Author’s response to reviews

Title: Comparison of double filtration plasmapheresis with immunoadsorption therapy in patients with anti-glomerular basement membrane nephritis

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Author’s response to reviews: see over
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Title: Comparison of double filtration plasmapheresis with immunoadsorption therapy in patients with anti-glomerular basement membrane nephritis

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Reviewer's report

**Title:** Comparison of double filtration plasmapheresis with immunoadsorption therapy in patients with anti-glomerular basement membrane nephritis

**Version:** 5  **Date:** 28 April 2014

**Reviewer:** Weixin Wei Hu

**Reviewer's report:**

Comments on “Comparison of double filtration plasmapheresis with immunoadsorption therapy in patients with anti-glomerular basement membrane nephritis”

The study was aimed to compare the efficiency of removing anti-GBM and efficacy of improving renal function between two procedures of therapeutic apheresis, DFPP and IA. The study is interesting, but many serious deficiencies have been found in the manuscript, especially in the methods and results.

**Major revisions:**

1. Detailed procedure of IA is missing. Methods of DFPP is also incomplete, no description of blood flow, anticoagulant, plasma amount treated in each session and total sessions for one course of DFPP.

   We have completed some details of DFPP in the manuscript. Low molecular weight heparin was used for anticoagulants. The blood flow was set to 100~120ml/min. After each session, 200~400ml fresh frozen plasma was used for supplement.

   IA was performed using Immunosorba PH-350 (Asahi Kasei Medical, Tokyo, Japan). Each course of treatment consisted of three sessions of IA. Each session was carried out daily or every other day. Three litres of plasma was processed at each session. Anticoagulant was the same as DFPP. No plasma substitution was needed as the clean plasma was returned to the patient.

2. Immunosuppressive therapy, including methylprednisolone and MMF or CTX should be clearly stated, eg the time, doses, duration of treatment. The author should explain why MMF was selected to treat anti-GBM disease because CTX is recommended as the first choice of immunosuppressive drug.

   Immunosuppressants are not the main research topics of this study. While we are pleasant to answer the doubt of reviewer. Methylprednisolone was administered intravenous 500mg daily for three days. Patients subsequently proceed to pulse IV cyclophosphamide at 0.5-1.0g/(m² BSA) monthly for 6-9 courses. Since the effect of MMF was observed in the therapies for severe lupus nephritis, some patients received MMF at 0.5g daily for first week, then the dose was increased to 1.0g/d. Monitoring of serum concentrations (MPA-AUC0-12h) was kept lower than 30mg/h.L.

3. The authors should analyse the clinical efficacy of the therapies in details rather than the effects of DFPP and IA to remove anti-GBM, this is most important for a new therapy, eg proportion of patients withdrawing from the RRT after 3 months or 12 months follow-up, or ESRD.

   We also have compared the clinical efficacy of the therapies in the part of “follow-up and outcome”. We observed the patient survival and the renal survival, but did not find significant differences between the two groups.
4. In regarding to compare the removal effects between the two therapies, because treatment sessions in a course were different between DFPP and IA, and different among patients, so it would be better to compare the reduction rate of serum anti-GBM after the same DFPP and IA sessions, and after a course of treatment. Also we want to know how the authors make the decisions of treatment sessions and how many patients became anti-GBM negative after a treatment course? It is recommended that plasmapheresis should be continued for 14 days or until anti-GBM antibodies are no longer detectable in the KDIGO guideline.

For the limit of this retrospective study, the treatment was depending on the clinical situation at the time it is difficult to collect such many cases if we selected patients strictly according the KDIGO guideline. For the same reason, we cannot collect detect of anti-GBM titer before and after each session. So we cannot compared the reduction rate of serum anti-GBM after the same DFPP and IA sessions.

5. Unit of laboratory measurements should be added in table 2
The unit of laboratory measurements has been added in table 2.

6. The most commonly used replacement fluid in TPE is human albumin solution, plasma is used as a replacement fluid in a limited number of diseases, for example TTP, It is inappropriate that the authors stressed the shortage of TPE in the section of introduction, discussion and abstract because of its requiring large amount of plasma as compared with DFPP or IA. Also, no plasma is needed in the procedure of IA.
We have revised some describe of IA in the manuscript.

7. In the section of “clinical and pathologic data”, authors need to record the number of patients presenting with pulmonary hemorrhage; the number of patients requiring RRT in the text is inconsistent with the number in table 1
The number of patients requiring RRT in table 1 was the patient requiring RRT at onset, while some patients had their Scr increasing during the treatment, so the number in text was more than in table 1.

Minor revisions:
1. The treating volume of plasma usually describe as 1.5 or 2 plasma volumes rather than “a double volume”
The sentence “A double volume of plasma was processed during each DFPP session.” has been changed to “1.5 or 2 plasma volumes was processed during each DFPP session.”
2. Fig 1 is not necessary.
We think Fig1 is helpful in understanding the manuscript. We add the schematic depiction of IA in Fig 1.
3. Some urine markers (NAG, RBP…) have nothing to do with this study.
These markers has been delete from the manuscript.
4. Table 5 is of little value.
5. In the last paragraph of the discussion, authors made a contradictory comments: “unless….., patients with high initial SCr and crescent formation do not require DFPP or IA.” “patients with higher percentage of cellular crescents should be treated with DFPP…”

What we mean is that the remove of antibody did not make sense for the prognosis if the crescent formation was more than 85% or constitute of many fibrous crescent. However, if the crescent was fresh formed and was consisted of mainly cellular crescents, it was necessary to be treated with DFPP to remove anti-GBM antibodies, thus avoiding further damage.

6. The authors should make a conclusion what the different efficacy they have found between DFPP and IA, this is the main purpose of this study

We compared the effect of the two therapies and find no significant differences. So we think DFPP could be another choice in treatment of anti-GBM nephritis.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
The authors and I are working in the same department. I have no financial competing interests.
Reviewer's report
Title: Comparison of double filtration plasmapheresis with immunoadsorption therapy in patients with anti-glomerular basement membrane nephritis
Version: 5
Date: 15 April 2014
Reviewer: ANDRE KAPLAN

Reviewer's report:
The data is clear and easy to understand. I found no particular problem with the presentation of results or the discussion.
Figures 2 and 3 are blurry and can be made easier to read
The figures has been changed to be more clear.

on table 2, provide a legend for terms which may not be understood by all, such as: NAG, RBP, Upr, pScr, URBC, etc..
We has made some changes to make the table easier to read.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
i have no competing interests