Author’s response to reviews

Title: The Effects of Two Vitamin D Regimens on Ulcerative Colitis Activity Index, Quality of Life and Oxidant/Anti-Oxidant Status

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The Effects of Two Vitamin D Regimens on Ulcerative Colitis Activity Index, Quality of Life and Oxidant/Anti-Oxidant Status

Nutrition Journal

Dear Dr. Clare Collins,

Nutrition Journal

Thank you very much for your email regarding the evaluation of our manuscript and the opportunity to revise and resubmit the paper. We have taken each comment very seriously, and now submit a revised version in response to the reviewers’ comments.

Once again, thank you for inviting us to respond to the reviewers' comments and revise our manuscript.
Reviewer reports:

Reviewer #1:

1. The authors did not measure serum vitamin D levels and they should therefore not use that term throughout the manuscript.
Response: Thanks for your comment; It was replaced with 25-hydroxy vitamin D throughout the manuscript.

2. The authors should add some nomenclature to the blood levels of 25-hydroxyvitamin D in the abstract presumably its nanograms/mL?
Response: Thanks for your comment; it is added.

3. The assay for 25-hydroxyvitamin D is not sensitive to 2 decimal places.
Response: We rounded the numbers to one decimal.

4. It is quite surprising that the blood level of 25-hydroxyvitamin D was the same at the end of the study for both the low and high dose group. This would suggest there was no difference?
Response: As it is shown in Table 3, mean 25-OH vitamin D increased significantly in high dose group from 21.8 to 29, and from 24.3 to 28.7 in low dose group. So it increased in both groups; however, the rise was not as much as healthy people because of the malabsorption due to inflammation.

5. A dose of 1000 IUs and 2000 IUs daily have been reported to increase blood level of 25-hydroxyvitamin D on average by 10 and 20 ng/mL respectively. Rule of thumb is for every 100 IUs ingested blood levels increase by approximately 1 ng/mL. This was not observed in either group raising concerns that may have been malabsorption due to the underlying inflammatory bowel disease. It would have been very helpful to have seen what the change i.e. delta was in serum 25-hydroxyvitamin D for each individual and to take those changes and provide a mean. This might give better insight as to what had occurred i.e. some of the subjects may have had poor absorption while others had moderate or normal absorption of vitamin D.
Response: Thanks for your comment; changes in both groups were analyzed and added in Results page 7, lines 182-184 as follow:

The mean changes in low dose and high dose groups were 0.2±2.2 and 6.7±3.8 respectively, which was significantly higher in high dose group compared with low dose group (p<0.0001).

6. Authors should carefully review the literature. There are a multitude of studies relating improvement in vitamin D status to varying doses of vitamin D including 1000 IUs and 2000 IUs daily. Also there are several studies that have evaluated vitamin D absorption in patients with ulcerative colitis and other inflammatory bowel disorders.

Response: We agree with you that vitamin D absorption reduces in patients with IBD. Our results are similar to other studies results that evaluated vitamin D supplementations in IBD patients (Garg et al., 2018, Jun et al., 2018, Tan et al., 2018) if it would be adjusted by dose and duration of supplementation.


Reviewer #2: This article investigated the effects of two dosages of vitamin D supplementation on serum vitamin D concentration, oxidative stress, quality of life, and disease activity in Ulcerative colitis patients.

The paper is well structured although some more explanations are needed with regards to:

- which therapy patients were taking during the study and if it was different between the two groups.
Response: Thanks for your comment; Medications were similar between two groups. It is shown in Table-2.

- Were the baseline Vit D serum concentrations significantly different between the two groups? (In the high dosage group the concentration was lower than in the low dosage group).
Response: No, it is explained on page 7, lines 180-185 as follow:

Serum 25-OHD level was not significantly different between two groups at the beginning (p=0.37), and the end of study (p=0.93). In the high dose group, serum 25-OHD significantly increased during the study, while this increase was not significant in the low dose group (Table 3). The mean changes in low dose and high dose groups were 0.2±2.2 and 6.7±3.8 respectively, which was significantly higher in high dose group compared with low dose group (p<0.0001).

- The high dose group had a basal Clinical Activity Indicator Questionnaire score and a IBDDQ respectively higher and lower than the lower dose group, could it influence the results?
Response: In ANCOVA analysis, we adjusted for baseline values; however, there were not significantly different at baseline.

- Has been evaluated the systemic phlogosis by biochemical markers (e.g. CRP or ESR)?
Response: No, our outcomes were serum 25-hydroxy vitamin D, oxidative stress status, disease activity, and quality of life.

- Why was a daily VitD supplementation chosen and not a monthly or weekly one?
Response: We chose daily supplementation only because it was more convenient for us for blinding the trial and using placebo control.

Have you evaluated patients’ compliance in taking pills?
Response: Yes, it is added on page 6, line 148 as follow:
Patients’ compliance was assessed using capsules count remained in the box at each visit.

Minor issues:
- Few words should be written as introduction in the abstract.
  
Response: Thanks for your comment; it is added as follow:

Due to malabsorption induced by inflammation in Ulcerative colitis (UC), the optimum dosage for vitamin D supplementation has not yet been elucidated.

- The are numerous missing blanks throughout the manuscript.
  
Response: Thanks for your comment; all were corrected.

- Table 2 could be synthetized reporting only bmi (the waist/hip ratio or waist circumference…are not necessary to the aim of the study)
  
Response: Thanks for your comment; we deleted them.

- In table number 5 "p values" should all reported in the table or all in the footnotes.
  
Response: All were entered in the table.