Author's response to reviews

**Title:** Potentially Modifiable Factors Associated with Non-Adherence to Phosphate Binder Use in Patients on Hemodialysis

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**Author’s response to reviews:** see over
We thank the editor and reviewers for your valuable comments on our manuscript “POTENTIALLY MODIFIABLE FACTORS ASSOCIATED WITH NON-ADHERENCE TO PHOSPHATE BINDER USE IN PATIENTS IN BRAZIL ON HEMODIALYSIS”. All comments were taken into consideration. You may find below our detailed responses to the comments and description of the changes that were made in the text. We hope that you will find the revised manuscript acceptable for publication in BMC Nephrology.

1. Editorial Office:

After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further. We advise you to seek the assistance of a fluent English speaking colleague, or to have a professional editing service correct your language. Please ensure that particular attention is paid to the abstract. Please also ensure that your revised manuscript conforms to the journal style.

Our response:

I would like to thank you for the comment that was important to improve the quality of the article. This new version of the manuscript was reviewed carefully by the co-authors in addition to professional collaboration of English expert in scientific writing. As indicated we paid particular attention to the abstract but as you may see modifications were made in every section of the manuscript. We have worked to ensure that the revised manuscript conforms to the journal style.

2. Reviewer 1:

2.1 Is there any consensus on indication of prescribing phosphate binder (PB)?

Our response:

There are recommendations to the use phosphate binder for dialysis patients but the current recommendations cannot be viewed as a consensus among specialists. According to K/DIGO guidelines, in patients with CKD stage 5D, the K/DIGO Work Group suggests using phosphate-binding agents in the treatment of hyperphosphatemia (GRADE 2B). The strength of a recommendation is graded as Level 2. Level 2 means that different choices may be appropriate for different patients. The recommendation is likely to require debate and involvement of stakeholders before policy can be determined. The evidence quality is graded as B, meaning Moderate. This indicates that the true effect is likely to be close to the estimate of the effect, but that there is a possibility that it will be substantially different.

We agree that is important to call attention to this information and we added it to the introduction on page 4 (“The use of a phosphate-restricted diet, in combination with an oral phosphate binder, has become well established in the management of patients on
dialysis, although there is not yet consensus among experts regarding this. It is important to note that according to the K/DIGO Work Group, the strength of indication for prescribing phosphate binder to patients with CKD stage 5D is graded as Level 2 (suggested) and the evidence quality grade is B (moderate”).

2.2 It seems that no matter adherence to PB or not, mineral parameters (Ca, P, CaxP, product, etc.) are not different among patients. How to explain that?

**Our response:**

The serum concentrations of Ca, P, CaxP product and other mineral parameters do not depend only on the use of PB. Dietary and dialysis adherence, comorbidities, hypercatabolism, and nutritional and hormonal status are also factors that contribute to the serum concentration of nutritional parameters. The higher phosphorus concentration in the group of patients who were adherent to phosphate binder in our study is an intriguing finding that needs further investigation. Possible explanations for this finding are described on page 14 of the revised manuscript.

2.3 What is the major information of this work?

**Our response:**

Modifications were included in the Discussion section to emphasize major pieces of information described in the work. As described on page 15, it is possible to increase adherence to phosphate binder in hemodialysis patients by improving the quality of patient-staff interaction and educate the patients about the correct use of phosphate binder. Nurses, dietitians and nephrologists are likely to contribute to improve adherence to PB by increasing their interaction with patients, explaining about PB use, its effects and importance, and listening to and clarifying patients’ feelings related to the medication. Encouraging patients feel more independent in their self-care and take responsibility for their treatment will likely result in reduction of non-adherence to PB.

The questionnaire used to assess phosphate binder adherence may also been viewed as a contribution of the study. The questionnaire is easy to use and may help to evaluate systematically the patients regarding phosphate binder adherence. Based on the results of the study, the questionnaire should be reviewed to become even more informative. To the best of our knowledge, there is no validated questionnaire available to evaluate specifically the degree of adherence to phosphate binders. The questionnaire used in the present study was
developed to provide a comprehensive assessment of adherence to phosphate binder by hemodialysis patient, in addition to information regarding the patient’s knowledge/understanding and myths about the medication use. The knowledge gained by the responses provided by the patients should be useful to guide interventions aimed at improving adherence and ensure the correct use of the medication. We hope that our study and the proposed questionnaire will stimulate new investigations and more systematic assessments of phosphate binder adherence in hemodialysis settings. These comments are addressed in the Discussion section of the article.

2.4 Based on these so-called modifiable factors, what can nephrologists or nursing managers do to improve mineral disorders of these patients?

Our response:
The association between the perception of the patient that was educated by the nephrologist about the use of phosphate binder and lower odds of non-adherence was the strongest one observed in the study. Unfortunately the study did not provide data specifically about the nurse-patient interaction. However, the major role played by nurses in the hemodialysis team is largely recognized. Our findings provide strong support to the role of the hemodialysis team in improving phosphate binder adherence in hemodialysis patients. We hope that our results will stimulate nephrologists, nurses and dietitians to educate patients about phosphate binder use and evaluate systematically the adherence of the patients to their recommendation.

2.5 The discussion is well written and most of them are closely related to results and findings of this work, however, the text is still too long. Please if possible, try to reduce wordings and make it more concise to read.

Our response:
Thank you for this important contribution. We reviewed the discussion and removed some points that were not closely related to our results, as can be noted in the new version of the manuscript (page 15). The Discussion section is more concise now, despite the fact that it was necessary to include new text in great part to address comments of the reviewers and editor.

2.6 Needs some language corrections before being published.

Our response:
The latest version has been re-edited.
Results do not differ from those found in the literature, which does not justify specifying in the title of the article that it is a study carried out in Brazil. The title could be POTENTIALLY MODIFIABLE FACTORS ASSOCIATED WITH NONADHERENCE TO PHOSPHATE BINDER USE IN PATIENTS ON HEMODIALYSIS.

Our response

Thank you very much for your assessment.

We agree with this suggestion and have therefore changed the title.