Reviewer’s report

Title: Effects of vitamin D supplementation on liver fibro-genic factors in non-alcoholic fatty liver patients with steatohepatitis: study protocol for a randomized clinical trial

Version: 1 Date: 10 Jan 2019

Reviewer: Thomas Hiemstra

Reviewer’s report:

The revised version of the manuscript is an improvement. However, there are some unresolved issues without which I cannot recommend this paper for publication.

1) Sample size calculation.

The authors now state ‘considering the serum laminin mean of 136.7 ng/ml (12), based on the suggested formula for parallel clinical trials, we reached a sample size of 18 patients in each group’. First, I can find no evidence of a mean of 136.7 ng/mL in the reference (12 - Santos et al 2005). Second, without providing the data distribution and the magnitude of the anticipated treatment effect, AND detail of the magnitude of the treatment effect for which the study is powered, it is impossible to replicate the sample size calculations. Unless this is provided explicitly, it is not possible to recommend this manuscript for publication.

2) Safety

The authors have not adequately addressed my point concerning the use of PTH to monitor safety. In reply the authors reference the use of PTH as a surrogate for hypovitaminosis D. While this is of course true, this is irrelevant in the context of this trial. The IMP is cholecalciferol, and measures of safety in the trial should assess the safety of the IMP. Here, HYPOvitaminosis D is not a concern, but vitamin D toxicity potentially is. The authors need to explain how the safety of the intervention will be assessed, and PTH will not achieve this. Without adequately addressing this point, the manuscript cannot be recommended for publication.

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