

Author’s response to reviews

Title: Therapeutic plasma exchange in a tertiary care center: 185 patients undergoing 912 treatments - a one-year retrospective analysis

Authors:

Julius Schmidt (schmidt.julius@mh-hannover.de)
Firas Asper (asper.firas@mh-hannover.de)
Gunilla Einecke (einecke.gu@mh-hannover.de)
Gabriele Eden (gabriele.eden@freenet.de)
Casten Hafer (c.hafer@comlink.org)
Jan Kielstein (kielstein@yahoo.com)

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Author’s response to reviews:

Dear Sir,

Thank you very much for your mail from July 23rd in which you ask for a revision of our manuscript BNEP-D-17-00360 “Therapeutic plasma exchange in a tertiary care center of 185 patients undergoing 912 treatments - a one-year retrospective analysis”.

We would like to thank you and the reviewers for your time and effort to review the manuscript. An addition to an itemized response to each point we implemented all changes and marked them in red.

We would be happy if you would find the revised paper suitable for publication in BMC Nephrology.

Sincerely yours

J. T. Kielstein, MD
Response to reviewer # 1:

Thank you for the important findings, corrections and suggestions.

Background:

line 12 - "fresh frozen plasma is used as the exchange fluid' appears out of place in this sentence.
Thank you for picking up our mistake. The sentence was corrected and reads now as follows:
“TPE can also replenish missing plasma components, e.g. ADAMTS13 in TTP, if fresh frozen plasma is used as exchange fluid.”

line 22- please elaborate why treatment numbers are increasing in the transplant population

We extended the sentence and added a reference [Garonzik Wang JM, Montgomery RA, Kucirka LM, Berger JC, Warren DS, Segev DL: Incompatible live-donor kidney transplantation in the United States: results of a national survey. Clin J Am Soc Nephrol 2011, 6:2041-2046.] The sentence reads now as follows: “Treatment numbers are especially increasing in the transplant setting as the use of incompatible kidney transplantation is growing as a response to the organ shortage, hence more and more recipients of a live-donor kidney transplant as well as deceased donor organ need to be pretreated by TPE.”

line 51 - please define what the abbreviations cTPE and mTPE are

Thank you for identifying this mistake. We now introduce the abbreviations centrifugal therapeutic plasma exchange (cTPE) and membrane therapeutic plasma exchange (mTPE at their first use in the interdiction.

Statistical analysis: Data is not normally distributed - suggest using non parametric stats not t tests/ paired t tests.

We now use Wilcoxon and Mann-Whitney tests. None of the previous results changed in terms of significance level. The one-way analysis of variance (ANOVA) was used to determine statistically significant differences between the four treatment categories.
Results:

line 40 - is the difference in calculated plasma volume statistically significant - please clarify

The difference in the calculated plasma volume is statistically significant if you compare the different groups. The significance level is now indicated.

Interestingly there is also a significant difference if you compare the two formulas that were used for the calculation of the plasma volume (p value < 0.0001).

line 55 - relative exchanged plasma volume in vasculitis is stated in the text as 0.87 (0.79-0.99) but is stated as 0.88 in the table.

Thank you for identifying this typo. The correct number (0.88) was also used in the text not only the table.

treatment time and no of treatments - this paragraph jumps between figure 5 and table 1 (although reference to table 1 is not listed - please amend this).

We now include the reference to table 1 that now also contains the reference to the correct figure (Figure 3).

Adverse events paragraph was hard to read. It is unclear how the statement that the mode of TPE influenced the adverse event rate. Similarly, it is not clear from table 2 or elsewhere that cTPE pts had a lower AE rate. Suggest the last 4 lines of this paragraph are moved to become the first 4 lines.

We rewrote the paragraph on the adverse events.

Tables and Figures

Table 1: add in abbreviations

We did add all abbreviations.
Table 2: suggest add line at bottom of table showing there were 6 severe AEs and 34 mild or moderate AEs. Also spell out AE. The text below table 2 does not belong there - belongs with ?? table 1??

We corrected the legends and put them on a separate page.

Figure 1 and 2: add in % so you can easily interpret the proportions.

We added the % to interpret the proportions.

Figure 3 and 4 - r² value should be discussed in text and how this was derived in the statistical analysis section.

Relationship between the exchanged and the calculated plasma volume was calculated by linear regression (r²) using GraphPad Prism (La Jolla, CA, USA).

Discussion: page 2 line 22 'bods' weight should be body weight. Can you explain or speculate what some of the other reasons for variations in AE rates between studies might be?

We corrected this typo.

Conclusion: first word should be 'In'. The conclusion needs revision - it outlines the main finding and limitations rather than giving a clear explanation of their importance and relevance.

We corrected the typo.
Response to reviewer # 2:

1. Results section:

1.1. They mentioned in the background that Guillain-Barre Syndrome is one of the recommended indications for plasma exchange but in their results section under neurological disease (line 11 and 12), only multiple sclerosis and acute disseminated encephalitis were listed. Does this mean that they did not have any cases of Guillain-Barre syndrome in their data?

For each disease category we just mentioned the main/leading diagnosis. As we only had seven cases of Guillain-Barre syndrome we did not mention these patients specifically.

1.2. They have presented results of most of their comparisons which they presented as significant with confidence intervals but it will provide more robust information for the general nephrologist and others if they also include p-values. Can they also indicate if the confidence intervals were 95% or other?

We added more details on the statistical analysis.

1.3. Table 1 needs to be clearer. It is not clear whether the 'patient group' represent the variables down the column or the variables across the rows. If this represented variables down the column, it does not make any sense. I would recommend they change the label in this to make it clearer.

The four groups (“all” patients, “neurology”, “vasculitis and immunological” and “others”) are shown in the columns, the variable are across the rows. We changed the label to make this clearer.

1.4. Their definition of serious adverse event needs to be clearer. They have said severe is "clinically unstable due to adverse event, termination of procedure required". Do they mean that severe was defined by both terms? If so, in table 2 they have 6 serious adverse events which conflicts with their statement in the adverse events section where they mentioned that there were 2 out of 185 serious adverse events leading to treatment stoppage.
There were a total of 6 severe adverse events. The severe adverse events were either clinically unstable due to adverse event or termination of procedure required.

2. Discussion

2.1. I would recommend that they need to include a detailed critique of the limitations of the study in the discussion section rather than the conclusions section as I think the limitations are crucial in this study although the results have got significant implications for clinical practice.

We moved the limitat