-14 05:41

**Reviewer performed review:** 2020-12-14 08:11

**Review time:** 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

1.It is a pity that the participant got mild intellectual disability. Despite the author's explanation, this case does not show the effect of the drug on normal intellectual patients who are the major part. Did the authors enroll and complete only one patient in the trial, which began in 2016? What about the other two patients who didn't complete the experiment? Why was the experiment designed to include three patients?No other eligible patients in 4 years? 2.A blood examination was conducted 2 and 6 weeks after the start of the trial, however the authors do not show any relevant results. 3.In the part of discussion: We conducted a clinical trial to examine the use of blonanserin to treat gambling disorder. The results suggested that blonanserin might be effective in mitigating gambling behaviors but that it may also carry a risk of adverse effects. But in the part of abstract: Conclusion: This case suggests that blonanserin is an effective treatment for patients with gambling disorder who resist standard therapies. Inconsistent conclusions need to be revised. 4.The authors should provide an informed consent with the patient's signature.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 61517

**Title:** The possible effect of blonanserine on gambling disorder: A clinical study protocol and a case report

**Reviewer's code:** 03593176

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Panama

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2020-12-14

**Reviewer chosen by:** Li Ma

**Reviewer accepted review:** 2020-12-15 01:24

**Reviewer performed review:** 2020-12-28 23:23

**Review time:** 13 Days and 21 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

Criteria Checklist for New Manuscript Peer-Review 1 Title. Does the title reflect the main subject/hypothesis of the manuscript? YES 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? BACKGROUND IS INCOMPLETE: SHOULD MENTION WHY (SUPPORTIVE INFORMATION) BLONANSERIN WAS SELECTED FOR THIS WORK. METHOD IS INCOMPLETE: IT SHOULD CLEARLY STATE THE SIZE OF THE SAMPLE (N = 1), GENDER, RANGE OF AGE OF THE PARTICIPANT. ALSO, AT LEAST FEW LINES ABOUT THE "STUDY PROTOCOL". 3 Key words. Do the key words reflect the focus of the manuscript? KEY WORDS ARE FINE. 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? YES IT DESCRIBED THEM JUST A COMMENT: THERE ARE YELLOW HIGHLIGHTED NUMBERS (REFERENCES). THE YELLOW SHOULD BE CLEARED. 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? THE INCLUSION CRITERIA SHOULD ADD THE LANGUAGE PROFICIENCY OF PARTICIPANTS (EDUCATION OR SCHOLARITY ENOUGH FOR UNDERSTANDING THE INSTRUMENTS, QUESTIONS, SUBJECTS WERE JAPANESE NATIVE SPEAKERS). THEY MENTION THE SOUTH OAKS GAMBLING SCREEN (SOGS), BUT A REFERENCE SUPPORTING ITS USE SHOULD BE ADDED (NONE INCLUDED). SIMILARLY FOR THE MADRS, YMRS, AND DIEPSS, REFERENCE SUPPORTING THEY USE SHOULD BE ADDED (NONE INCLUDED) IN THE PARAGRAPH DESCRIBING THE DOSE (PAGE 8): 2 TO 12MG/DAY, REFERENCE SUPPORTING THEY USE SHOULD BE ADDED (NONE INCLUDED). IN THE PARAGRAPH DESCRIBING THE GSAS, PG-YBOCS, BIS-11, the DIEPSS, the MADRS, and the YMRS (PAGE 9): REFERENCE SUPPORTING THEY USE SHOULD BE ADDED

(NONE INCLUDED). 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? IN THE DESCRIPTION OF THE PATIENT, IT IS LISTED THE DIFFERENT MEDICATION SHE IS RECEIVING. THE AUTHORS SHOULD EXPLAIN ABOUT THE ABSENCE OR PRESENCE OF INTERACTIONS BETWEEN THESE DRUGS AND BLONANSERIN (PAGE 10) YES, RESEARCH OBJECTIVES WERE ACHIEVED. THIS STUDY CONTRIBUTION IS TO SHOW THAT BLONANSERIN CAN REDUCE GAMBLING DISORDER PROBLEM, BUT ITS LIMITATION IS EXCESSIVE SALIVATION SIDE EFFECT. 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? YES, THE DISCUSSION IS FINE BASED ON THE QUESTIONS LISTED. JUST A COMMENT: THERE ARE YELLOW HIGHLIGHTED NUMBERS (REFERENCES). THE YELLOW SHOULD BE CLEARED. 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? THE FIGURE NEED TO HAVE A NUMBER (FIGURE 1), DESPITE BEING THE ONLY OF THE MANUSCRIPT. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? A DOCUMENT WAS SENT, BUT IT STATES THERE WERE NOT STATS IN THE MANUSCRIPT 10 Units. Does the manuscript meet the requirements of use of SI units? YES 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? I DETECT OMISSIONS IN DIFFERENT SECTIONS OF THE

MANUSCRIPT. THEY WERE DESCRIBED IN THOSE SECTIONS. MOREOVER, REFERENCES ARE NOT SO UPDATED. NEED TO ADD MORE REFERENCES FROM 2015 TO 2020 PERIOD. I CHECK AND FOUND THAT 8 OUT OF 35 REFERENCES (23%) ARE FROM 2015 TO 2019 (NO INCLUSION OF 2020) 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? YES, IT IS FINE BASED ON THESE QUESTIONS. 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? IT WAS INCLUDED IN THE ATTACHMENT THE CONSORT 2010 STATEMENT. 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? YES, THEY HAVE THE NEXT: CLINICAL TRIAL REGISTRATION STATEMENT (ATTACHED) INSTITUTIONAL BOARD REVIEW APPROVAL (ATTACHED) INFORMED CONSENT FORMS OR DOCUMENTS (ATTACHED) OTHERS COMMENTS: In "Conflicts of Interest and Source of Funding" (page 2) of manuscript, it should be included the number of the grant (ID or Grant code). Please make your specific comments/suggestions to authors based on the above-listed criteria checklist for new manuscript peer-review and the below-listed criteria for comments on writing. The



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criteria for writing comments include the following three features: First, what are the original findings of this manuscript? THE BLONANSERIN IS POTENTIALLY USEFUL FOR TREATING GAMBLING DISORDER (HOWEVER, SALIVATION IS A SIDE EFFECT) What are the new hypotheses that this study proposed? TARGETING GAMBLING DISORDER BY MEANS OF D3 RECEPTORS TARGETING DRUG (BLONANSERIN) COULD REDUCE GAMBLING DISORDER What are the new phenomena that were found through experiments in this study? THE POTENTIAL OF BLONANSERIN TO DECREASE GAMBLING DISORDER What are the hypotheses that were confirmed through experiments in this study? THE REDUCTION OF GAMBLING DISORDER BY MEANS OF BLONANSERIN Second, what are the quality and importance of this manuscript? IT IS THE FIRST STUDY TO EXPLORE THE USE OF BLONANSERIN FOR TREATING A BEHAVIORAL ADDICTION (AND IMPULSIVE/COMPULSIVE BEHAVIOR). IT WOULD BE BETTER IF A LARGER SAMPLE AND BLINDED DESIGN, BUT IT IS GOOD FOR PRELIMINARY DATA FOR FURTHER EXPLORATION. IT IS NOT GREAT QUALITY, BUT ACCEPTABLE. What are the new findings of this study? BLONANSERIN CAN REDUCE GAMBLING DISORDER BUT IT CAN INDUCE SALIVATION AS SIDE EFFECTS. What are the new concepts that this study proposes? TARGETING D3 RECEPTORS FOR TREATING GAMBLING DISORDER What are the new methods that this study proposed? REALLY THERE IS NO NEW METHODOLOGY, ONLY A NEW DRUG FOR TARGETING GAMBLING DISORDER. Do the conclusions appropriately summarize the data that this study provided? YES, IT IS FINE. THEY ALSO DESCRIBE THE LIMITATIONS AND FURTHER STUDIES NECESSARY. What are the unique insights that this study presented? A POTENTIAL RELATIONSHIP BETWEEN A BEHAVIORAL ADDICTION (GAMBLING) AND PHARMACOLOGY FOCUS IN D3 RECEPTORS (BLONANSERIN). What are the key problems in this field that this





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study has solved? THERE IS STILL ABSENCE OF A SATISFACTORY DRUG TREATMENT FOR GAMBLING, AND BLONANSERIN POTENTIALLY COULD FURTHER STUDY (THIS IS SORT OF PRELIMINARY FINDINGS) Third, what are the limitations of the study and its findings? - IT IS A SINGLE CASE STUDY - THE MAGNITUDE OF THE PLACEBO EFFECT IS DIFFICULT TO DETERMINE IN OPEN-LABEL TRIALS. - THIS STUDY DID NOT QUANTITATIVELY EVALUATE COGNITIVE FUNCTION. What are the future directions of the topic described in this manuscript? BLONANSERIN SHOULD BE EVALUATED IN THE FUTURE BY MEANS OF DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS FOR COMPREHENSIVELY MEASURE THE EFFECTS OF BLONANSERIN. FURTHER INVESTIGATION IS NEEDED TO PURSUE THE POSSIBILITY THAT THE PARTICIPANT'S GAMBLING PROBLEMS WERE MITIGATED THROUGH IMPROVED COGNITIVE FUNCTION What are the questions/issues that remain to be solved? FUTURE STUDIES SHOULD INCLUDE: LARGER SAMPLES, DOUBLE BLINDED WITH BOTH GENDERS FOR ELIMINATE PLACEBO OR RELATED BIAS AND CONFIRM THE ABSENCE OR EXISTENCE OF GENDER DIFFERENCES OF BLONANSERIN. What are the questions that this study prompts for the authors to do next? 1- CAN BE CONFIRMED BLONANSERIN EFFECTIVENESS FOR REDUCING GAMBLING DISORDER IN LARGE SAMPLE AND DOUBLE BLIND STUDIES? 2- ARE POTENTIAL GENDER DIFFERENCES IN BLONANSERIN EFFECTS (THE PARTICIPANT OF THE STUDY WAS FEMALE)? 3- CAN BA BLONANSERIN COMBINED WITH OTHER DRUG (COMBO) FOR REDUCING THE SALIVATION SIDE EFFECT WITHOUT DECREASING THE BENEFIT ON GAMBLING DISORDER? How might this publication impact basic science and/or clinical practice? IT FOSTER MORE STUDIES (LARGER SAMPLE, DOUBLE BLINDED, BOTH GENDER, DIFFERENT ETHNIC GROUPS) FOR CONFIRMING BLONANSERIN EFFICACY FOR





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TREATING GAMBLING DISORDER.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Title:** The possible effect of blonanserine on gambling disorder: A clinical study protocol and a case report

**Reviewer's code:** 05426634

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Director

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2020-12-14

**Reviewer chosen by:** Han Zhang (Part-Time Editor)

**Reviewer accepted review:** 2021-01-11 07:59

**Reviewer performed review:** 2021-01-11 08:43

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The manuscript had been revised according to my suggestion. I believe this research will be helpful for the treatment of gambling in the future.