Author’s response to reviews

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

Authors:

Heidi Moretti (hmoretti1@gmail.com)

Vincent Colucci (Vince.Colucci@providence.org)

Bradley Berry (Bradley.Berry@providence.org)

Version: 3 Date: 12 Sep 2017

Author’s response to reviews:

September 12, 2017

Dear Dr. Cottini,

Thank you very much for the opportunity to revise our manuscript for possible publication in BMC Cardiovascular Disorders. This is an honor for us. You will find the requested revisions in green highlight and markup in the manuscript. We addressed each of the reviewers concerns, and revised according to their suggestions.

Reviewer 1 comments

Discussion, Vitamin D status, page 22, row 10 A question remains as to whether heart failure patients require vitamin D3 treatment only in the cases of 25(OH)D <20-30 ng/ml or if all patients with heart failure would benefit from supplementation despite normal circulating 25(OH)D levels…

-Discussion, Vitamin D status, page 22, row 17 In the case of vitamin D, one flaw of previous research may be the lack of identification of highest risk patients by not measuring 25(OH)D levels less than 20-30ng/ml. With the potential benefit that we found for QOL and neurohormonal indices, monitoring 25(OH)D and subsequent repletion has some scientific merit. Further research is needed to elucidate whether vitamin D should be given with or without monitoring serum levels. Commentary. These assertions fuel the suspicion that Authors may regard use of vitamin D as a beneficial resource in chronic heart failure(CHF) patients, in terms of improved quality of life and neurohormonal indexes, even if such a liberal use is indiscriminately applied, namely even in the absence of a proven vitamin D deficiency. Unfortunately, a liberal use of vitamin D, taken isolatedly, has not been shown to be adequately
beneficial and resolutive, not even in osteoporosis therapy, that is, in a field of application more directly related to the pharmacodynamic features of vitamin D, i.e., the ability to increase intestinal dietary calcium absorption and thereby at least partially antagonize heightened osteoclastic activity in bone tissue, that is present in postmenopausal osteoporosis. Conversely, in my opinion, vitamin D administration is not useful except for selected cases of CHF, as well as in cases of chronic kidney disease associated to it, namely in cardio-renal and reno-cardiac syndromes. On the contrary, authors seem to agree with the hypothesis of a possible utility of vitamin D in all cases of CHF, without not even affirming the diriment and mandatory role reasonably played by a preliminary determination of serum vitamin D. This statement seems to confer to vitamin D a feature of crucial drug in CHF management, which is certainly misleading and/or exaggerated with respect to the subsidiary and marginal role, that vitamin D therapy really plays in pharmacologic management of chronic heart failure.

Author comments:

Thank you for your commentary. We have removed any misleading suggestions that may overstate or extrapolate the benefit of vitamin D. This was removed in the abstract, discussion, and conclusion sections on pages 3 line 6-9, pg 22 line 23, page 23 line 1-2, pg 24 line 5-8.

Reviewer 2

The authors have made the suggested changes to the manuscript. But, some changes should be made as in the following. In page 17, line 19: but a more recent supplement trial (Babar, et al) -> Instead of Babar, et al, the number of reference should be inserted. "Table 1. Baseline characteristics" should be above the Table 1. Below the Table 1, this sentence [Data are expressed as mean ± standard deviation (SD) or number and percentages] would be located. "Table 2. Baseline and Post-Treatment/Placebo Laboratory Parameters" should be above the Table 2. Below the Table 2, this sentence [Data are expressed as mean absolute values ± standard deviation (SD)] would be located. "Table 3. Changes in Laboratory Parameters and KCCQ" should be above the Table 3. Below the Table 3, this sentence [Data are expressed as mean ± standard deviation (SD), 95% CI] would be located. "Table 4. Changes in Cardiopulmonary Exercise Tests" should be above the Table 4 Below the Table 4, this sentence [Data are expressed as Δ ± standard deviation (SD), 95% CI] would be located.

Thank you for your editorial suggestions. We have made changes to all of the tables to reflect the reviewer suggestions above.
The authors express sincere gratitude for this opportunity. Please let us know if there are any further requests or changes desired.

Best regards,

Heidi Moretti, MS, RD