Reviewer's report

Title: Study protocol: A randomized placebo-controlled clinical trial to study the effect of vitamin D supplementation on glycaemic control in type 2 Diabetes Mellitus SUNNY trial

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Reviewer: Chia-Chao Wu

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General comments:

The authors propose this double blind, randomized placebo-controlled trial (SUNNY trial) to investigate the effect of vitamin D supplementation on glycemic control and quality of life in patients with type 2 diabetes mellitus (DM). Three hundred diabetic patients will be enrolled to analysis and compare the outcome parameters, quality of life between patients treated with vitamin D3 (50,000IU monthly) and placebo. This study was well written and organized, but vitamin D plays several roles in insulin resistance including immunoregulatory function, control inflammation and other molecular actions (hypocalcemia, hyperparathyroidism) to alter glucose homeostasis.

Specific comments:

1. In background section, the author should address the roles of vitamin D in insulin resistance, especially in immunoregulatory function and associated pro-inflammatory cytokine.

2. The author proposed the diabetic patients in study are excluded when serum 24OHD < 15nmol/l or > 150nmol/l. However, if these patients are supposed to be have sufficient vitamin D, the study design and recruitment flow chart should be revised to study only in patients of type 2 DM with vitamin D deficiency.

3. In inclusion/exclusion criteria, other divalent ion disturbances, like hypocalcemia, hyper/hypophosphatemia, abnormality of PTH regulation should be added in exclusion criteria.

4. As we know, the oral glucose tolerance test can provide the pancreas beta cell function. We suggest add the test to clarify. Otherwise, the immunoregulatory or pro-inflammatory cytokines are also considered to be addressed in this study.

5. The authors design to treat patient with oral vitamin D3 (50,000 IU monthly) for 6 months, however daily oral vitamin D supplement seems to be reasonable.

6. The authors also detect the skin AGE accumulation by skin autofluorescence during 6 months to evaluate the microvascular or macrovascular complication caused by oxidative stress associated with vitamin D deficiency. However, the study period seems to be so short that AGE may not accumulate during these 6 months. Other biomarkers of oxidative stress, for example serum nucleic acid
oxidation of 8-oxo-dG, 8-OH-dG, are suggested to more reasonable.

7. The authors should clarify the method and how to presentation of quality of life.


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.