Author’s response to reviews

Title: Acute alcohol intoxication may cause delay in stroke treatment - Case reports

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Author’s response to reviews:

Answers to Reviewer #1 (Auwal Abdullahi, MSc)

Dear Auwal Abdullahi,

We thank you for the effort and time in reviewing our manuscript, entitled „Acute alcohol intoxication may cause delay in stroke treatment – Case reports” written by Tamas Arokszallasi et al. We appreciate very much for your constructive comments and suggestions. Each comment has been carefully considered point by point and responded. Responses are indicated bold and italics. Please find enclosed the revised version of our manuscript with and without revision marks.

Abstract
Page 2, Background
-Line 2: Remove 'to'

Done
Case Presentations

-Lines 24-39: Please you should mention some demographic characteristics such as age and sex of the participants. Also you need to state how the acute intoxication and the stroke were diagnosed and for how long the treatments were delayed.

Answer: We thank you for this suggestion. We changed this part of the abstract accordingly. 'Case presentation' paragraph was rewritten and detailed description of the cases was given.

'Case presentations: cases of three patients with alcohol intoxication and stroke are presented. The first patient (female, 50-year old) had dysarthria, nystagmus and trunk ataxia on admission. Her blood alcohol content was 2.3‰. After forced diuresis her symptoms improved, however, 5.5 hours later there was a progression, and in addition to the initial symptoms, diplopia and dysphagia appeared. Angiography showed basilar artery occlusion. Intraarterial thrombolysis was performed. After drinking 4 units of alcohol, the second patient (male, 62-year old) noticed diplopia, dysarthria and trunk ataxia, which symptoms were attributed to alcoholic intoxication. Two hours later, neurological examination revealed dysphagia and mild right sided hemiparesis as well, which made the causal relationship between alcohol consumption and the symptoms unlikely. Cerebral CT was negative. Intravenous thrombolysis was done. The third patient (male, 55-year old) drank 10 units of alcohol after that he fell asleep. Three hours later his relatives tried to wake him up. He did not answer, therefore his status was attributed to alcoholic intoxication. He woke up 8 hours later, when right sided hemiparesis and aphasia were found, and cerebral CT already revealed irreversible ischemic changes.'

Conclusion

-Lines 41-58: While all that you mentioned here is important, it is good that you summarize the passage and make it clear. Especially now that you need more things under the case presentations section.

Answer: Thank you very much for this comment. We rewrote the 'Case presentation' paragraph in order to summarize and make clear the passage. Moreover, the 'Conclusion' paragraph was also slightly modified to make the message more clear, and to remain within the 350-word limit.

Page 3

-Line 2: Please consider using appropriate key words (MesH terms)

Answer: We thank you for this suggestion.

Key words were changed according to the MesH terms.
We appreciate very much your suggestions regarding the correction of our grammatical errors.

Page 4

Background

-Line 2: Add 'help' after 'time is important to'
Done
-Line 5: Replace 'he/she is' with 'they are'
Done
-Line 7: This should be 'intravenous tissue plasminogen activator (IV tPA)'
Done
-Line 9: Replace 'i.e.,' with 'and therefore'
Done
-Line 12: Replace 'Diseases' with 'Conditions'
Done
-Line 17: Add 'One of the conditions that may mimic stroke is acute alcohol intoxication'
Answer: This sentence was added to the manuscript.

-Lines 19-24: This should be changed to 'Specifically, alcohol intoxication results in symptoms very similar to vertebrobasilar ischemia (cite here); and thus simultaneous occurrence of vertebrobasilar stroke and alcohol intoxication may result in misdiagnosis of stroke.'
Answer: We thank you for your comment. We changed this part of the manuscript accordingly. Two new citations were added (7,8), which explain the brain stem and cerebellar signs and symptoms in alcoholic intoxication.


-Lines 24-34: This should be changed to 'The common signs and symptoms, dizziness, dysarthria, nystagmus, ataxia with or without double vision and somnolence shared by vertebrobasilar stroke and alcohol intoxication, can easily be attributed to the effect of acute alcohol consumption, and the misdiagnosis may consequently cause delay in stroke recognition and failure to perform proper therapy (cite here).'

Answer: We thank you for this suggestion. We changed the sentence according to your recommendation. We added a new citation '(9)'.


-Line 44: Change 'to our best knowledge' to 'to the best of our knowledge.'

Done
Done

-Line 12: Remove the colon (:) and add 'and this showed that'

Done

-Lines 17-22: This should be 'However, early in the afternoon (2 p.m.), the control examination revealed worsening symptoms as she became somnolent again; and severe horizontal nystagmus, double vision, dysarthria and dysphagia developed.'

Answer: Thank you. The sentence was changed according to your suggestion.

-Line 24: 'which was also' not 'which was'

Done

-Lines 24-34: This should be 'Similarly, Duplex ultrasound did not show stenosis of the carotid or vertebral arteries; however TCD revealed high pulsatility index and low flow velocity in the basilar artery. Due to the fast progression and the sound suspicion of the basilar artery occlusion, DSA was performed. DSA showed basilar artery occlusion; and therefore intraarterial thrombolysis was done.'

Answer: We agree with your suggestion. This part of the manuscript was changed accordingly.

-Line 24-34: Write TCD and DSA first in full before abbreviating them

Done

-Line 46: 'ethanol' not 'etanol'

Done

-Line 48: Add 'and' after 'speech'

Done

-Line 51: trunk not trunc

Done

-Line 53: It should be 'consumption; however'

Done
Page 6

-Line 9: It should be 'improvement, and the NIHSS'
Done

-Line 19: It should be 'early in the morning (5 a.m.), the patient opened……'
Done

-Line 22: drunk not drunken
Done

-Line 27: It should be 'the relatives realized that he had facial asymmetry,'
Done

-Line 29: It should be 'on admission,'
Done

-Line 29: Do you mean 'right facial nerve palsy'? Or what do you mean by right central palsy? I am hearing this terminology for the first time, even though my mind tells me that, the central may refer to CNS involvement. Better still, do you mean cranial?

Answer: In neurology, central facial palsy is used to describe the weakness of the lower half of the face that is caused by lesion of the supranuclear innervation of the facial motor nucleus. Since that part of the nucleus that is responsible for innervation of the muscles of lower half of the face (around the mouth) has been under only contralateral upper motor neuron control, damage to upper motor neurons of the facial nucleus results in weaknes of the perioral muscles contralateral to the lesion. Patients with central facial palsy can wrinkle his/her forehead, can close his/her eye, but cannot move the perioral muscles contralateral to the lesion, therefore they cannot show their teeth on one side and their smile is asymmetrical.

We changed ’right central facial palsy’ to ’paresis of the lower half of right side of the face’.

-Line 34: Write MCA in full at first mention
Done

Discussion and Conclusion

-Line 53: This citation (7) should be placed after 'older' in line 48
Done
Page 7
- Line 5: 'immediate' not 'immediately'
Done
- Line 7: Resemble 'to'
Done
- Line 36: Merge this paragraph with the previous one
Done
- Line 51: Condition not disease
Done

Page 8
- Line 2: Cite a study or studies from the literature that used diffusion weighted MRI to diagnose stroke

Answer: We added the following citations:


- Line 14: Merge this paragraph with the previous one
Done

-Line 22: You can add a sentence at the end of the paragraph like 'Thrombolysis therapy helps prevent complications and improve outcomes after stroke (citation here). This is to help you have at least one citation in the paragraph since it is not conventional to have a whole paragraph without citation.

Answer: The following sentence was added: 'It is well known that thrombolytic therapy helps dissolve blood clots and restore cerebral blood flow, and thus improves outcome in acute ischemic stroke (14).'

The citation that we added is as follows:


-Line 32: There should be a comma after 'consumed'

Done

Page 9

-Line 9: 'With' not 'wit'

Done

-Line 17: 'for' not 'of'

Done

General Comment

-This is a very good study that will help us understand the differential diagnosis of stroke more.

We thank you very much for your interest in our work.

-The CARE guideline requires that, submission of a case report be accompanied with study timeline which will include statements on the perceptions of the patients about the management or treatment. However, I cannot see any timeline accompanying your submission.
Answer: We thank you for calling our attention to this point. In fact, we considered this issue when the manuscript was written and we felt that it is difficult to make a timeline of these cases. However, we reconsidered this point and according to your comment we made and inserted a figure with timelines of our cases. We hope that this figure improves the understanding of our manuscripts and points to the delay of the treatment caused by alcohol intoxication. The following Figure legend was added:

Figure 1. Timeline of the 3 cases. The delay of the treatment due to alcohol intoxication is indicated by diagonal lines. Bold text highlights those symptoms that helped differentiate stroke from alcohol intoxication. TCD: transcranial Doppler; DSA: digital subtraction angiography; CT: computer-tomography; CTA: CT angiography; MCA: middle cerebral artery

Other changes:

Since 5 new citations were added [(7), (8), (9), (12), (14)], the numbering of citations were changed.

One figure (timeline) was added, therefore the numbering of figures was also modified.

We thank you very much for your thoughtful and thorough review of our work, as well as for your helpful comments and suggestions. We greatly appreciate your efforts to improve our manuscript. We hope that you find our revised manuscript acceptable for publication in BMC Neurology.

Yours sincerely,

Tamás Árokszállási

corresponding author

04/November/2018

Answers to Reviewer #2 (Yasmin Ali O'Keefe)
Dear Yasmin Ali O'Keefe,

We greatly appreciate your efforts and time to evaluate our manuscript, entitled „Acute alcohol intoxication may cause delay in stroke treatment – Case reports” written by Tamas Arokszallasi et al. Your comments has been carefully considered and responded. Responses are indicated bold and italics. Please find enclosed the revised version of our manuscript with and without revision marks.

-Comment: I think this is a very practical issue within the world of stroke care, thus a relevant publication. It needs some slight editing due to just nuance in grammar and flow, consider a formal editing service.

Answer: We thank you for your suggestions. We edited our manuscript regarding the grammatical errors and flow. Reviewer #1 also highlighted these mistakes and suggested corrections.

-Comment: I would like to see more discussion regarding why this is a pertinent issue, from a care and resource utilization standpoint (ex tpa and ICU stays, angiography, etc...). I did appreciate how you point out the caution that must be taken with each case to not be susceptible to premature closure or anchor biases that all symptoms are related to alcohol, and that objective and unbiased evaluation is necessary in each case.

Answer: We added a sentence to highlight why it is important to treat patients with alcohol intoxication and stroke in stroke unit or ICU.

‘Since patients with alcohol intoxication and stroke within the thrombolytic time window require increased medical attention, CT examination, angiography, and IV tPA treatment, observation of these patients is ideal at the neurological ICU or well-equipped stroke unit.’

In fact, other parts of the manuscript also underlines the importance of a thorough observation and care, as well as resource utilisation in these patients. See the 3rd and the last paragraphs of the 'Discussion and Conclusions’ chapter.

We thank you very much for your evaluation of our manuscript and we greatly appreciate your interest in our work. We hope that you find our revised manuscript acceptable for publication in the journal 'BMC Neurology'.

Yours sincerely,
Tamás Árokszállási

corresponding author

04/November/2018