Reviewer’s report

Title: Hypoglycaemia in Diabetes: Do we think enough of the cause? An observational study on prevalence and causes of hypoglycaemia among patients with type 2 diabetes in an out-patient setting in Sri Lanka

Version: 0 Date: 15 Feb 2018

Reviewer: Thomas Barber

Reviewer's report:

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In this observational study by Dissanayake and colleagues, hypoglycaemia severity was assessed in 1000 patients with Diabetes Mellitus attending a private sector diabetes clinic in Sri Lanka. Furthermore, an attempt was made to ascertain the possible causes of hypoglycaemia. This field is certainly topical, and is of interest and relevance to the readership of BMC Endocrine Disorders. There are however a number of points that the authors need to address in a revised version:

1. It is important to provide more details on the type of Diabetes (ie. type 1 vs type 2) in the 1000 subjects recruited. Subgroup analyses for each type of Diabetes would be of interest, and relevant. As it is written, it is not possible for the reader to make any inferences about the risk of hypoglycaemia in each type.

2. Although the severity criteria for hypoglycaemia are outlined in a table, there is little if any reference to the tables in the text of the paper, and this needs to be addressed. Also, an explanation is needed for these criteria: some criteria for hypoglycaemia class any event that requires 3rd party assistance as severe, but this does not appear to have been used by the authors. Furthermore, the use of the term 'comatose' for severe is a bit vague. What is meant by 'comatose'? Can this be defined on the basis of GCS, or timing of the event etc.?

3. What is really of interest here with regards to therapies, is how many of those who had a hypoglycaemic event were on a sulphonylurea drug at the time, and how many were on insulin therapy. The way the paper is written makes these important details unclear. How many of those who had hypos were not on insulin or an SU therapy? That subgroup is of
particular importance, as theoretically they should not have had a hypo from their therapies, and so there may be other causes perhaps?

4. There are some grammatical and typo errors. (Declaration for example). Also, please avoid use of the term 'diabetic': should use 'patient with diabetes' instead.

6. As the authors correctly state, a limitation is that the data are self-reported and rely on memory. Furthermore, many of the events did not have capillary blood measurements of glucose which does limit conclusions that can be made. Also, there is no way to assess asymptomatic hypos. Clearly, CGMS data would have been useful, but it is clearly understood that this would not be feasible or practical in such an epidemiological study.

7. 'Unaccustomed exercise' is a bit vague. Can the authors elucidate on this term. Also, the timing of the hypo in relation to the 'unaccustomed exercise' would be useful to know.

8. For the readers who do not live in the Indian subcontinent, it would be useful to know a few more details of the foods identified as potential causes of hypoglycaemic episodes. What are their sugar contents for example, what kinds of food are they, and what are the proposed mechanisms for hypoglycaemic precipitation? Are there any lessons that can be learnt for western diets from these results?

9. Why was frequency (in addition to severity) of hypos not explored?

10. It is perhaps not surprising that a higher A1C associates with more severe hypoglycaemic episodes and the possible reasons the authors outline seem reasonable. This would certainly fit with clinical experience. It may be worth mentioning also that these data are consistent with those from ACCORD in which greater effort in reducing A1C (in those with less well controlled A1C) appeared to be most at risk: those with higher A1C are more likely to be advised by HCP to increase insulin dose for example.

11. This reviewer completely concurs that the main utility and importance of this study should be from an educational perspective (both from the patient and HCP angles) and this important point should be elaborated and expanded upon in the discussion section.

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?
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