Reviewer’s report

Title: Mechanism of Worsening Diabetic Retinopathy with Rapid Lowering of Blood Glucose: The Synergistic Hypothesis

Version: 0 Date: 25 May 2017

Reviewer: Telma Soares

Reviewer’s report:

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This paper discusses the synergistic hypothesis to explain the occurrence and worsening of diabetic retinopathy (DR) that may occur due to insulin treatment in patients with diabetes mellitus. Insulin treatment, in spite of decreasing blood glucose, may increase DR, with paradoxical effect in some diabetic patients. The exact mechanisms of this insulin effect are still unclear. The authors support the hypothesis that high doses of exogenous insulin may act by increasing the expression of vascular endothelial growth factor (VEGF) in retinal microvascular endothelial cells via the activation of reactive oxygen species, inducing neovascularization. The subject under debate is very interesting and the authors have shown good argumentation on the subject. The introduction was presented in a clear manner with objectives and a summary of the existing literature with many current references. The body of the text was presented in subsections with relevant discussions on the topic. The authors conclude that the hypothesis presented has therapeutic potential and may benefit patients with type 1 and type 2 diabetes. However, minor changes are important.

Pag 2, Line 7 - remove underline

Pag 2, Line 19 - put abbreviations for type 1 and type 2 diabetes

Pag 5, Line 18 - change …lowering of blood pressure by lowering of blood glucose

Pag 5, Line 57 - put rats in lowercase

Pag 7, Line 26 - remove to before with

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
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Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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