

## Format for ANSWERING REVIEWERS

July 22<sup>th</sup> , 2014

Dear Editor,



**Title:** Polydipsia, hyponatremia and rhabdomyolysis in schizophrenia: A case report

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**Name of Journal:** *World Journal of psychiatry*

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The manuscript has been improved according to the suggestions of reviewers:  
Format has been updated

Dear Editors :

Thank you for reviewing our article. We appreciated your good comments very much. Our point-to-point responses to the editor's and reviewers' comments are listed in the following pages respectively. We also revised our manuscript according to these suggestions and comments. We hope that now this article will be found suitable for publication in the "**World Journal of Psychiatry**".

Sincerely Yours

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### Reviewer 1.

1. How was the CK level during the time on the emergency ward?

Ans: Creatine kinase(CK) was 247 U/L on the emergency ward.

2. Did the patient receive paliperidone during the time on the emergency room?

Ans: He didn't prescribe Paliperidone after patient was sent to the emergency ward for three days.

3. How was his psychopathology in these and the following days?

Ans: Thanks for your kind comment. The patient was discharged on the 31th day, and the psychiatric condition remained stable until now, only mild loosening speech was noted without disturbing behavior.

#### Reviewer 2.

1. Abstract and MS: CK values are not always clearly expressed: e.g., line 8 Abstract, should read 30505 IU/l or 30505 U/l etc.

Ans: Thank you, we corrected it. (marked by yellow color)

2. Format should be checked, e.g. "[3-7]." or ".[9-11]"

Ans: Thank you, we corrected it. (marked by yellow color)

3. Discussion, after "[12-14]" there is in my view something missing, should read e.g. "Delayed CK Level" elevations

Ans: Thank you, we corrected it. (marked by yellow color)

4. It should be added that CK elevation is not necessarily associated with rhabdomyolysis and that (free) myoglobin in serum (and urine) are most likely more sensitive (first sign) and specific (muscle cell damage) than CK levels.

Ans: Thanks for your kind comment. However, we do not have the serum or urine level of myoglobin.

5. It could be mentioned that massive CK elevations have been reported with quetiapine (Klein et al. 2006), Risperidone (Holtmann et al. 2003), olanzapine (BMJ 2008) and other typical and atypical antipsychotics without diagnosis of rhabdomyolysis.

Ans: Thanks for your kind comment. We added it in the discussion section. (marked by yellow color)

#### Reviewer 3.

1. What was the reason for 15mg of paliperidone, as is the maximally dose 9mg/day?

Ans: Thank your comment. Although the recommended maximum dose for paliperidone is 12mg/day when it was launched, recent clinical evidences have suggested higher dose is required for patients with severe psychotic condition. And recently we Taiwan have established the consensus that paliperidone 12-15mg/day can be prescribed for patients in acute phase, and the results was reported in the 2014 Schizophrenia international research society (SIRS) annual meeting. .

2. What was the reason for 1200mg of quetiapine, as is the maximally dose 800mg/day?

Ans: Thank your comment. Again, the maximum dose of quetiapine for schizophrenia is in debate for many years. In clinical practice, many schizophrenia patients needed more than 800mg/day to stabilize the psychiatric condition. In this case, His polydipsia was controlled by 800mg of quetiapine. Because of the persistent disorganized speech (loosening of association), so we gradually titrated quetiapine to 1200mg, and now the patient was in a stable condition.

3. Which antipsychotics did he become in earlier episodes?

Ans: The patient was diagnosed as schizophrenia for 20 years. He has received many antipsychotics, including haloperidol, risperidone, and aripiprazole and some other antipsychotics that their family didn't know the name. But the psychiatric condition was fluctuated. So this is the reason why the patient needed higher dose of paliperidone and quetiapine.

4. What kind of polydipsia (approximately how much water drunk the patient per day) occurred at the dose of 12 and at the dose of 15mg of paliperidone?

Ans: According to the report of the nurses in the nursing home, the patient always tried to drink water even they monitored his drinking behavior. They estimated the amount must be more than 3L /day.

5. The authors should use the internationally accepted SI units for laboratory findings.

Norm – perhaps normally. The typical antipsychotics can cause the polydipsia as well as risperidone. If the patient was treated with typical antipsychotics in the past what were the doses? Did he have a polydipsia too?

Ans: Thank you comment. The normal range in our laboratory test of CK level is 25-200 U/L. We revised the sentence as "After hydration, the CK level gradually decreased to 212 U/L (normal range 25-200 U/L) on the 16<sup>th</sup> day, and down to 75 U/L on the 24<sup>th</sup> day". And because the nurses of the nursing home changed, whether the patient also had polydipsia was not available.

#### Reviewer 4.

1. The assertion that "there were (sic) no articles as detailed as our article" in the Core tip appears to be misplaced and should be changed.

Ans: Sorry, we can't find this sentence: "there were (sic) no articles as detailed as our article", could you kindly identify the comments more clearly? Thank you very much.

2. This 40-year-old single man was diagnosed with schizophrenia with the presentation of auditory hallucination, persecutory delusions and bizarre behavior when he was 21 years old. Authors have to explain what they mean by "bizarre behaviour."

Ans: Thank your comment, we added the description: self-talking, poor self-hygiene, and wandering out as the disturbing behavior. (marked by yellow color)

3. Polydipsia is usually accompanied by polyuria. No mention of polyuria has been made in this case report.

Ans: Thank your comment, we added "more than the 3L /day" with the polydipsia on page 1 line 17. (marked by yellow color)

4. Approximately how much water/fluids was the patient drinking daily?

Ans: Thank your comment, on page 2 line 7 we have described "After admission, the patient was prescribed paliperidone 6mg/day initially for his psychotic symptom, and polydipsia was still noted with total water intake of 4000CC/day" (marked by yellow color)

5. Several issues regarding the diagnosis of the patient's renal problems are not clear: ? Was a diagnosis of psychogenic polydipsia (and polyuria) made? ? Was diabetes insipidus of central or nephrogenic origin ruled out? ? Were other medical causes of polydipsia and hyponatremia ruled out? ? Was the patient evaluated by a nephrologist for this purpose?

Ans: Thank your comment. When the patient was sent to the emergency room, the medical nephrologist was consulted. The patient was evaluated the medical condition and other causes of hyponatremia. According to the patient's history and clinical presentation, the nephrologist diagnosed the hyponatremia was related with polydipsia.

6. This patient appears to have developed water intoxication. Some mention of the fact that only about a quarter to half of the patients with psychogenic polydipsia develop such serious complications has been made in the abstract, but not in the discussion section of the paper.

Ans: Thank your comment. But we did have mentioned the prevalence of psychogenic polydipsia both in the abstract part and discussion section.

(Page 2 line 14) Discussion section:" The prevalence of polydipsia among patients with schizophrenia is 6%-20%."

(Page 2 line 17) Discussion section: "Previous studies showed 10%-20% of subjects with polydipsia may develop hyponatremia."

7. The management of chronic polydipsia usually requires intensive behaviour therapy. It is not clear from this report whether this was attempted in this patient.

Ans: Thank your comment. After the patient was admitted to the psychiatric ward, we have the behavior therapy that the nurses had reminded and monitored the patient's water intake, but the patient still find the opportunity to take water, even the tap water. We revised the sentence: page 2 line 7: [polydipsia was still noted with total water intake of 4000CC/day, although the behavior modification was done.]

(marked by yellow color)

8. There are several grammatical mistakes in the text, which need to be corrected.

Ans: Thank your comment. We have this manuscript reviewed by an English native speaker. Hope it's better now.

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