Author's response to reviews

Title: A case report of the successful clozapine administration in the face of myocardial infarction, pulmonary embolism and hyperlipidaemia resulting in the termination of long-term seclusion

Authors:
Alex Till (alextill54@gmail.com)
Ed Silva (ed.silva@merseycare.nhs.uk)

Version: 2 Date: 14 Dec 2018

Author's response to reviews:

We thank our reviewers for their comments which we feel have greatly strengthened this article. Our responses are below, alongside being incorporated at the end of our manuscript. We look forward to hearing your further decision.

Yours sincerely,
Alex Till and Ed Silva

---

REVIEWER COMMENTS

Dong-Bin Cai, MD (Reviewer 1):

Background

1. Please provide some references about the impact of clozapine on metabolism.

Thank you, this is already provided in the second paragraph of the background, references 6 and 7.

2. Please describe what is unique about this case directly?

Thank you, this is described in the opening line of the case presentation and is supported with subsequent description. We re-emphasise this and the “take-away”, as further requested below, in the discussion and conclusion section.
Case presentation

1. Please provide the de-identified demographic information about the patient (such as family history) Thank you, this information was limited but where available, was provided in the second paragraph of the case presentation.

2. Please provide more clinical materials of this case (such as PE, laboratory testing, image) Thank you. Unfortunately images are not available. We have provided laboratory values where possible and a description of the CTPA and ECG findings.

3. Please describe the diagnose criteria of schizophrenia, myocardial infarction, pulmonary embolism, hyperlipidaemia. Thank you. Although for conciseness of the case presentation and the well recognised diagnostic criteria of these conditions we have not elaborated on this further, although, bearing in mind overlap with reviewer 2’s comments, we have specified the criteria for treatment resistant schizophrenia and normal triglyceride values.

4. In case presentation, Line 52:" Accepting oral medication, his mental state made a rapid and dramatic improvement." It would make me misunderstand, can you provide any specific objective evaluation to measure the improvement of the condition before and after intervention? Thank you. We have provided this in the following sentences with reference to his time in seclusion before and after clozapine, compliance incidents and transfer to medium secure services.

5. Please describe the dose of clozapine one day, it is better for you to describe the whole administration of intervention (such as dosage, strength, duration). Thank you. The patient received treatment in accordance with BNF guidance and therefore is not elaborated on in further detail as this is well known and easily accessible within the additional reference that we have now provided.

Discussion

1. I think the discussion is too short, please provide more information.

Thank you, we have now elaborated further on this.

2. Please discuss the strengths and limitations in your approach in your case.

Thank you, this is now provided in the final line.
3. Please discuss the relevant medical literature of your case.

Thank you, the relevant medical literature is well referenced in the background to the case and is avoided within the discussion and conclusion to prevent repetition.

4. Please discuss the rationale for your conclusions (including assessment of possible cause)

Thank you, this is now provided in the final line.

5. It is important to describe the "take-away" lessons of this case report for the reader.

Thank you, this is now provided in the final line.

Shu I. Wu (Reviewer 2):

Abstract:

1. There are 404 words, should reduce the number of words to 350 as requested by the journal. Thank you, although this is not the case, the abstract is 349 words.

Case presentation:

2. Page 5, Line 30 of the PDF file: please provide literature regarding increased risk of myocardial infarction in people with severe mental illness. Thank you. We have included a reference.

3. Please specify the diagnosis and the criteria fulfilled for diagnosing his psychotic condition. Thank you. Rather than addressing this within the case presentation we feel this is an important point and have addressed this within the ‘Background’ section, starting on line 2.

4. It may read more clearly if the two 'aged 21' and 'aged 28' in the second paragraph be changed to 'at age 21' and 'at age 28'. Thank you. We have amended this.

5. Perhaps describe or list a little more about the thirteen different antipsychotics that he used and how they he has used them would be helpful in letting the readers know how treatment resistant the patient is. Thank you, we have included a description of this which in conjunction with the following paragraph we feel provides a good overview. It was not possible to provide further descriptions due to the limited information available.
6. Please explain more about what the 'assertive approach' is, does this required only for clozapine? Or for all other antipsychotics? and its relations and indication for this patient. Thank you, we have updated the reference now our work has been published in BJPsych Bulletin and feel that this, alongside the following sentence, adequately addresses this point.

7. Why didn't the authors consider using injections? I know this may have been used or considered, but the article just lack the description of such decision making process. Could it just because previous treatments with other antipsychotic medications were not long enough to see the effects? Thank you. We have addressed this in paragraphs 2 and 4 of the case presentation.

8. Line 54 on page 6 of the PDF file: Is it cardiologist or psychiatrist consider that 'the risk of both restraint and clozapine administration were not markedly increased comparatively to baseline'? Thank you. We have addressed this at the start of that sentence. By what criteria or findings did the doctors consider and evaluate such risk? Thank you. Sentence reviewed and altered to address this. What other antipsychotic has been tried during that time? Thank you. We have incorporated this at the end of that sentence.

Discussion

9. Please be more conservative about the conclusion part on page 10 that 'clozapine can be initiated despite significant concerns...'. After all, this is just one case report describing symptom reductions after the initiation of clozapine. Longer follow up and regular monitoring on cardiovascular risks are still needed for this and other patients. Thank you. This is a very important point that we have addressed in the concluding paragraph.