Reviewer’s report

Title: Effects of human insulin and insulin aspart preparations on levels of IGF-I, IGFBPs and IGF bioactivity in patients with type 1 diabetes

Version: 1 Date: 19 December 2013

Reviewer: Peter van Dijk

Reviewer’s report:

This manuscript reports the effect of different insulin aspart preparations of parts of the GH-IGF-IGFBP axis in patients with T1DM. The manuscript is well written and the study has been performed meticulously. Although the clinical consequences of these findings are limited, this study adds to the growing knowledge concerning the effects of different insulin regimes and -administration techniques on the aforementioned axis.

I have some suggestions for the authors.

Introduction

1. “Type 1 Diabetes”. Please use the term “Type 1 Diabetes Mellitus” and abbreviate as “T1DM” throughout the manuscript

2. “…as differences in IGFBP-1 may lead to secondary changes in bioactive IGF” Please provide an reference for the assumption that differences in IGFBP-1 may lead to changes in IGF (IGF1 or IGF2?)

3. The claim that alterations in the GH-IGF-1-IGFBP-1 axis may contribute to the development of long-term complications is still very speculative at the moment. The authors do provide 2 references. However, I would like to invite the authors to give some additional thoughts on this topic as this may improve the clinical significance of their findings.

4. Please provide an testable hypothesis in the introduction or the patients and methods section.

Methods

5. The authors state that patients with impaired renal and hepatic function were excluded. How did the authors test this? Please provide the exact cut-off values for i.e. eGFR. How was a “recurrent major hypoglycaemia” defined?

6. What was the rationale for the 7-day interval between study visits?

7. Did the patients receive any instructions for the period between the study phase/visits?

8. The authors state that “outcomes were controlled for baseline levels if necessary”. How was this performed?
Results
9. Please provide standard deviation for the mean values.

10. Did the patients use other medication than insulin?

11. “Nineteen patients (15 men and four woman)”. Should be: Nineteen patients (15 men and 4 woman). Please change this.

12. “…as defined a priori by the study protocol…”. Please remove “a priori”. A study protocol is always a priori.

13. Four patients had an extended profile day because glucose levels > 16 mM, were there any reasons for this? Were these patients included in the analysis?

14. Were there any correlations between IGF-1 bioactivity and total IGF-1 and IGFBP-1?

Discussion
15. The discussion is very well written. Nevertheless, as this study was not intended to investigate the safety of the different formulations of insulin the final conclusion of the authors that there is no reason to concern when using insulin aspart containing preparations is not justified. I would suggest to keep the conclusions mention in the discussion section in line with the, deliberate, conclusion in the abstract.

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests