Serum vitamins A and E deficiencies in patients with inflammatory bowel disease

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Chronic inflammatory bowel diseases (IBD) include ulcerative colitis (UC) and Crohn's disease (CD), the etiologies of which are not certainly defined, and are hypothesized to be an interaction between environmental, genetic, and immunologic factors.[1] Recent studies show a gradually increasing rate of IBD in developing countries in Africa, South America, and Asia.[1] There has been a reported increase in the incidence and prevalence of IBD in the West during the past 50 years, 120-200/100000 for ulcerative colitis and 50-200/100000 for Crohn's disease (CD).[1] Inflammatory bowel disease patients usually suffer from mal-absorption and mal-digestion, especially in the flare-up phase of the disease when increased requirement and decreased food intake are reported. Nutritional deficiency and malnutrition have been documented in IBD patients notably in CD, which may lead to adverse outcomes.[2] Vitamins B12, A, E, and D need to be monitored and supplemented. When a large amount of the small bowel is resected, all nutrients will be absorbed poorly.[3] This case-control study was designed to measure and compare serum levels of vitamins A and E between IBD patients and a healthy normal population in northeastern Iran. Due to the large differences in feeding habits in different areas, the aim of this study was to compare the levels of these vitamins in the patients and healthy cases.

This case-control study was carried out from November 2011 to April 2012 in Golestan Province, Northern Iran. In this study, 94 pathologically confirmed IBD cases, and 94 healthy age and gender-matched controls with no gastrointestinal problems over the previous 2 years were recruited. The inclusion criteria for IBD patients were based on clinical diagnosis and pathology, and the exclusion criteria were based on those who did not receive vitamin supplements in the last 6 months.

A fasting blood sample was taken. Measurement of vitamins A and E was carried out by the high-performance liquid chromatography (HPLC) technique (KNAUER V 7057-3; Smartline pump 1000 V 7603; Smartline UV Detector 2500 V 7604 and Smartline manager 5000 V 7602, (Berlin, Germany). Values of less than 30 µg/dl for vitamin A and 0.5µg/dl for vitamin E were considered as deficiencies. Retinol acetate (Retinyl palmitate [all-trance-retinol palmitate]; Sigma LN 68F0645, St. Louis, MO, USA) was used as the internal standard with a final concentration of 2 µg/ml.

To extract vitamins, 200 µl methanol (Merck & Co., Inc., Rahway, NJ, USA), 200 µl Ethanol (Merck & Co., Inc., Rahway, NJ, USA, 11727), 50 µl internal standard (Retinol acetate) and 500 µl n-Hexan (Merck & Co., Inc., Rahway, NJ, USA, 04391) were added to 200 µl of plasma. The surface phase was gathered after centrifuge and 500 µl n-Hexan added, and then vaporized by nitrogen gas. The remaining was dissolved in 200 µl methanol, and 50 µl of sample was injected for HPLC (flow rate: 1.5 ml/min, time: 20 min, sample: 50µl, wavelength [0 min–7 min]: 325 nm, wavelength [7 min -15 min]: 292 nm)]. The ethical committee of Golestan University of Medical Sciences (No=1453) approved this study, and the patient consents were obtained.

Fifty percent of both case and control groups were male. The mean (standard deviation [SD]) age of patients was 38 (15), and of controls was 38 (14) years (p=0.8).

Table 1 - The mean (standard deviation) levels of vitamins A and E in inflammatory bowel disease patients and controls in different age and gender groups.

Variable	Vitamin E	*P*-value	Vitamin A	*P*-value
Group				
Case	0.40 (0.37)	0.001*	46.85 (32.23)	0.03*
Control	1.29 (1.80)		58.25 (27.56)	
Gender				
Male	0.87 (1.31)	0.21*	54.46 (29.82)	0.42*
Female	0.82 (1.43)		50.26 (31.23)	
Age group				
<29 years	0.57 (1.03)	0.001**	50.51 (26.13)	0.3**
30-42 years	0.56 (1.03)		51.92 (33.14)	
>43 years	1.41 (1.76)		54.82 (32.76)	

*Student t-test, **One-way ANOVA

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The mean level of vitamin A was not significantly different between males and females (p=0.42) as well as different age groups (p=0.3) (**Table 1**). The vitamin E level was not significantly different between the genders (p=0.21). The levels of vitamin E were significantly higher in older (> 43 years) compared with other age groups (p=0.001) (**Table 1**). Vitamin A had no significant relationship with age (p=0.24). There was no significant difference in proportion of vitamin A (p=0.4) and E (p=0.32) deficiencies between males and females in the control group. In the IBD group, the proportions of vitamin A deficiency were 22.7% in males, and 43.6% in females (p=0.04), and regarding vitamin E deficiency, they were 65.5% in males, and 78.7%, in females (p=0.1). The means of both vitamins A (p=0.03) and E (p=0.001) were significantly lower in IBD cases than controls (**Table 1**). In this study, 32.5% of patients and 18.2% of controls had vitamin A deficiency (p=0.03). Vitamin E deficiency was seen in 72% of IBD cases, and 46% of controls (p=0.001). The duration of disease in those with vitamin A deficiency was 3.3 years, and 2.9 years in those with normal levels of vitamin A (p=0.21). These values were 3.9 years in those with vitamin E deficiency, and 2.9 years in those with normal vitamin E levels (p=0.18). No significant relationship was found between the duration of disease and the proportion of vitamin deficiencies in IBD patients.

In the present study, the serum levels of vitamin A and E were significantly lower in IBD patients compared with healthy controls. This finding was similar to some other investigations. Vagianos et al[2] evaluated 126 consecutive adults with IBD regarding biochemical markers of nutrition, and concluded that even if the nutritional status of the IBD patient seems well, vitamin and mineral deficiencies may exist. They showed a high proportion of deficiency for some nutrients, including vitamin E (63%), vitamin D (36%), vitamin A (26%), calcium (23%), folate (19%), iron (13%), and vitamin C (11%). They suggested a routine multivitamin supplementation in IBD patients.

In the study of Alkhouri et al,[4] they investigated the prevalence of vitamin and zinc deficiencies in patients with newly diagnosed IBD in comparison with a control group. This was a retrospective chart review of all patients diagnosed with IBD from 2006-2010, ages 1-18 years. A total of sixty-one IBD patients, and sixty-one age and gender-matched controls were included. None of the sixty-one patients with IBD had folate or vitamin B12 deficiency. Vitamin D deficiency was found in 62% of the patients, vitamin A deficiency in 16%, vitamin E deficiency in 5%, and zinc deficiency in 40%. The control group had vitamin D in 75%, vitamin E deficiency in 8%, and zinc deficiency in 19%. They concluded that vitamin B12 and folate deficiencies are rare in children with newly diagnosed the ulcerative colitis (UC). Vitamin A, and zinc deficiency are common in patients with newly diagnosed IBD and levels should be assessed at the time of diagnosis so that internal repletion can commence. Vitamin D deficiency is common in all children in the Buffalo, New York area and routine screening for this deficiency is warranted.[4]

In the study of Vavricka et al,[5] it was shown that vitamin B(12) and folic acid supplementation may be necessary in IBD patients, especially those with CD with either inflammation of the terminal ileum or after resection of the terminal ileum. It is also recommended during therapy with sulfasalazine as this compound inhibits the absorption of vitamin B(12). They investigated that patients with high or continuous inflammatory CD activity and frequent therapy with steroids have an increased risk of low bone mineral density and vitamin D deficiency. These should be monitored regularly, and vitamin D should be supplemented. In a recent trial[5] a trend towards a reduced risk of relapses in CD patients treated with vitamin D was reported. Only limited studies and case reports exist on other vitamin deficiencies, for example vitamins A, B(1), B(2), niacin, B(6), C, E, and K, found in IBD patients. Regular nutritional monitoring in IBD patients is warranted and requires the special attention of treating physicians and dieticians.[5]

The limitation of this study was that the degree of severity of illness was unknown. If there were information on the severity of disease in comparison with the vitamin levels, better results could have been obtained.

In conclusion, we found vitamin A and E deficiencies in IBD patients. It may be concluded that without maintaining the optimum level of vitamins in IBD patients, they would be trapped in a cycle of low vitamin level, increased oxidant factors, increased tissue injury in the intestine, and again, further decrease in vitamin levels. A cohort study design is recommended, in addition to controlling the levels of vitamins, other micronutrients should also be evaluated and compared with the severity and progression or remission of disease.

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