Reviewer's report

Title: Switching from glargine+insulin aspart to glargine+insulin aspart 30 before breakfast combined with exercise after dinner and dividing meals for the treatment of type 2 diabetes patients with poor glucose control - A prospective cohort study

Version: 0 Date: 24 Feb 2018

Reviewer: Marco Gallo

Reviewer's report:
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The Authors aim at comparing an insulin regimen with glargine + premixed insulin (before breakfast) with a "basal-plus" regimen (glargine + once daily insulin aspart) in patients with T2DM and poorly controlled blood glucose levels. The main limit of the article is that it is an observational prospective single-arm cohort study without either a control group or a cross-over design: therefore, it is not possible to state if the regimen proposed is better than others. Furthermore, no conclusion about patients satisfaction and compliance can be drawn, since these aspects have not been presented or discussed in the paper. Lastly, the article needs to be revised by an English native medical translator.

Specific issues
1) The paper needs a revision as there are some orthographical and typographical mistakes in the text. I think it should be better if the paper was revised by an English native speaker, since it is often hard to read and understand.
2) This was an observational, prospective, single-arm study, without a cross-over design and with the limitation of an 'intervention bias': therefore, it is not possible to state if the insulin regimen proposed is better than others. As stated by the Authors in the discussion, "No control group was neither included, nor other types of insulin regimen." It is impossible to say how many patients would have achieved a better HbA1c level replacing glargine+premixed with glargine+once daily aspart.

3) Many kinds of premixed insulin exists, but the article took into consideration only a specific type (Insulin Aspart 30). The article should specify just from the title that this specific type of premixed insulin has been tested, instead of "glargine+premixed insulin"

4) the follow-up was very short (4+12 weeks) to draw any conclusion about the efficacy of this regimen

5) Abstract: "Blood glucose levels were well controlled and 58.7% of the patients achieved the HbA1c targets compared to 33.1% before switching." This pertains more to the section results than to the section Methods. Furthermore, in the section Results, no information about insulin doses, BMI, 2h-PG, hypoglycemia events, and patients' satisfaction is given.

6) Methods: Were the 185 patients (fulfilling inclusion criteria) screened for participation consecutively seen? Why the age range of 50-82 years has been chosen as an inclusion criteria? (this limitation is admitted in the discussion)

7) Melbine: do you mean metformin?

8) Results: The Authors state that "Switching to glargine+premixed insulin before breakfast resulted in lower breakfast, lunch, and dinner 2hPG and HbA1c, as well as a higher proportion of patients reaching the HbA1c target". However: "1) the initial dose of premixed insulin analogues was set as 1.5 times of the dose of breakfast insulin aspart in the original "1+1" mode; 2) furthermore, the insulin aspart 30 was gradually adjusted until at least one of the 2hPG levels after breakfast or lunch met the standard level"; 3) "For patients with 2hPG
failing to meet the requirement after one meal or two meals (except for patients with 2hPG failing to meet the requirement at both breakfast and lunch), they had to select smaller servings; 4) Thirdly, "30min exercise after dinner and/or reduced servings were adopted". Therefore, a real comparison between the same insulin doses of the two regimens has not been performed.

9) Was the rate of hypoglycemia higher, equal, or lower vs the previous insulin regimen? Not stated in the text

10) What was the effect on weight/BMI? Not stated in the text

11) Discussion: "Results showed that blood glucose levels were well controlled and 58.7% of the patients achieved the HbA1c targets compared to 33.1% before switching […] Therefore, for patients with T2DM that is poorly controlled under the 1+1 regimen, switching to glargine+premixed insulin analogues after breakfast showed promising benefits": see major issues #2

12) "glargine could steadily play its fundamental role at dinner, since it is an α-glucosidase inhibitor playing a synergistic hypoglycemic effect." Not clear to me: glargine is an α-glucosidase inhibitor?!?

13) Conclusions: "In conclusion, for patients with T2DM that is poorly controlled under the 1+1 regimen, switching to glargine+premixed insulin analogues after breakfast showed promising benefits, as well as good satisfaction and compliance". Satisfaction and compliance results have not been presented or discussed in the paper, even if they represent two outcomes of the study, according to the abstract.

Minor issues:
1) Glycated hemoglobin sometimes written as HbA1c, sometimes as HbA1C. Please, unify
2) "What is GAUC"??
3) "especially for patients with seriously impaired insulin metabolism who had been diagnosed with diabetes for >5 years". Do you mean glucose metabolism?

**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.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Unable to assess

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Not relevant to this manuscript

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