Reviewer’s report

Title: Sodium valproate induced acute pancreatitis in a bipolar disorder patient: a case report

Version: 1 Date: 25 Feb 2019

Reviewer: Jiraganya Bhongsatiern

Reviewer's report:

This is a case report featured sodium valproate-induced acute pancreatitis in an adult male patient aged 54-56 years old, treated for his chronic bipolar disorder. The patient received sodium valproate (VPA) 1500 mg/day, quetiapine (the author wrote quetiapie) 800 mg/day, and lithium carbonate 0.75 g/day. The author reported that the patient has been taking VPA for 1 year before pancreatitis occurred, and have been admitted to two institutions before the institution where the authors treat the patient. The laboratory results revealed increased amylase throughout the treatments at three institutions with VPA level remained in the normal range reported by the first institution. The patient was diagnosed as acute pancreatitis following the CT results of increased volume of pancreas and swelled peripancreatic fat. At the third institution, VPA was switched to other mood stabilizer. The authors reported the normal amylase level (with no quantitative numbers provided), and stated that the patient was discharged and being follow-up by telephone which the most recent amylase level reported was increased.

In spite of confusing written report, this is an interesting case due to VPA-induced pancreatitis is considered rare, particularly in patients with bipolar disorders. Trivedi and Pichumoni 2005 and Tenner 2014 reported VPA as a Class I medications associated with acute pancreatitis which is defined by the criteria of >20 reported cases with at least one documented case following rechallenge excluding all other causes such as alcohol, gallstones, hypertriglyceridemia, and other drugs. Majority of the patients in these two studies were treated for epilepsy, not bipolar disorders. Although I support additional evidence of VPA induced pancreatitis, I would have to ask the authors to revise their case report. My major comments are the followings:

1) How did the author rule out comedications such as quetiapine and lithium carbonate? I would encourage the authors to discuss this point. Quetiapine 800 mg/ day is a recommended maximum dose. There are reports on quetiapine-induced acute pancreatitis with lower dose of quetiapine such as 600 mg/day - not an evidence suggesting dose-dependent reactions, just an example. Some evidence shows that quetiapine induces hyperglycemia and hypertriglyceridemia causing acute pancreatitis in patients. For example, Liou 2014 and Franco 2015 reported aggravation of hypertriglyceridemia and acute pancreatitis in patients treated with quetiapine. However, there are cases that reported no elevated lipid levels or metabolic syndrome, similar to the authors’ case, such as those of Gropper and Jackson 2004 and Chang 2014. While Gropper and Jackson reported three cases describing patients using quetiapine alone and comedication of quetiapine and VPA, interestingly, Chang reported two episodes of acute pancreatitis with the first episode was during comedication of quetiapine and VPA, and the second episode was quetiapine alone.
2) What was the normal range for amylase, lipase, and blood fat? I would encourage the authors to report the normal range at least for amylase if the word count is limited. In the abstract, the authors stated amylase did not go back to the normal level. In contrast, line 37 page 4, Case presentation, the authors stated amylase was normal. For the lipase and blood fat, the authors would report these measurements or at least lipase level if considering quetiapine.

3) Even though there are some spelling and grammatical errors, I think the most important weakness of this report is that it is not scientific enough. For example, the patient is either 54 or 56 years of age; other mood stabilizers to which the patient was switched from VPA may be important to be disclosed; Two admission dates with the first one (October 19, 2017) was not the date that VPA was started; the authors did not mention whether the patients was treated with the same medications (VPA, quetiapine, and lithium carbonate) throughout his admission in three hospitals or not; bellyache versus stomach ache or abdominal pain

a. Examples of spelling and grammatical errors include:
   i. Abstract, line 22; Case presentation, line 16: peripancreatic fat
   ii. Background, line 51: severe
   iii. Discussion and conclusion, line 15: dosis tolerata (I personally do not think this word should be used here)

b. Case Presentation, lines 12 and 14: another, instead of other
v. Case Presentation, line 10: the advices, instead of the advises
vi. Case Presentation, lines 4 and 27: quetiapine, instead of quetiapie
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

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Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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