Author's response to reviews

Title: Treatment of hepatic encephalopathy by on-line hemodiafiltration: A case series study

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Version: 4 Date: 7 April 2010

Author's response to reviews: see over
April 7, 2010
Dear Editor of BMC Emergency Medicine:
Object: MS: 1214835103063241
Treatment of hepatic encephalopathy by on-line hemodiafiltration: A case series study
Thank you for considering our paper. We have reviewed the above manuscript according to your reviewer’s comments.

Reviewer’s report
Title: Treatment of hepatic encephalopathy by on-line hemodiafiltration: A case series study
Version: 3 Date: 8 March 2010
Reviewer: Vanessa Stadlbauer

Reviewer’s report:
The authors have answered to all my questions. However, there are still some small issues, that should be resolved before publication.
I am still missing the inclusion of some key references (as suggested by the two other reviewers and by myself in the first review). Please include those papers.


The sentence in the methods section of the text has been changed as follows:
Hepatic encephalopathy was assessed using the West Haven criteria of altered mental state [13] and the Glasgow Coma Scale in accordance with the recommendation of a working party on studies in hepatic encephalopathy [14].

The sentence in the discussion section of the text now appears as:
In more recent randomized controlled trials, Hassanein et al reported that 5 days treatment with extracorporeal albumin dialysis using molecular adsorbent recirculating system is effective in 62% of cirrhotic patients with severe hepatic encephalopathy [36]. This system thought to be one of hopeful methods. However, 40% of the patients who treated with the standard medical therapy alone also improved their hepatic encephalopathy by 2 grades from baseline, and 34% of the patients whose hepatic encephalopathy did not respond to the any treatment survived after 2 weeks. There is a possibility that their experience cannot be just applied to the patients with acute liver failure.

I think the data on the excluded patients are very interesting - you should include at least the data on NH3 in the congestive heart failure patients in the results.

We described about the changes of the bilirubin and ammonia levels in 5 patients who were excluded in the discussion section of the text and added figure 6. The sentence in the discussion section of the text now appears as:

Figure 6 shows the changes of the serum bilirubin and ammonia levels in 5 patients who were excluded from the study because of improvement with no need of ALS. The serum bilirubin levels increased even during the good clinical course, whereas the serum ammonia levels decreased rapidly. Figure 2 and 6 suggested that the change of serum ammonia levels may be a more useful predictor of survival compared with that of serum bilirubin levels.

Reviewer's report

Title: Treatment of hepatic encephalopathy by on-line hemodiafiltration: A case series study

Version: 3 Date: 23 March 2010

Reviewer: Norman Sussman

Reviewer's report:

MINOR ESSENTIAL REVISIONS

1. I do not disagree with the diagnosis of ALF in patient 11, but I don’t believe that this was alcohol-induced. How can you be so certain that he did not take an overdose of acetaminophen – APAP would have been undetectable by the time of admission. Did you confirm with APAP adducts? If not, please acknowledge the possibility of another insult to the liver.

In Japan, acetaminophen induced ALF is very very rare. People in Japan can buy an over-the-counter drug that was encased by the
small quantity. The patient 11 did not have suspicious circumstantial
evidence of overdose, no past history of the suicide attempt or a mental
illness, and no empty box of any drugs, but he had a history of alcohol
abuse two days before onset. The sentence in the methods section of
the text has been changed as follows:
The etiology of acute liver failure was hepatitis B virus infection in 10 patients,
non-A~G hepatitis virus infection in 2 (indeterminate), alcoholic suspected with the
medical history in 2, congestive liver in 1, infiltration of leukemia cells in 1, and
acetaminophen overdose in 1.

2. Please update your reference list to include recent work in artificial liver.

We examined 2 articles which other reviewers recommended
and added these to the reference (Ferenci P, Lockwood A, Mullen K,
Tarter R, Weissenborn K, Blei AT: Hepatic encephalopathy--definition,
nomenclature, diagnosis, and quantification: final report of the
working party at the 11th World Congresses of Gastroenterology,
Stange J, Blei AT: Randomized controlled study of extracorporeal
albumin dialysis for hepatic encephalopathy in advanced cirrhosis.

The sentence in the methods section of the text has been
changed as follows:
Hepatic encephalopathy was assessed using the West Haven criteria of altered
mental state [13] and the Glasgow Coma Scale in accordance with the
recommendation of a working party on studies in hepatic encephalopathy [14].

The sentence in the discussion section of the text now appears
as:
In more recent randomized controlled trials, Hassanein et al reported that
5 days treatment with extracorporeal albumin dialysis using molecular adsorbent
recirculating system is effective in 62% of cirrhotic patients with severe hepatic
encephalopathy [36]. This system thought to be one of hopeful methods. However,
40% of the patients who treated with the standard medical therapy alone also
improved their hepatic encephalopathy by 2 grades from baseline, and 34% of the
patients whose hepatic encephalopathy did not respond to the any treatment
survived after 2 weeks. There is a possibility that their experience cannot be just
applied to the patients with acute liver failure.

3. I don't think ref 23 is the final word on hepatic encephalopathy. You may want to include other references or state that this is one theory.

   We revised the sentence in the discussion section of the text has been changed as follows:
   At present, it is proposed as one opinion that the causal agents of hepatic encephalopathy are presumed to be middle molecules [24].

4. Please add a footnote to Table 1 that some patients had a higher AST at sometime during their illness, and that the value in the Table reflects the value at the start of treatment.

   We added the highest AST in the Table 1. The sentence in footnote of the Table 1 now appears as:
   Highest AST, Highest values that could be recorded during illness.

We think that we could cope with your concerns point by point. We hope that you will find our revised manuscript suitable for publication in your journal and look forward to hearing from you.

Sincerely yours,
Shinju Arata