ORIGINAL ARTICLE

Oman Medical Journal [2015], Vol. 30, No. 2: 115–118

Vitamin D Deficiency in Patients with Irritable Bowel Syndrome: Does it Exist?

Yasir Khayyat[1]* and Suzan Attar[2]

[1]Department of Medicine, Umm Al Qura University, Makkah, Saudi Arabia
[2]Department of Internal Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

ARTICLE INFO

Article history:
Received: 26 June 2014
Accepted: 22 February 2015

Online:
DOI 10.5001/omj.2015.25

Keywords:
Vitamin D; Vitamin D Deficiency; Irritable Bowel Syndrome.

ABSTRACT

Objectives: Vitamin D has been found to be strongly associated with many systemic disorders. There has been an augmented interest within the medical community in vitamin D, especially its deficiency, in various systemic disorders. Although the role of vitamin D deficiency in irritable bowel syndrome (IBS) has not yet been established, studies are underway to clearly establish its role in the disease. The objective of our study was to elucidate and establish the role of vitamin D deficiency in IBS patients compared to a healthy control group. ***Methods:*** This study is a comparative case control study of vitamin D deficiency in patients with IBS diagnosed with ROME 3 criteria of classification (the third ROME foundation classification) to an age and gender matched healthy control group. The vitamin D level was measured in both cohorts for comparison and the results interpreted statistically. Sixty patients with IBS and 100 healthy individuals were included as test and control groups, respectively, in the study. The mean serum vitamin D level (nmol/L) of IBS patients was compared to the control group. ***Results:*** Vitamin D deficiency was detected in 49 patients (82%) in the IBS group and 31 patients (31%) in the control group. There was a statistically significant difference in the mean vitamin D level (p=0.025) between the IBS group and control group. ***Conclusions:*** Our study shows that vitamin D deficiency is highly prevalent in patients with IBS and these results seem to have therapeutic implications. Vitamin D supplementation could play a therapeutic role in the control of IBS.

Vitamin D has of late been the point of discussion in the medical domain and has been found to be strongly associated with many systemic disorders.[1,2] There has been an augmented interest within the medical community in vitamin D, especially its deficiency, in various systemic disorders. The association of vitamin D in skeletal and extra-skeletal health[1] is an established medical fact. More than 80% of metabolic vitamin D is derived from sunlight and the rest through dietary supplementation.[2]

Irritable bowel syndrome (IBS) is a gastrointestinal disorder marked by disorganized bowel function due to neurohormonal bowel wall-gut axis dysfunction.[3] IBS patients are managed using a pharmacological regimen and modified dietary protocol that is devoid of milk and other calcium-rich dairy products. Additionally vitamin B_{12} and riboflavin supplements are taken to minimize painful bowel spasms and regulate bowel function.[4] However, there are published comparative study reports from Sweden that contradict the efficacy of these modified dietary protocols in IBS patients.[5]

Although the role of vitamin D deficiency in IBS has not yet been determined, studies are underway to clearly establish its role in the disease. The recent report on the successful treatment of diarrhea predominant IBS with high doses of oral vitamin D supplementation—culminating with the resolution of the associated anxiety and depression as well—has sparked a gush of medical blogs and interest from the scientific community.[6]

The objective of the present study has been to elucidate and establish the role of vitamin D deficiency in IBS patients compared to a healthy control group. The study is a comparative case control study of vitamin D deficiency in patients with IBS diagnosed with ROME 3 criteria of classification (the third ROME foundation classification) to an age and gender matched healthy control group. Vitamin D level was measured in both groups for comparison and the results interpreted statistically.

*Corresponding author: ykhayyat@imc.med.sa

Box 1: Irritable bowel syndrome (ROME 3 Criteria*) for Diagnosis.

Recurrent abdominal pain or discomfort at least three days/month in the last three months associated with two or more of the following:**

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

Criterion fulfilled for the last three months with symptom onset at least six months prior to diagnosis.

***"Discomfort" means an uncomfortable sensation not described as pain.*

Table 1: Demographic characteristics of the irritable bowel syndrome (IBS) patients and control group.

	IBS n=60	Control n=100	*p*-value
Age (years)*	44.2±16	47±14.55	0.250
Male: Female ratio	23:37	11:89	0.510
25(OH)D (nmol/L)*	21.1±12	31.37±16.35	0.025
Deficiency < 50nmol/L**	49(81.67)	31(31)	

*mean±SD; **n(%)

METHODS

This prospective comparative analysis was conducted at the International Medical Centre (IMC), a tertiary centre in Jeddah, Saudi Arabia. Patients presenting to the gastroenterology clinic of the IMC with symptoms of IBS diagnosed by ROME 3 criteria (defined in Box 1) were compared to a healthy control group. The control group were age and gender matched attendants to the general clinic checking their vitamin D level, and were free from symptoms of IBS.

Information pertaining to age and gender were collected from both groups. The serum concentration of vitamin D was measured by 25-hydroxycholecalciferol (25(OH)D) levels utilizing liquid chromatography-tandem mass spectrometry (LC-MSMS) technique (Roche Diagnostics, Germany) in both groups. Vitamin D deficiency for the study was defined as serum 25(OH)D levels less than 50nmol/L as standardized in published research literature.[7]

Statistical analysis was accomplished using SPSS (version 19). Qualitative data were presented in the form of number and percentage values. The quantitative data were presented in the form of mean and standard deviation (±SD) values. Chi-square test was employed as a test of significance for ordinal data. Student's *t*-test and linear correlation (Pearson's coefficient-2-tailed) was utilized to compare the mean vitamin D levels in the control and IBS group with a *p*-value (significance level) less than 0.050.

Informed consent of all the participants was documented and ethical approval was obtained from the institutional review board of the hospital.

RESULTS

A total of 60 IBS patients and 100 healthy individuals from the control group were included in the study, which took place over a period of three months. The study population was mostly female (79%) with a mean age of 42±5 years. The mean serum level of 25(OH)D in IBS patients was 21±12 nmol/L compared to the matched control of 31±16 nmol/L. There was a statistically significant difference in the mean 25(OH)D level between the IBS and control groups (p=0.025) [Table 1].

Vitamin D deficiency was detected in 49 of the 60 patients (82%) in the IBS group and 31 of the 100 patients (31%) in the control group. A positive Pearson's correlation coefficient (r=0.264, p=0.001) was found to exist between age and serum 25(OH)D levels indicating a proportionality of 25(OH)D levels to age. Scatter plotting showed a linear relationship between age and vitamin D levels. Gender had no significant effect on vitamin D levels. Vitamin D supplementation in terms of consumption over the study period was excluded in both groups due to poor recollection response.

DISCUSSION

The study revealed three statistically significant results. Firstly, the mean serum level of 25(OH)D in IBS patients was 21±12 nmol/L compared to the control group 31±16 nmol/L. Secondly the frequency of vitamin D deficiency was found to be high in the IBS group (82%) and thirdly, a significant positive correlation between age and vitamin D level was found.

In this context, it is worth mentioning that bone loss associated with vitamin D has been an observed in numerous abnormal abdominal conditions such as celiac disease, inflammatory bowel disease, and post-gastrectomy cases. Given the fact that the areas of the gut involved in vitamin D absorption[8] is centered predominantly in the ileum (70–80%), with most of the vitamin D receptors and regulatory mechanisms

in the cecum and colon regions,[9,10] the importance of vitamin D deficiency needs to be addressed seriously in IBS patients as well.

This can be substantiated by recent published studies showing that alterations in the vitamin D mechanisms in the receptor cells could cause altered cellular growth and promote adenoma and carcinoma in vitro.[11] Furthermore, it has also been observed that immune activation was part of this oncogenesis process in such cases with elevated levels of cytokines such as tumour necrosis factor (TNF-α) and interleukins (IL-1β and IL-6).[12] It should also be acknowledged that the gut, rich in micro flora, acts as an excellent region for activation of an immune response, promoting the effect of type-1 helper T cells and thus, maintaining hemostasis.[13] In this context, it has to be acknowledged that vitamin D inhibits T-cell proliferation and thus is capable of inhibiting the immune response.[1]

From such a point of view, the link between IBS and vitamin D deficiency can be theoretically established to the alterations in the immune response. It is no doubt a questionable fact whether vitamin D deficiency could be taken into account as a causative factor relating to the pathogenic aetiology in the development of IBS as in the case of vitamin deficiency induced fibromyalgia cases.[14] The present study has shown significant difference in the mean level of vitamin D in the IBS group compared to control. It is worth mentioning that the authors see no published clinical study that looks into the pathological explanation of such an association.

Attention needs to be drawn into the psycho-social behavioral patterns of these IBS patients who often tend to avoid food items like fortified milk, which are rich in vitamin D and calcium, leading us to the conclusion that an altered vitamin D absorption mechanism could be an underlying reason for such observed social behaviours.[15] The case report by Sprake et al[8] has shown a probable treatment response associated with active diarrhea symptoms of IBS.

Thus, if the immune response alteration observed in IBS is a major contributory response and it could be proved experimentally that vitamin D suppresses immune function response by type-1 helper T cells and potentiates the function of natural killer cells,[16] it would be a breakthrough study in this grey area of gastrointestinal research. Interestingly, similar medical conditions such as inflammatory bowel disease that have been extensively studied with reference to vitamin D replacement showed no improvement of its clinical exacerbations.[17] Although vitamin D deficiency has an established link with poor exposure to sunlight, there has been no significant difference between male and female population with reference to vitamin D levels in this study. However, advancing age has been found to have a positive correlation with vitamin D deficiency. This could be attributed to the fact that the middle aged tend to be more cognizant of their dietary habits and take over-the- counter vitamin supplements. This, in fact, has been substantiated by the CHMS (Canadian Health Measures Survey) Cycle 2 data for the period from August 2009 to November 2011.[18] This study is limited by the fact that vitamin D balance is dependent on numerous physiological and social factors like exposure to sunlight, physical activity, and dietary habits that serve as the determinants of serum vitamin D levels.

Though these factors, in fact, contribute to the actual measured vitamin D levels, they are not accurately quantifiable elements to be included in the study and acquiescent to recall bias. Additionally, the geographic region where the study has been conducted is hot throughout the year and hence, the population most often are in cultural attires that minimize their physical exposure to sunlight. Thus, patient responses to interventions using supplemental vitamin D to treat IBS should rely more on improvement of the symptoms.

CONCLUSION

With an enhanced attention on the role of vitamin D deficiency in the pathogenesis of several chronic illnesses, deficiency of vitamin D in IBS has recently caught the interest of medical professionals. There have been numerous attempts of therapeutic application of vitamin D to improve IBS symptoms. More research is needed to establish the therapeutic role of vitamin D in the management of IBS patients and deficiency should be addressed in the diagnosis and the treatment of the condition. Vitamin D supplementation should be considered as a part of the therapeutic protocol in patients with IBS henceforth. Further research to determine a quantifiable amount of vitamin D supplementation is needed to establish the optimal dose response effect.

Disclosure
The authors declared no conflicts of interest. No funding was received for this study.

Acknowledgements
We would like to acknowledge the effort of Mr Mohammed Janish for his assistance with the statistical analysis.

REFERENCES

1. Pakpoor J, Pakpoor J. Vitamin d deficiency and systemic lupus erythematosus: cause or consequence? Oman Med J 2013 Jul;28(4):295.
2. Attar SM, Siddiqui AM. Vitamin d deficiency in patients with systemic lupus erythematosus. Oman Med J 2013 Jan;28(1):42-47.
3. Holick MF. Vitamin D deficiency. N Engl J Med 2007 Jul;357(3):266-281.
4. Mead MN. Benefits of sunlight: a bright spot for human health. Environ Health Perspect 2008 Apr;116(4):A160-A167.
5. Eshraghian A, Eshraghian H. Interstitial cells of Cajal: a novel hypothesis for the pathophysiology of irritable bowel syndrome. Can J Gastroenterol 2011 May;25(5):277-279.
6. Atkinson W, Sheldon TA, Shaath N, Whorwell PJ. Food elimination based on IgG antibodies in irritable bowel syndrome: a randomised controlled trial. Gut 2004 Oct;53(10):1459-1464.
7. Bohn L, Storsrud S, Simren M. Nutrient intake in patients with irritable bowel syndrome compared with the general population. Neurogastroenterol Motil. 2013 Jan;25(1):23-30 e1.
8. Sprake EF, Grant VA, Corfe BM. Vitamin D3 as a novel treatment for irritable bowel syndrome: single case leads to critical analysis of patient-centred data. BMJ Case Rep 2012;2012(007223):2012-007223.
9. Holick MF. Vitamin D status: measurement, interpretation, and clinical application. Ann Epidemiol 2009 Feb;19(2):73-78.
10. Vestergaard P. Bone loss associated with gastrointestinal disease: prevalence and pathogenesis. Eur J Gastroenterol Hepatol 2003 Aug;15(8):851-856.
11. Christakos S. Recent advances in our understanding of 1,25-dihydroxyvitamin D(3) regulation of intestinal calcium absorption. Arch Biochem Biophys 2012 Jul;523(1):73-76.
12. Christakos S, Dhawan P, Porta A, Mady LJ, Seth T. Vitamin D and intestinal calcium absorption. Mol Cell Endocrinol 2011 Dec;347(1-2):25-29.
13. Peterlik M, Cross HS. Vitamin D and calcium deficits predispose for multiple chronic diseases. Eur J Clin Invest 2005 May;35(5):290-304.
14. Karaahmet F, Basar Ö, Yüksel I, Coban S, Yuksel O. Letter: vitamin D supplementation and the irritable bowel syndrome. Aliment Pharmacol Ther 2013 Feb;37(4):499.
15. Ghoshal UC, Shukla R, Ghoshal U, Gwee KA, Ng SC, Quigley EM. The gut microbiota and irritable bowel syndrome: friend or foe? Int J Inflam. 2012;2012:151085.
16. Jesus CA, Feder D, Peres MF. The role of vitamin D in pathophysiology and treatment of fibromyalgia. Curr Pain Headache Rep 2013 Aug;17(8):355.
17. Nicholson I, Dalzell AM, El-Matary W. Vitamin D as a therapy for colitis: a systematic review. J Crohns Colitis 2012 May;6(4):405-411.
18. Whiting SJ, Langlois KA, Vatanparast H, Greene-Finestone LS. The vitamin D status of Canadians relative to the 2011 Dietary Reference Intakes: an examination in children and adults with and without supplement use. Am J Clin Nutr 2011 Jul;94(1):128-135.