Reviewer’s report

Title: The effects of treatment with liraglutide on atherothrombotic risk in obese young women with polycystic ovary syndrome and controls: a case control study.

Version: 1 Date: 25 March 2014

Reviewer: Michelle Jones

Reviewer’s report:

This manuscript reports the results of an important pilot study investigating the effects of GLP-1 agonist liraglutide on weight loss in PCOS and matched controls. The study reports interesting results; primarily that although changes in weight loss are small and similar between the two groups, they were statistically significant and coupled with reduction in atherosclerosis markers. The author’s hypothesis is that women with PCOS and weight/age matched controls respond to liraglutide in a similar fashion.

Major Reviews

1. Please include a reference for the statement “Weight loss has been found to reduce many CV risk markers in PCOS including inflammation, and insulin resistance (IR).”; lines 53-55. A suitable reference would be Thomson et al, Hum Repro 2012 27(7):2169-76.

2. Please update the reference used on line 63 of the paper, there are several large trials of liraglutide published recently that would be a good addition to this older reference (ie. Wadden et al, Int J Ob 2013 Nov; 37(11):1443-51).

3. Please include some explanation for the dose selected in this trial. Several doses are seen in the literature of similar trials.

4. Power calculations: the power calculations provided are only for a single trait (P-selectin expression). Although this is important, the results from a number of other traits are reported. Perhaps a power table showing multiple effect sizes would give the reader a better opportunity to interpret the results of this study. The authors should also comment on the difference between the number of subjects needed per the power calculation and the number of subjects who completed the study, and how this difference affects the interpretation of the results of the study.

5. In defining differences between the two groups at baseline, the addition of significant P values to Table 1 (as a symbol) would be extremely helpful. Although the P values (of presumably all significant traits) are given in line 162-164, they would be more informative in the context of the table. There is also no mention of any difference in baseline glucose between the two groups.

6. In comparing the response of the two groups the addition of P values in the same fashion requested above is needed. A statistical test to compare the changes in the traits between cases and controls and the respective P value
should be included in both the text of the manuscript (line 172-175) and line 202 and Table 1. At very least this should be given for weight loss (delta weight).

7. Figure 1: please define the abbreviation SEM.

8. Figure 2: the legend panel should either be added to each panel or included once, not included in three of the five panels. Please move the legend explaining the asterisk used into the text of the figure footnote.

Minor Essential Reviews

1. Please define the abbreviation SD (line 145).

2. It seemed quite interesting that there was no increase in HOMA-%B. While this is an imperfect measure of beta cell function, it might be helpful to include a comment in the discussion on the lack of improvement in HOMA-%B in this study (including if other studies detect an increase in this trait).

3. There isn’t a clear and concise statement in the opening of the discussion that reintroduces the reader to the initial hypothesis of the paper (stated in lines 73-74) and comments how the primary findings of the paper fit with it. Adding this to the beginning of the discussion would significantly improve the first paragraph of the discussion.

4. The discussion would benefit from a few in depth sentences describing the mechanism of action of GLP-1 in insulin secretion, glucose homeostasis and body weight.

5. In comparing the results of this study to previous studies (line 241) the authors should add that the cited study also included diet and/or exercise interventions, and these could be important in cIMT.

6. In the footnote of Table 1 please add that the P values listed are from comparing baseline to 6m within each group. (Also see Major revisions for requests to add P values comparing the groups at baseline and 6m). Only significant P values need to be added to this table with symbols.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests