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:

Answer to Reviewer#1 (Auwal Abdullahi, MSc)

Dear Auwal Abdullahi,

We thank you very much for the effort and time in reviewing our manuscript, entitled „Acute alcohol intoxication may cause delay in stroke treatment – Case reports” written by Tamas Árokszallási et al. Each comment has been carefully considered and the manuscript was modified according to yours suggestions. Please find enclosed the revised version of our manuscript with and without revision marks.

Comments:

Page 2

Abstract

Case presentation

- Line 26: Please capitalize C in the word 'cases'

We were asked by Reviewer#3 to improve the English of the manuscript. When the manuscript was revised, the position of the ‘cases’ was changed (it was moved from the beginning of the sentence), therefore we could not fulfill your request.
'Cases of three patients with alcohol intoxication and stroke are presented.'
was changed to
'Three cases of alcohol intoxication and stroke are presented.'
- Line 29: Add a comma after 'forced diuresis'

We added a comma, although this sentence was also changed. The new sentence is: 'The symptoms improved after forced diuresis, but 5.5 hours later progression was observed, and the patient developed diplopia and dysphagia in addition to her initial symptoms.'

Thank you again for your thorough review of our work. We hope that you find our revised manuscript acceptable for publication in BMC Neurology.

Yours sincerely,

Tamás Árokszállási

23/December/2018

Answers to Reviewer #3 (Francisco Alvarez, MD, PhD)

Dear Professor Alvarez,

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.

- The English grammar should be reviewed.
- Answer: a native English speaker (who is a medical doctor) checked the English grammar and style of the manuscript that was revised according to her suggestions.

- Had these patients conduct symptomatology?

- Answer: no, none of our patients had conduct disorders or behavioural problems. The first and third patients were social drinkers with very rare binge episodes. (Before admission to the hospital, the first patient celebrated her birthday, while the third patient participated on a wedding ceremony.) The second patient was an occasional drinker who drank about 2 units of alcohol once or twice a week.

- In the first case, authors say that Angio-CT was negative. Was it completely normal? After some hours the same patient had a basilar thrombosis, therefore in the first moment she had not a stroke?

Answers:

- We checked again the angio CT together with a neuro-radiologist and no abnormalities in the basilar artery were found on the source images at admission. TCD flow parameters in the basilar artery at 75-90 mm depth were also normal when the patient was admitted.

- Although the cerebral CT and angio CT were negative and the patient’s symptoms improved during the forced diuresis, it cannot be excluded that in addition to alcohol intoxication the patient had a simultaneous vertebrobasilar stroke already at the admission. We discussed this question in the manuscript: „The cause of the initial symptoms cannot be clearly determined. They could be due to alcohol intoxication alone or to alcohol intoxication with simultaneous presence of vertebrobasilar stroke with improving symptoms.”

We completed this statement and made it more clear.

The new statement is: „Although cerebral CT and angio-CT were negative and the patient’s symptoms improved during forced diuresis, the cause of initial symptoms cannot be clearly determined. They could be due to alcohol intoxication alone or to alcohol intoxication with concomitant vertebrobasilar stroke with improving symptoms.”

- In the first case, authors say that the patient was treated with forced diuresis. Could that dehydration collaborate in the posterior development of stroke?
Answer: This is possible, but cannot be proven. We discussed this topic in the manuscript as well, and wrote:

„It remains unclear whether vertebrobasilar stroke was induced by alcohol and dehydration due to forced diuresis, or was independent of these conditions.”

- It will be interesting to give the alcohol levels in mg/dl or similar units. The time between the intake of alcohol, the determination of this blood concentration, and the development of symptoms should be discussed.

Answers:

- We changed the percent values to mg/dL [1% means 1 g/dL = 1000 mg/dL, 1‰ means 100 mg/dL]. The table was completed.

| Ethanol(%) | 2,3 | UK | <0,1# |
| Ethanol (mg/dL) | 230 | UK | <10 mg/dL |

- We added the next paragraph to the Discussion chapter:

„According to heteroanamnesis, all of our 3 patients undoubtedly drank significant amounts of alcohol before admission to our clinic. However, the time between alcohol consumption and blood alcohol level measurements varied (about 6 hours in the first patient, and at least 12 hours in the third patient), therefore the blood alcohol level measured after admission did not reflect the amount of ethanol consumed. Since the symptoms of alcohol intoxication and stroke overlapped and in the first and third patients the symptoms were only noticed after awakening, it was impossible to determine the precise onset of stroke. Based on our assessment, symptoms developed within 2 and 3 hours of alcohol consumption in the second and third patients, respectively. The onset-to-door time was about 2 hours in the second patient, but due to the delay in the recognition of stroke it was more than 8 hours in the third patient. In the first patient, neurological symptoms were noticed within 5 hours of alcohol consumption, however, these symptoms were most likely to be caused by alcohol intoxication, and obvious stroke symptoms developed later, already in the hospital.”

- As a final conclusion: what could be (if there are) the clinical guides to diagnose a stroke in a drunken patient?

Answer: as it was mentioned in the Discussion chapter, diffusion-weighted MR (DWI) could be the most sensitive diagnostic method to differentiate ischemic stroke and alcohol intoxication. While DWI is negative in alcohol intoxication, it becomes positive already several minutes after the onset of ischemic stroke.
As we discussed: „If the diagnosis of stroke cannot be excluded, diffusion-weighted MRI, if available, can be useful to determine the etiology of symptoms (13,15).”

We also discussed the clinical signs and symptoms, which may help recognise stroke in case of simultaneous occurrence of alcohol intoxication. As it was written: „…unusual alcohol-related clinical symptoms, such as dysphagia or hemiparesis, and disproportion between the symptoms and the amount of alcohol consumed may help the recognition of stroke in the background of symptoms”.

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

23/December/2018