Reviewer's report

Title: The Effect of Vitamin D Supplementation on Hemoglobin Concentration: A Systematic review and Meta-analysis

Version: 0 Date: 08 May 2019

Reviewer: Marjolijn Akkermans

Reviewer's report:

My compliments to the authors for having performed an extensive meta-analysis regarding the effect of vitamin D supplementation on Hb concentrations in adult patients. My question, why did you focus on adults specifically and not also include children or older people above 68 years of age? Furthermore, I have a few other remarks/questions, see below.

Introduction

What are the details of the reverse relationship between vitamin D levels and anemia in adults (line 66)? Please elaborate. A little more information on this is found in the Discussion but I believe this should also be mentioned in the introduction. Why are you investigating the relationship between vit D supplementation and Hb? What is the hypothesis? Maybe include an illustration to summarize the possible effects of vit D, PTH, hepcidin etc. on iron status/Hb?

Materials and Methods

Based on which criteria where patients assigned to one of the subgroups (line 138-140)? Please provide more details. And I believe that it is to expect that non-active vit D supplementation will not have a big effect on Hb when administered to patients with chronic kidney patients since the activation of vit D in the kidney might not be fully possible?

Results

What is the mean vit D dosage?

Where did most studies took place? Close to the equator with more sun exposure?

When did most studies took place? Summer/winter?

Did the studies reporting on ferritin levels take into account the acute phase protein aspect of ferritin? In other words, did the authors of these studies check for elevated CRP levels? If possible infection was not considered/checked, ferritin levels could have been falsely elevated
and hereby making analyses unreliable regarding the possible effect of vitamin D supplementation on ferritin levels.

Transferrin saturation and serum iron are unreliable iron status markers because serum iron has a diurnal pattern. I assume blood draws have not all been performed at the same time of the day. I suggest to remove these two parameters. Furthermore, both parameters do not differentiate between the possible presence of absolute iron deficiency (low/depleted iron stores) and functional/relative iron deficiency (restricted iron stores based on the increased expression of hepcidin leading to reduced availability of ferritin for iron demanding organs and cells).

Discussion

See also my remarks under Introduction and Results.

Tables/figures

Table 1 could be supplemental/online.

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