

Effect of Vitamin D on Irritable Bowel Syndrome

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Abstract:

Irritable Bowel Syndrome (IBS) impacts the quality of life; its incidence has been increasing over last two decades to become the commonest gastrointestinal disease is. Pharmacological agents going to target the underlying illness mechanisms have been developed with an increasing awareness of IBS pathophysiology. Possible mechanisms implicated in IBS pathogenesis can be modulated by vitamin D, Owing to its possible role as immune modulator, and anti-microbial and anti-inflammatory agent.

The aim of this research was to evaluate the impact of food rich in vitamin D and supplementation on irritable bowel syndrome symptoms in undergraduate medical students with vitamin D deficiency, as part of Nutritional Assessment of Medical Students of Ain Shams University (NAMS/ASU).

Subjects and Methods: This is a prospective cohort study done as a part of The Nutritional Assessment of Medical Students of Ain Shams University (NAMS/ASU), the project was designed to evaluate the nutritional status of 1225 medical student of the undergraduate medical students.

This sector of the project included 40 vitamin D deficient (<20IU), IBS (according to ROME IV criteria) undergraduate medical students

Those students were selected after:

- History taking stressing on demographic data, IBS symptoms according to ROME IV criteria and chronic illness (DM, HTN, IBD,.....)

-Vitamin D level by ELISA (Ain Shams University Central Labs) with deficiency diagnosed at (<20 IU), (50 nmol/liter)

Those students were further subjected to:

-Diet instruction for irritable bowel syndrome and lifestyle advice (eg. Regular eating pattern, Limiting the intake of triggering agents, ensuring a good hydration and regular physical activity, take the time to eat, sit down to eat, chew the food carefully)

-An advice to increase intake of vitamin D rich food and Vitamin D Oral Drops Cholecalciferol 42000 IU / week.

Enrolled students were reassessed after 12 weeks through:

Re-evaluation of IBS symptoms using ROME IV criteria by the same investigator

Vitamin D level by ELISA using the same kits at the same laboratory (Ain Shams University Central Labs).

Informed written consent was obtained. Approval by the ethical committee was obtained.

Data collection was done, tabulated and analyzed (SPSS Inc., Chicago, Illinois, USA).

Probability (P-value) – The P-value of >0.05 was deemed insignificant.

Results: Forty undergraduate medical students were involved in this sector of (NAMS/ASU) with mean age= 22.33±1.37, mean BMI=23.75±3.02, 65% of included

students were females. The included students had mean vitamin D= 11.68±8.17 and 44.30±16.18 before and after 12 weeks of VIT D supplementation respectively, 97.5% of the participants achieved vitamin D normalization by the end of the study, After three months of vitamin D supplementation, 47.5% (19 students) of the study population did not fulfill ROME IV criteria any more (no IBS symptoms), while 52.5% (21 students) of them continued to have ROME IV criteria, yet with partial relief of symptoms with a significantly higher vitamin D levels in the students with complete resolution of symptoms at the end of the study duration (P value=0.013)

Conclusion: Vitamin D supplementation plays a therapeutic role in the control of IBS in vitamin D deficient IBS patients.

Key Words: Vitamin D, irritable bowel syndrome, nutrition, therapeutic role

INTRODUCTION:

Irritable Bowel Syndrome (IBS) impacts the quality of life [1] In recent years IBS has become prevalent worldwide between the young adult community and university students [2] Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder which shows symptoms of recurrent abdominal pain coupled with changes in digestive behavior without organic abnormalities [3]. It is a chronic gastrointestinal (GI) tract disorder with a relapsing/remitting course that is possibly disabling [4, 5].

Irritable bowel syndrome is described as per the Rome IV criteria, as recurrent abdominal pain for at least 4 days each month over a period of at least 2 months, correlated with one or more of the following: defecation-related, changes in stool frequency and/or changes in the shape or appearance of the stool [6]. Diet and stress exposure (involving early life events) were proposed as contributing factors to IBS [7].

Diet and lifestyle recommendations should have been the first method in IBS dietary management, if symptoms persist while following general diet and lifestyle advice, manipulations to relieve symptoms such as low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diets, should be involved in dietary management [8].

Pharmacological treatments for IBS therapy should be directed at the predominant symptom of the patient that may be dominant abnormal intestines, abdominal pain or bloating. Cognitive behavioral therapy, multi-component psychological therapy and dynamic psychotherapy can also be used [9].

With increasing awareness of IBS pathophysiology, pharmacological agents going to target the underlying illness mechanisms have been developed [10].

It's been shown that all possible mechanisms implicated in IBS pathogenesis are modulated by vitamin D [11], as the impacts of vitamin D on improving the function of the intestinal barrier were reported in in vitro [12], experimental [13] and human studies [14].

Vitamin D2 (ergocalciferol) derived from plant sources (yeast and fungi) and vitamin D3 (cholecalciferol), which is synthesized in human skin and ingested in the diet via the consumption of animal-based foods, are two major types of vitamin D [15]. Oily fish are a

good source of vitamin D3 [16], yet not sufficient to substantially boost human vitamin D status [17].

Dietary vitamin D (either vitamin D2 or D3) has been typically absorbed along with other dietary fats in the small intestine [18]. Yet, vitamin D obtained from exposure to the sun, food and supplementation (either vitamin D2 or D3) has been biologically inactive and must be activated by two consecutive enzymatic hydroxylation reactions in the liver and kidney [15]. 1, 25-dihydroxyvitamin D (1, 25[OH] 2D) , referred to as the active vitamin D hormone or calcitriol-is derived primarily from 25(OH) D renal hydroxylation and is more reliant on mineral metabolism regulators (e.g., parathyroid hormone (PTH), phosphate or fibroblast growth factor-23 (FGF-23)) or renal function than on substrate accessibility of 25(OH) D. The vitamin D metabolites in circulation are predominantly bound to vitamin D-binding protein (DBP) and, to a smaller degree, to albumin and lipoprotein, with only a tiny fraction (less than 1%) circulating unbound (free) in their form [19].

Beside its known role in Calcium and phosphorus metabolism and bone mineralization [20], Vitamin D enhances endothelial function by lowering vascular inflammation, managing blood pressure, hindering vascular smooth muscle cell proliferation, and antagonizing foam cells formation [21].

Since 1 α -hydroxylase and vitamin D receptors are expressed by macrophages, dendritic cells and activated B and T lymphocytes, active vitamin D modulates the immune response by interacting with innate and adaptive cells of the immune system, regulating cytokine expression [22]. Adequate vitamin D reduces incidence of infections of the upper respiratory system [23], improves brain health [24].

The possible role of vitamin D in IBS may be explained by its role as an immune modulator, anti-microbial and anti-inflammatory agent [25].

Diagnostic criteria of vitamin D status [26]

	Severe deficiency	Deficiency	Insufficiency	Optimal concentration	Risk of toxicity
25(OH)D3 concentration (ng/ml)	0-10	10-20	21-29	30-80	> 100

The aim of this research was to evaluate the impact of food rich in vitamin D and supplementation on irritable bowel syndrome symptoms in undergraduate medical students with vitamin D deficiency, as part of Nutritional Assessment of Medical Students of Ain Shams University (NAMS/ASU)

SUBJECTS AND METHODS:

This is a prospective cohort study done as a part of The Nutritional Assessment of Medical Students of Ain Shams University (NAMS/ASU). The project was designed to evaluate the nutritional status of 1225 medical student of the undergraduate medical students.

This sector of the project included 40 students who were selected after:

- History taking:

1) Abdominal pain (site, character, duration, relieving and precipitating factors, relation to defecation)

- 2) Any change in stool frequency or consistency
- 3) Chronic illness (DM, HTN, IBD,.....)

-General clinical examination: Anthropometric measurement:

- 2) Weight in kilogram (kg): the participants being bare – foot and in minimal clothing, weight measure with electronic scales (In-Body 770).
- 3) Height in centimeters (cm).
- 4) Body mass index (BMI): is recognized as weight (in kg) divided by height (in m²)

Laboratory data:

Vitamin D level by ELISA (Ain Shams University Central Labs) with deficiency diagnosed at (<20 IU), (50 nmol/liter) [27].

(25(OH) D has greater serum concentrations and longer half-life (approximately 3 weeks vs. 1 day), thus deemed to be the best vitamin D supply predictor).

The 40 students included in the study were diagnosed to have vitamin D deficiency and IBS according to ROME IV criteria (Diagnostic criteria for Rome IV for IBS: on average, in the last 3 months, recurrent abdominal pain of at least 1 d/wk, linked to at least 2 of the following criteria:

1. Correlated to defecation
2. Linked to changes in stool frequency or form (appearance). For the last 3 months, criteria met with symptom onset of at least 6 months prior diagnosis.

Those students were further subjected to:

Diet instruction for irritable bowel syndrome and lifestyle advice:

- A regular pattern of eating.
- Restrict the intake of possible dietary causes like alcohol, caffeine, fat, and spicy foods.
- Ensuring a good hydration and regular physical activity.
- Avoid skipping meals, long gaps or eating late at night.
- Avoid large meals.
- Take the time to eat, sit down to eat.
- Chew the food carefully.

An advice to increase intake of vitamin D rich food like:

- Fatty Fish, like Tuna, Mackerel, and Salmon.
- Foods fortified with vitamin D, like some dairy products, orange juice and cereals.
- Beef Liver.
- Cheese.
- Egg yolks.
- Vitamin D Oral Drops Cholecalciferol 42000 IU / week in half glass of water or milk.

Re-evaluation of the included students was applied after 12 weeks of life style and dietary modification and Vitamin D Oral Drops Cholecalciferol 42000 IU / week administration by:

- 1) Re-evaluation of IBS symptoms using ROME IV criteria by the same investigator
- 2) Vitamin D level by ELISA using the same kits at the same laboratory (Ain Shams University Central Labs).

Ethical Considerations:

A written informed consent of each student and their legal guardians has been obtained before enrolment in this study after explaining the aim of the study and all the procedures

done. Privacy and confidentiality were concerned. Approval was obtained from the ethical committee.

Using the statistical package for social sciences, version 20.0, using assessment methods, data collection was done, tabulated and analyzed (SPSS Inc., Chicago, Illinois, USA). Mean \pm standard deviations (SD) express quantitative data, frequency and percentages express qualitative data. Independent-samples t-test Probability (P-value) – The P-value of 0.05 was deemed insignificant.

RESULTS:

Forty undergraduate medical students were involved in this sector of (NAMS/ASU) with mean age= 22.33 \pm 1.37, mean BMI=23.75 \pm 3.02, 65% of included students were females. The included students had mean vitamin D; 11.68 \pm 8.17 and 44.30 \pm 16.18 before and after 12 weeks of VIT D supplementation respectively, 97.5% of the participants achieved vitamin D normalization by the end of the study

Table 1): Mean Vitamin D level and frequency of deficiency among study group (n=40).

Vit.D	Total (n=40)
Vit. D at the start Mean \pm SD	11.68 \pm 8.17
Vit. D after 12 weeks of Vit D supplementation Mean \pm SD	44.30 \pm 16.18
Difference Mean \pm SD	32.63 \pm 11.79

After three months of vitamin D supplementation, 47.5% (19 students) of the study population did not fulfill ROME IV criteria any more (no IBS symptoms), while 52.5% (21 students) of them continued to have ROME IV criteria, yet with partial relief of symptoms.

Table 2: Comparison between students according to their Vit.D in relation to degree of relief of IBS symptoms:

	ROME IV criteria		t-test	P-value
	No symptoms	Partially relieved symptoms		
Vit. D at the start Mean \pm SD Range	14.74 \pm 10.27 5-43	8.90 \pm 4.29 3-17	2.691	0.022*
Vit. D after 12 weeks of Vit D supplementation Mean \pm SD Range	50.84 \pm 15.25 30-86	38.38 \pm 14.96 18-62	4.797	0.013*
Difference Mean \pm SD Range	36.11 \pm 11.01 19-56	29.48 \pm 11.84 13-50	2.142	0.041*

This table shows statistically significant difference between vitamin D level and degree of IBS symptoms resolution or relief.

DISCUSSION:

Regarding Rome IV criteria; (52.5%) out of the study students showed improvement and (47.5%) showed no symptoms. There was statistically significant improvement regarding Rome IV criteria (IBS symptoms) in included students which was proportionate to vitamin D level, with $P=0.02$, 0.013 before and after 12 weeks of vitamin D supplementation. Abbasnezhad et al. (2016) [28] also found that patients having received vitamin D had a substantially higher degree of improvement in IBS symptoms. Sparke et al., (2012) [29], recorded that 70 % of 37 patients with IBS reported improvement in their symptoms with supplementation with vitamin D, and most of these persons reported deficiency of vitamin D prior to supplementation. Moreover, Cho et al., (2018)[30] reported that in adolescents with IBS, the average vitamin D level was low (16.25 ± 6.58 ng/mL). Tazzyman et al. (2015)[31] recorded no substantial enhancement in IBS symptoms following 12 weeks of vitamin D supplementation in adults with IBS, contrast to our findings, but this may be due to either sufficient vitamin D in this study population or non compliance.

CONCLUSION

Vitamin D supplementation plays a therapeutic role in the control of IBS in vitamin D deficient IBS patients.

LIMITATION:

Selected study population with stressful life style
Subjective nature of IBS symptoms with multiple relieving and precipitating factors

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