Reviewer's report

Title: Glucagon like Peptide Analogues for Type 2 Diabetes Mellitus: Systematic Review and Meta-analysis

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Reviewer: Kristine Juul Hare

Reviewer's report:

Shyangdan and co-authors aim to review data regarding the effectiveness of GLP-1 analogues in patients with type 2 diabetes who are not achieving satisfactory glycaemic control with one or more oral glucose lowering drugs. The relevant analogues are tested alone against placebo, traditional treatment, in combination with traditional oral agents or against other comparable treatment (e.g. LEAD-6). It is important to the authors that the studies included in the meta-analysis follow the prevailing treatment guideline, this makes the review very relevant further the aim is clear and well arguemented. All studies run for at least 8 weeks there relevant effects should have been obtained.

The authors describe the method very thoroughly and argue why the chose the 28 analysed studies and that not all data in all studies are included resulting in an evaluation of only clinically relevant data. The studies analysed are of a high quality and by highly recognized authors.

Discretionary Revisions

This review draw the relevant comparisons regarding effect parameters in diabetes treatment, being glycaemic control and reaching the goal given by both ADA and EASD together with the other clinical important data being FPG/PPG, body weight gain/reduction. Further other parameters, which seems to be affected by treatment with GLP-1 analogues are listed being blood pressure, lipid profile and beta cell function are addressed. In the introduction the authors list glucagon inhibition as a primary effect of GLP-1 based treatment, however nothing further is discussed about this. Very little data is available; however it would have been relevant to put this in the discussion.

The authors acknowledge that more studies needs to be done in order to fully recognize this new drug class. Here only studies going on for up to 52 weeks are described; data on longer studies are sparse - however needs to be done. Exenatide, being the oldest of these analogues on the marked, has been used for 5 years now; still no one knows the long time effects, which could include carcinomas and pancreatitis. Also, the long term beta cell benefits are still only speculative as are the ability to maintain a loss in body weight. These facts are correctly included in the discussion as could be the clinical relevant compromise regarding reaching sufficient glycaemic control at an affordable cost and with minimal risk of hypoglycaemia and no weight gain. The compromises made by the treating physician and the patient.
All together the authors manage to give a review aiming towards a clinical setting – with references to the latest treatment guidelines, they systematically list the effect parameters/obtained results, and quite neutrally the GLP-1 analogues seems superior to previous treatment regarding the given data. Whether this treatment obtains the right place in the treatment guidelines are not discussed, however the data needed for guideline changes are called for.

The review is thorough and well written, I advise it for publication.

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

**Quality of written English:** Acceptable

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