Reviewer's report

Title: Effect of Glycemic Control on Soluble RAGE and Oxidative Stress in Type 2 Diabetic Patients

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Reviewer: Katerina Kankova

Reviewer’s report:

The MS of Motawi TMK et al. “Effect of glycemic control ... in Type 2 Diabetic Patients” describes the results of case - control study focusing on the effect of glycemic control on various routine as well as experimental parameters ascertained in well vs. poorly controlled T2DM subjects and healthy controls.

Major Compulsory Revisions:

The basic idea is not novel since sRAGE and parameters reflecting oxidative stress in diabetes are widely studied. Comparison of various parameters between study groups doesn’t constitute the study hypothesis. I am missing clearly stated research hypothesis and aims and, therefore, justification why the study was done. In the current form of the MS there are numbers of observations presented without clear pathogenic sequel. Overall MS is very busy and not transparent.

However, my major concern is the interpretation of the results. With such a large number of comparisons correction for multiple comparisons have to be performed. Although authors claim to use Bonferoni correction they still set the significance level at P<0.05!! Considering only data in Table 2 for example – 9 variables compared between 3 groups – the corrected P level should be <0.003. Following this correction, fewer significances would probably hold than shown currently and the whole Result and Discussion section would be modified. Multiple comparisons obviously stress the problem of large number of parameters being studied without clearly stated purpose.

Discussion is far too long and the reader gets soon lost. This section should be structured according to biological significance of the results – the elaborated research hypothesis would help.

Minor essential revisions:

1. Abstract
   - Result section is misleading – it is not clear which control group authors mean (healthy subjects or well controlled diabetics?)

2. Background
   - The statement “RAGE can be blocked by usage of soluble RAGE …” is incorrect since it implies that RAGE binds to RAGE while in fact it competes with RAGE for binding for AGEs (if that is the case with RAGE at all). The word
“neutralises” would be preferable.

3. Materials and Methods
- Subjects – since the level of plasma transaminases were used as one of the selection criteria it is not clear why authors compare the ALT and AST levels between the groups later on.

4. Results
- The reason for splitting of parameters between the Table 1 and 2 is not justified.

5. Discussion
- The whole section needs to be rewritten according to corrected and completed results as suggested above.
- Discussion on the relationship between sRAGE and kidney disease (proteinuria) in diabetics (the 1st paragraph) could benefit from including reference to the paper by Kankova K et al. in Arch Physiol Biochem 2008 describing the dependence of sRAGE on kidney function.
- Conclusions and description of the novelty aspects of the study should be incorporated into Discussion.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests