Reviewer's report

Title: Metformin associated lactic acidosis: a case series of 28 patients treated with sustained low efficiency dialysis (SLED) and long-term follow-up

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Reviewer: Ramin Sam

Reviewer's report:
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This article reviews all cases of metformin associated lactic acidosis at a single hospital in Italy. In recent years there have been large studies showing the incidence of lactic acidosis with metformin administration is very low and may be similar to other antihyperglycemic agents. However, there continues to be case reports of this condition. We need to give a chance to both sides of this debate to present their case. This article goes a long way in doing that and I think is clearly worthy of publication. I only have minor comments.

1. The authors define MILA as lactic acidosis exclusively due to metformin and MALA as lactic acidosis with intake of metformin and other co-morbidities. The authors then go on to describe their patients as having MALA, however they fail to mention what are the other co-morbidities that has led to lactic acidosis in these patients. In my opinion this classification is not helpful as patients with diabetes very often have co-morbidities and it is difficult to state what has led to what. Also many of the co-morbidities can be caused by the lactic acidosis itself and there will be the question of the chicken and the egg.

2. The authors states that 86% of their patients were volume depleted as they had nausea and vomiting. But it is clear that severe lactic acidosis can also lead to nausea and vomiting. Do
the authors have any solid data that the nausea and vomiting preceded the lactic acidosis? Were there other evidence for volume depletion (for example orthostatic hypotension)?

3. The authors talk about 57% of their patients had SIRS. Is the reason for SIRS just severe lactic acidosis or is there another cause for it?

4. In the patients with sepsis. Did all the patients have positive blood cultures and what did they grow?

5. The patients with contrast exposure, did they receive contrast while on metformin without holding it?

6. The authors state that hyperkalemia was corrected very slowly on the patients. It would nice to provide actual lab values on how slowly the potassium value was corrected and also what was the exact potassium bath that was used with hemodialysis?

7. It would be nice to supply lactate and bicarb values right before and after SLED if available.

8. The authors state 21% of the patients died after the first hemo treatment. Did anyone die prior to the first hemodialysis treatment?

9. The English needs to be improved a little.

10. On Table 2. can the authors fill in the second column for hemoglobin, potassium, glycemia and CRP.

11. The authors states that the serum lactate was 13.7 and the anion gap 36 at time zero. Was the serum lactate and anion gap drawn at exactly the same time on all of the patient? In our experience the two values usually coincide pretty well.

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**

If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**

If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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