

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Hyperkalemia prevalence, recurrence, and treatment in patients on haemodialysis in China: protocol for a prospective multicentre cohort study (PRECEDE-K)
AUTHORS	Ni, Zhaohui; Jin, Haijiao; Lu, Renhua; Zuo, Li; Yu, Weimin; Ren, Yuqing; Yang, Qiongqiong; Xiao, Jie; Zhang, Qinghong; Zhang, Lihong; Zhang, Xinzhou; Chen, Qinkai; Chen, Chaosheng; Shao, Guojian; Luo, Qun; Yao, Li; Qin, Shuguang; Peng, Hui; Zhao, Qing

VERSION 1 – REVIEW

REVIEWER	Bhuwania, Puneet KG Hospital and PG Institute
REVIEW RETURNED	16-Aug-2021

GENERAL COMMENTS	<p>The study design is well thought of and includes most of the factors influencing hyperkalemia. I would like to suggest certain points which would be beneficial in analysis of the study</p> <p>1- ESRD patients with uncontrolled asthma [i.e. not on stable doses of bronchodilators (Beta-agonists) be excluded from the study].</p> <p>2- Ultrafiltration rates performed during the dialysis be also mentioned in the profile of the patients as it does impact potassium levels, especially in patients with LIDI.</p> <p>3- If possible a note on potassium content in the baths be made and mentioned in dialysis vintage of the patients (zero K, 1K, 2K or 3K).</p>
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REVIEWER	De la Flor, Jose Central Defense Gomez Ulla Hospital, Nephrology
REVIEW RETURNED	21-Sep-2021

GENERAL COMMENTS	<p>Thank the authors for preparing a clear and concise protocol, but I have some doubts that I would like to comment:</p> <p>-To increase the power of the study and avoid bias, I consider it appropriate to include the other new potassium binder, the patiromer, in the management of hyperkalemia, it is not included in the management of the protocol.</p> <p>-Apart from the primary objectives of prevalence and recurrence, it would be interesting to add as secondary objectives to the</p>
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	<p>treatment the efficacy, safety and tolerability of the options for the management of hyperkalemia in hemodialysis (HD).</p> <p>-It would be interesting to estimate the frequency of clinical events of interest (hyperkalaemia, hypokalaemia, hospitalizations and mortality) in patients with hyperkalaemia in HD, treated with the different potassium binders.</p> <p>-Analyze the evolution of the different ions (K +, Na, Mg, Ca and P) on a monthly basis, during the follow-up time with the different potassium chelators in patients on HD.</p> <p>-Explain in the protocol some other procedures carried out for the control of hyperkalemia in addition to the therapeutic.</p> <p>-Improve the classification of hyperkalemia according to its severity levels.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Puneet Bhwania, KG Hospital and PG Institute

Comments to the Author:

The study design is well thought of and includes most of the factors influencing hyperkalemia. I would like to suggest certain points which would be beneficial in analysis of the study

Query

1- ESRD patients with uncontrolled asthma [i.e., not on stable doses of bronchodilators (Beta-agonists) be excluded from the study].

Response

Dear reviewer, thanks for your suggestion, this study intend to explore the disease burden of hyperkalemia in hemodialysis patients under real world conditions, so we think it may be meaningful to enroll these patient but we will set a subgroup analysis of complications (asthma) and combination therapy (beta-agonists) for further observation.

Query

2- Ultrafiltration rates performed during the dialysis be also mentioned in the profile of the patients as it does impact potassium levels, especially in patients with LIDI.

Response

Dear reviewer, Thank you for your suggestion. We will mention the Ultrafiltration rates at each dialysis visit in the protocol. We have added this information in the Table 1 (Study plan).

Query

3- If possible, a note on potassium content in the baths be made and mentioned in dialysis vintage of the patients (zero K, 1K, 2K or 3K).

Response

Dear reviewer, Thank you for the suggestion. We have added this information in the Method and analysis section.

Reviewer: 2

Dr. Jose De la Flor, Central Defense Gomez Ulla Hospital

Comments to the Author:

Thank the authors for preparing a clear and concise protocol, but I have some doubts that I would like to comment:

Query

-To increase the power of the study and avoid bias, I consider it appropriate to include the other new potassium binder, the patiromer, in the management of hyperkalemia, it is not included in the management of the protocol.

Response

Dear reviewer, Thank you for the suggestion. We agree that adding patiromer would be appropriate to increase the power of the study and avoid bias. But, due to non-availability of patiromer in China (not approved yet in China) , we can't include it in the study for now.

Query

-Apart from the primary objectives of prevalence and recurrence, it would be interesting to add as secondary objectives to the treatment the efficacy, safety and tolerability of the options for the management of hyperkalemia in hemodialysis (HD).

Response

Dear reviewer, Thank you for the suggestion. But the present study focusses on evaluating the clinical burden of hyperkalemia in hemodialysis patients. However, we'll set an exploratory sub-group analysis to evaluate efficacy, safety and tolerability of the options for the management of hyperkalemia in hemodialysis (HD) patients.

Query

-It would be interesting to estimate the frequency of clinical events of interest (hyperkalaemia, hypokalaemia, hospitalizations and mortality) in patients with hyperkalaemia in HD, treated with the different potassium binders.

Response

Dear reviewer, Thank you for the suggestion. The rate of use of potassium binders in hemodialysis patients in China is relatively low. Considering the sample size in the present protocol study, it will be difficult to analyze different clinical events with different potassium binders, but we'll collect the treatment pattern of different option. The idea that you have suggested is well noted, we may design a study on the efficacy, safety and clinical events of different options for the management of hyperkalemia in hemodialysis patients in the next stage, based on the disease burden and treatment pattern collected from this study.

Query

-Analyze the evolution of the different ions (K +, Na, Mg, Ca and P) on a monthly basis, during the follow-up time with the different potassium chelators in patients on HD.

Response

Dear reviewer, Thank you for the suggestion. We have added this information in the Method and analysis section

Query

-Explain in the protocol some other procedures carried out for the control of hyperkalemia in addition to the therapeutic.

Response

Dear reviewer, Thank you for the suggestion. We have explained in the introduction and method section some of the other procedures carried out for the control of hyperkalemia like control on dietary intake of potassium and dialysis prescription management that includes potassium dialysate concentration and number of hemodialysis sessions.

Query

-Improve the classification of hyperkalemia according to its severity levels.

Response

Dear reviewer, Thank you for the suggestion. We have added the classification of hyperkalemia according to serum potassium (sK) levels as mild, moderate and severe.

COI statements:

Reviewer: 1

Competing interests of Reviewer: None.

Reviewer: 2

Competing interests of Reviewer: I have no conflict of interest.

VERSION 2 – REVIEW

REVIEWER	Bhuwania, Puneet KG Hospital and PG Institute
REVIEW RETURNED	01-Nov-2021

GENERAL COMMENTS	All the queries have been answered
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REVIEWER	De la Flor, Jose Central Defense Gomez Ulla Hospital, Nephrology
REVIEW RETURNED	22-Oct-2021

GENERAL COMMENTS	Good afternoon, it is appreciated the effort made by the authors to make the modifications requested by the reviewers.
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