Reviewer’s report

Title: Ursodeoxycholic acid augmentation in treatment-refractory schizophrenia: A case report

Version: 0 Date: 01 May 2020

Reviewer: Upinder Kaur

Reviewer's report:

1. Do you believe the case report is authentic?
   Yes/No

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.
   Comments: NO

3. Does the Introduction explain the relevance of the case to the medical literature?
   Yes/No
   YES

4. Does the article report the following information? Where information is missing, please specify.
   YES
   a. The relevant patient information, including:
      - De-identified demographic information (age, gender, ethnicity)
      - Main symptoms of the patient
      - Medical, family and psychosocial history
      - Relevant past interventions and their outcomes
   b. The relevant physical examination findings YES

   c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.

   d. Diagnostic assessments, including:
      - Diagnostic methods
      - Challenges (e.g., financial, language/cultural)
      - Reasoning and prognostic characteristics (e.g., staging), where applicable

   e. Types and mechanism of intervention
f. A summary of the clinical course of all follow-up visits Yes

Comments:

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?
Comments:

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.
Yes/No

7. Is the Abstract representative of the case presented?
Comments:
YES

8. Does the case represent a useful contribution to the medical literature?
Comments:
NO

9. Additional comments for the author(s)?
Authors have described a case of Treatment Resistant Schizophrenia and marked improvement in positive and negative symptoms of schizophrenia merely with Urso deoxycholic acid. Following issues must be addressed:
1. Since it is a case report, Give Only One reference for the definition of TRS.
2. Page 2 Lines 48-51"Furthermore, there has been no convincing evidence—N methyl glycine: The statement needs clarification.
3. Page 3, line 26-27: What was the reason for Noncompliance to clozapine therapy?
4. Page 3, lines 41-42, mention the normal range for liver enzymes. Is this level an indication for discontinuation of Mirtazapine? Why was Mirtazapine stopped? What were the Liver function reports before Mirtazapine was started?
5. Remove the statement on t test. Just mention the PANSS and cognitive scores before and after the treatment.
6. If mirtazapine had to be stopped because of elevated liver enzymes, what was the effect of stopping mirtazapine and adding UDCA on liver enzymes.
7. Remove Figure2: Difficult to interpret.
8. Discussion: This part is poorly written, needs to be reframed. Statements at present seem to be directly taken from the paper by Ackerman HD 2016. The paper describes possible roles Bile acid paly in neurodegenerative disorders such as AD, HD, PD, Stroke etc. Role of bile acids in schizoaffective disorders or schizophrenia is not discussed in the review. Further, if authors suggest bile acids to block NMDA and GABA receptors simultaneously, how is this neurotransmitter disbalance going to be effective in schizophrenia. It is to note that glutamate NMDA receptor blockade is widely accepted to produce Schizophrenia.
Authors should try giving a de-challenge of UDCA and try giving placebo to the patient. At present it seems nothing but a placebo response to UDCA. This is the major issue authors should pay special attention to.

**Level of interest**
Please indicate how interesting you found the manuscript:

An article of limited interest

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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Were you mentored through this peer review?

No