

Review 00005191 firstly summarizes my paper as follows:

“The review discusses the forgotten issue of CO₂ load from dialysis solution, as acidosis by dialysate may occur causing early hypercapnia followed by respiratory failure. Another risk is the large amount of CO₂ moving from dialysis solution to the extracorporeal circuit. The Authors mention previous studies that have only partially addressed these issues but conclude that CO₂ as respiratory component of acid-base pattern is at least as important as the metabolic component in acid-base assessment also in hemodialysis patients. Clinicians must estimate the value of partial pressure of pCO₂ complying with the reduced HCO₃ concentration, but recommendations on what should be used are lacking. As formulas are different, results are often inconsistent. Textbooks provide some tips to easily calculate the expected pCO₂. The Authors stress that it has never been investigated whether different CO₂ loads should be recommended to a particular hemodialysis patient. Vascular access recirculation may be easily and profitably discovered by means of easy blood sampling. The issue of CO₂ load during renal replacement therapy has indeed been neglected so far and has not been in depth investigated. For this reason the paper brings an interesting message to the clinical community involved with renal replacement therapies. To infer and diagnose mixed acid-base disorders, physiologic respiratory response to metabolic acidosis should be considered and the expected pCO₂ value should be computed.”

Then, he/she states:

“The review could profit from some minor editing in style and some minor linguistic improvement but on the whole it is well written and well researched.”

I wish to thank him/her for this comment. Polishing of the text and minor changes have been made.

Review 02887546 states *“Please make the suggested grammatical corrections”*

I wish to thank reviewer for his/her help. All suggested grammatical corrections have been made.

Review 26955 suggests to take into consideration the following points:

- 1) *The abstract is a bit long and doesn't highlight the main points of the manuscript. In fact, there is significant overlap with the Introduction. I suggest writing a shorter abstract that highlights the main points the authors are trying convey.*

Thank you for this very helpful suggestion. Abstract has been entirely rewritten. The new Abstract is the follow:

"The large prevalence of respiratory acid-base disorders overlapping metabolic acidosis in hemodialysis population should prompt nephrologists to deal with the partial pressure of CO₂ (pCO₂) complying with the reduced bicarbonate concentration. What the most suitable formula to compute pCO₂ is reviewed. Then, the neglected issue of CO₂ content in the dialysis fluid is under the spotlight. In fact, a considerable amount of CO₂ comes to patients' bloodstream every hemodialysis treatment and "acidosis by dialysate" may occur if lungs do not properly clear away this burden of CO₂. Moreover, vascular access recirculation may be easily diagnosed by detecting CO₂ in the arterial line of extracorporeal circuit if CO₂-enriched blood from the filter reenters arterial needle.

- 2) *Define DOPPS study*

In the "Bicarbonate and beyond" paragraph the sentence *"Results from DOPPS study [2]"* has been replaced by: *Results from Dialysis Outcomes and Practice Patterns (DOPPS) study [2]....."*

- 3) *The article is written for a knowledgeable target audience, It would help broaden the audience if the authors provided a little more introduction that would benefit students new to the field. Imagine medical students reading the review.*

Many thanks for this suggestion. I have modified the Introduction section by replacing the following sentence:

“This approach clearly neglects serum HCO₃ modifications that are secondary to respiratory disorders” with “The finding of a low HCO₃ value has been always regarded as a sign of metabolic acidosis, but respiratory alkalosis also is featured by decreased HCO₃ concentration. Hence, diagnosing metabolic acidosis based on the latter parameter clearly neglects serum HCO₃ modifications that are secondary to respiratory disorders”.

Then, the sentence: *“Moreover, the surprising large prevalence of respiratory acid-base disorders, often coupled with metabolic acidosis, should prompt nephrologists to deal with the pCO₂ complying with the reduced HCO₃ concentration.* “ has been replaced by the followings: *“In these patients, respiratory acid-base disorders have been recently found in a large percentage and this should further prompt nephrologists to deal with the pCO₂ complying with the reduced HCO₃ concentration. Mixed disorders occur if measured pCO₂ is not consistent with the expected value.”* Finally, I further add this explanation: *“As a result of CO₂ clearance and of HCO₃ addition from dialysis solution, patient’s blood pH increases “*

4) *There are a modest number of grammatical errors and some language polishing is in order.*

The manuscript has been reviewed in order to improve English language.