Reviewer’s report

Title: Vitamin D versus placebo as adjunctive treatment of heart failure patient quality of life and hormonal indices: A randomized, double-blind, placebo-controlled trial

Version: 1 Date: 06 Jul 2017

Reviewer: Renato De Vecchis

Reviewer's report:

Commentary

In this article, authors report the results of their clinical randomized trial with supplementation of vitamin D in the diet of patients with chronic heart failure (CHF); subsequently they address the issue of the possible relationship between low serum vitamin D levels and increased risk of poor clinical outcomes in CHF.

- Authors should point out in the Discussion that although plausible evidences has been accumulated over the years in favor of pharmacologic supplementation with vitamin D (colecalciferol or ergocalciferol) for CHF patients, no consistent demonstration of systematic benefit has emerged so far with regard to hard clinical endpoints, that is, death from all causes, cardiovascular death, and frequency of heart failure hospitalizations. This is why the administration of vitamin D supplements is not suggested by the recent (2016) guidelines for CHF treatment released by the ESC. Please highlight this point in the Discussion.

- Severe hypocalcaemia associated with rickets must always be kept in mind among the causes of dilated cardiomyopathy and impaired cardiac function in infants. If diagnosed and treated in time, dilated cardiomyopathy and severe heart failure related to rickets respond well. However, while vitamin D deficiency has been shown to be a proven cause of HFREF in neonatal and pediatric age, it would be correct to recognize that heart failure caused by hypo-vitaminosis D (diagnosed by means of hemato-chemical determination of serum 25(OH)-vitamin D levels) is not a very common condition. Please discuss on this issue in the manuscript.

- Background."Vitamin D deficiency is common in heart failure; prevalence ranges between 89-98% [8-9]". In my opinion, this assertion is devoid of the necessary documentation (the cited references are inappropriate or misleading). Please rectify or clarify better.

- It's well known that for CHF treatment some beta-blockers(carvedilol, bisoprolol, metoprolol, nebivolol) have been validated, for which there has been a class 1A indication. Notably, use of these drugs for HFREF patients is not dependent on the demonstration of a high heart rate or a clinically evident excess of adrenergic tone. Indeed, they have been
strongly recommended even in HFREF patients with normal heart rate, namely put between 60 and 85 beats / min. Conversely, if a vitamin D3 treatment has to be started in a patient with HFREF, you could wonder whether a such treatment should be carried out in the presence of a proven nutritional deficiency (25 (OH) vitamin D <30 ng / ml) or, like in the case of beta-blockers, vitamin D should be administered to HFREF patients as many as possible. Please address this issue in the Discussion.

- Determination of vitamin D serum levels is present in the work-up of patients with chronic kidney disease; on the contrary it is not included in the hematochemical determinations usually performed in CHF patients who have not been diagnosed with a cardiorenal syndrome (i.e., CHF patients with normal serum creatinine). Please discuss on this point.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

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

No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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