Reviewer’s report

Title: 25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease

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Reviewer: Marco Contoli

Reviewer’s report:

In the manuscript titled “25-hydroxyvitamin D deficiency, exacerbation frequency and human rhinovirus exacerbations in chronic obstructive pulmonary disease” the authors aim to investigate whether deficient vitamin D is linked to increased exacerbation frequency in COPD. The topic of the study is relevant and it has been performed by a group with solid experience in the field. The authors found that low vitamin D levels are not associated with exacerbation frequency. I have only few minor comments to address to the authors.

1) The results are in line with a very recent large study (Kunisaki et al. AJRCCM 2012) showing that in patients with severe COPD, baseline vitamin D levels are not predictive of subsequent exacerbation. The authors should include and mention this study in the discussion.

2) At page 11, line 251. The authors conclude: “The next step in establishing the importance of 25-hydroxyvitamin D deficiency in COPD is to study supplementation in adequately powered clinical trials using relevant clinical outcomes.” This has been very recently performed in a single-centre, randomised, double-blind, placebo-controlled study (Lehouck et al. Ann Internal Medicine 2012). The study shows that high-dose of vitamin D supplementation in COPD patients does not reduce the incidence of exacerbations. However, the same study also documents that in participants with severe vitamin D deficiency at baseline (post hoc analysis) supplementation may reduce exacerbations. The authors should quote and address this study in the discussion.

3) The authors used the following definition to capture an exacerbation: “increase of two symptoms (at least one major) for two consecutive days, or if in the opinion of the attending clinician.” Did the author evaluate severe exacerbation frequency (i.e. requiring antibiotics or systemic corticosteroids) in relationship with vitamin D levels?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests