Author’s response to reviews

Title: Dialysate Temperature Adjustment as an Effective Treatment for Baroreflex Failure Syndrome in Hemodialysis Patient

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Author’s response to reviews: see over
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Version: 2 Date: 6 May 2014

Author's response to reviews: see over
Dear Editors,

I am re-submitting the following revised manuscript for your consideration: Dialysate Temperature Adjustment as an Effective Treatment for Baroreflex Failure Syndrome in Hemodialysis Patient.

Your comments and those of the referees were very helpful. We have worked through each of the comments and further improved the manuscript. My co-authors have all contributed to this revised manuscript and agree to this re-submission.

In the following pages are detailed out point-by-point responses to each of the comments and concerns of the editors and the reviewers. We indicated the page and line numbers in this point-by-point response.

We hope that the revisions in the manuscript and our accompanying responses are now sufficient to make our manuscript suitable for publication in the *Bio Med Central Nephrology*.

We shall look forward to hearing from you at your earliest convenience and we are very grateful for your consideration.

Yours sincerely,

Dr. Natsumi Tanabe
Minor Essential Revisions

1. It is opinion of the reviewer that table and figure legends could improve the readability of the text.

   Thank you for your advice. We have revised the figure and table legends. The table and figure legends have been written in more detail. (Page 10-13, Figure 1,2,4,5 Table 1,2)
Reviewer's report

Title: Dialysate Temperature Adjustment as an Effective Treatment for Baroreflex Failure Syndrome in Hemodialysis Patient

Version: 2 Date: 7 July 2014

Reviewer: Francesco Locatelli

Reviewer's report:

The paper: 'Dialysate Temperature Adjustment as an Effective Treatment for Baroreflex Failure Syndrome in Hemodialysis Patient' by Natsumi Tanabe et al describe an interesting case report however important information is missing.

1. How was the sodium measured?
   1. Thank you for asking this. The dialysis was done three times a week in the afternoon. The sodium was measured pre and post dialysis from the site of paracentesis. In order to remove the dialysate affection, sufficient amount of blood was drawn before the sample taken. (Page 6; Line 183-185)

2. What was the gradient between the Na plasma water concentration of the patient and dialysate Na concentration?
   1. Thank you for mentioning. The Na concentration of the dialysate was 140 mEq/L. The patient routinely had blood test every week before dialysis and the Na concentration was mostly controlled between 140 to 142 mEq/L. (Page 6; Line 181-183)

3. What about the interdialytic body weight increase?
   1. Thank you for asking. Since there was a hemodynamic instability during the dialysis, we should have mentioned the weight change inter- and inra- dialysis. Most of the time the patients weight increase was controlled between 1.5 – 1.7 kg and there was not a remarkable difference. (Page 4; 126-127)

4. Any data about blood pressure during the interdialytic period (possibly 24 hour measurements)?
   1. Thank you for asking this, we have done 24 hour ambulatory BP monitoring. The BP change during the day was extreme as well. And everyday, there were several timings when the BP dropped. One was after inserting food from the PEG and another was after
lying in bed. We considered both of these situations were when vagus nerve was stimulated and the patient was not able to have a vasovagal reflex. (Page 4; 135-137, Page 5; 163-165)

5. Any information about the blood pressure lying and standing?

1. Unfortunately we did not do a tilt test but the patient complained BP drop after inserting food from the PEG and when lying in bed.

6. Apparently it seems that the diffusive sodium balance during dialysis was negative, what about the amount of ultrafiltration?

1. Thank you for mentioning this, as you mentioned, ultrafiltration rate is very important for hemodynamic change during dialysis. We added the data. The ultrafiltration rate was 6.30 ml/hr/kg and 6.16 ml/hr/kg in convectional dialysis and temperature adjusting dialysis, respectively. This diffuse sodium balance and ultrafiltration rate was very similar between the two. From this similarity between convectional and temperature adjusting dialysis, we presume that the successful blood pressure control with temperature adjustment was mostly by the effect of peripheral temperature stimulation. (Page 8; Line 245-247, Line 252-255)

7. The sodium balance is of paramount importance in interpreting the blood pressure behavior during dialysis, much more than the stimulation of RAAS thus please correct the text accordingly.

1. Thank you very much for this advice, it is true we have focused on RAAS and did not mention about the sodium balance and ultrafiltration rate. In our case the diffuse sodium balance was negative and ultrafiltration rate was 6.30 ml/hr/kg and 6.16 ml/hr/kg in convectional dialysis and temperature adjusting dialysis, respectively. This diffuse sodium balance and ultrafiltration rate was very similar between the two. Negative diffuse sodium balance may affect the RAAS pathway and lead to blood pressure change but during both dialysis, the Plasma Renin Activity (PRA) did not change extremely and the Plasma Aldosterone Concentration (PAC) declined toward the end of the dialysis. From these results, the previous hemodynamic instability during dialysis was not likely to be caused by volume change nor RAAS effect but possibly cased by the overstimulation of autonomic nerve with no vasovagal reflex.

From this negative diffuse sodium balance and ultrafiltration rate similarity between convectional and temperature adjusting dialysis, we presume that
the blood pressure was successfully controlled through peripheral temperature stimulation in temperature adjusting dialysis. (Page 7-8; Line 245-259)

Thank you very much for your comment, this has been done.