Author’s response to reviews

Title: Zero Balance Ultrafiltration Using Dialysate during Nationwide Bicarbonate Shortage: A Retrospective Analysis

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Version: 1 Date: 18 Aug 2019

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Reviewer 1 Comments:

This paper reports a study examining the effects of changing solutions given during zero balance ultrafiltration from normal saline to a dialysate solution. The paper has a number of limitations
Page 2, line 26; the concentration of sodium chloride solution should have be stated.

Our response: Corrected - 0.9% sodium chloride

1. The introduction section should have concluded with a hypothesis and aim for the study.

Our response: We hypothesized that the use of dialysate as the replacement fluid for Z-BUF would show similar decreases in whole blood potassium levels and increases in serum bicarbonate levels when compared to Z-BUF with NaCl as the replacement fluid.
2. The authors state that the study had approval from their Institutional Review Board. The reference number and date of the letter of approval should have been supplied.

Our response: 752-17-EP, 11/22/2017

3. A description of how the electrolytes and bicarbonate were measured should have been provided along with any evidence to support the reliability of the technique.

Our response: Laboratory testing that was reviewed included pre- and post-Z-BUF whole potassium levels (measured via blood gas analyzers) and pre- and post-Z-BUF bicarbonate levels obtained from venipuncture or indwelling central venous catheters).

4. A description of how patients who underwent ultrafiltration were identified should have been presented.

Our response: Have updated in the text as to the indications.

5. An explanation why the study population sample size and why the time periods was were chosen should have been given.

Our response: We decided to review patients within the first 150 days of the change to utilize dialysate as the replacement fluid for Z-BUF as that coincided with the greatest restrictions to sodium bicarbonate administration at our institution.

6. The T-test is properly known as Student's t-test.

Our response: Corrected in the Methods section

7. An explanation of how the distribution of the data was examined to determine that is was normal would have been valuable.

Our response: Normal Probability Plots were created by the authors to determine that distribution of data (whole blood potassium values pre- and post-Z-BUF and serum bicarbonate values pre- and post-Z-BUF) was normal.
8. The results are reported as 'serum' concentrations. If they were measured by a blood gas analyser the concentrations were measured in whole blood so they should be reported as 'blood' concentration.

Our response: Corrected this throughout the paper.

9. Rather than using blood bicarbonate concentration as an estimate of metabolic acidosis, something like standardised base excess would have been better as it controls for arterial carbon dioxide tension (PaCO2). It would have also been useful to report PaCO2 as well.

Our response: Noted.

10. The design of the study is a retrospective, observational one using historical controls and this point should have been clarified in the methods section and abstract.

Our response: Clarified further in the abstract and methods section.

11. There is unnecessary duplication of information presented as text, tables and figures. Tables make data more accessible than text their use to report all the data would have sufficed with explanatory text in the results section. The figures added little value to the interpretation of the data and they could have been omitted.

Our response: We have omitted the figures.

12. Changes in variable would have been better presented as mean change with 95% confidence intervals as this would have enabled meaningful comparisons.

Our response: Noted.

13. Multiple statistical analyses have been undertaken inflating the risk of Type 1 statistical error. This of error could have minimised by nominating a primary outcome and controlling the risk in the secondary outcomes using something like Bonferroni's correction. In addition the number of tests could have been significantly reduced by comparing the changes variables groups rather than the point variables.

Our response: Noted.
14. Including the word safe in the conclusion and abstract is unjustified given the profound weaknesses of the study design and small sample size.

Our response: Corrected in the text.

15. The mean volumes of replacement fluid for each group should have been reported.

Our response: The mean volume of replacement fluid used in Z-BUF-S patients was 2413.16 mL while the mean volume of dialysate used as a replacement fluid in the Z-BUF-D group was 4428.38 mL (P < 0.01).

16. Page 6, sentence beginning line 43: presumably the authors mean sodium bicarbonate 8.4% solution rather that bicarbonate by itself.

Our response: Corrected in the text.

17. The author's might be interested in a study of similar design as a historical precedence for their study design. Alston RP, Theodosiou C, Sanger K: Changing the priming solution from Ringer's to Hartmann's solution is associated with less metabolic acidosis during cardiopulmonary bypass. Perfusion 22:385-9, 2007

Our response: Appreciate this.

Reviewer 2 Comments:

In the section of "abstract" Z-BUF-S must have its own explanation as was done in the main text.

Our response: Appreciate this and have corrected in the text.

In the section of "results", in the sentence of "The post-Z-BUF serum chloride levels were also similar in the Z-BUF-S and Z-BUF-D groups (111.08 ± 4.39 mEq/L versus 10.976 ± 2.84 mEq/L) (P = 0.06).", "10.976 must be 109.76.

Our response: Corrected in the text.
In the section of "conclusion", in the sentence of "Z-BUF with dialysate replacement fluid appears to be a safe and effective therapy for the treatment of hyperkalemia and metabolic alkalosis in patients undergoing CPB. "alkalosis" must be corrected as "acidosis".

Our response: Corrected in the text.