Impact of Low Vitamin D Level on Inflammatory Bowel Diseases

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Mini Review

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Introduction

The role of vitamin D in patients with inflammatory bowel diseases (IBD) has been for years underestimated [1]. This fat soluble vitamin is absorbed in jejunum and terminal ileum and directly and indirectly affects enterocytes leading to an increase in calcium absorption from the gastrointestinal tract [2]. The main role of vitamin D is regulation of calcium-phosphate homeostasis [2]. However, recently many studies indicate its pleiotropic effects, which is connected with the presence of vitamin D receptors (VDR) in different tissues [2,3].

Anti-carcinogenic activity of vitamin D comprises promotion of cell differentiation, induction of apoptosis, inhibition of cancer cell proliferation, regulation of expression of different proinflammatory cytokines and growth factors, as well anti angiogenic properties [2,3]. However, the evidence that vitamin D prevents development of colon cancer is inconsistent [3]. It is worth to underline that low serum vitamin D level might also result from many other malignancy risk factors such as: obesity (vitamin D sequestration in adipose tissue), lack of physical activity (less sunlight exposure), and difference in diet habits [3].

The deficiency of vitamin D has an important influence on the immune system function, and may interfere proper cellular immune response, especially of activated VDR-expressing monocytes, macrophages, dendritic cells, and lymphocytes [2,3]. Vitamin D promotes microbial killing in the macrophages and inhibits antigen-presenting capacity of the dendritic cells [3]. Acting through VDR in lymphocytes vitamin D inhibits their proliferation and differentiation to maturity, which results in suppression of the adaptive immune response [3].

Epidemiological studies show that prevalence of vitamin D insufficiency is common in patients with IBD - in children 55.6% of patients with Crohn's disease (CD) and 63.6% of patients with ulcerative colitis (UC) have its sub-optimal (≤ 32ng/mL) serum level [4]. Low vitamin D level, (with insufficiency (20-30ng/mL) in 37% and deficiency (<20 ng/mL) in 23%) is found in 60% of adult IBD patients [5]. Especially exposed to low vitamin D levels are patients with pouchitis-69.4% [6].

The most important risk factors of vitamin D insufficiency comprise: mal absorption, resection of small intestine, decreased sunlight exposure, winter and spring season, higher body mass index Z-score, smoking and higher erythrocyte sedimentation rate [2,4].

In IBD patients hypovitaminosis D is associated with severer course of the disease, enhanced use of medications (corticosteroids, biologics, narcotics), increased risk of surgery and hospitalizations, and quality of life deterioration [7-9]. Low vitamin D level may also contribute to an increased risk of the CD onset [10]. Ananthakrishnan et al. [10] in a large prospective cohort study showed that each 100-IU/day increase in total vitamin D intake resulted in a 10% reduction in UC risk and a 7% reduction in CD risk [10].

Hypovitaminosis D, as well male gender, Asian ethnicity, and corticosteroids use are risk factors for low bone mineral density in IBD [5].

However, deficiency of vitamin D might be also connected with several nonskeletal effects, for instance an increased risk of Clostridium difficile infection [11]. Ananthakrishnan et al. [11] found that each 1ng/mL increase of vitamin D level in plasma was associated with a 4% reduction in risk of Clostridium difficile infection.

Ananthakrishnan et al. [12] in a large IBD cohort (2809 patients) study showed an increased risk of colon cancer in subjects with vitamin D deficiency (<20ng/mL). Each 1ng/mL increase of vitamin D in plasma was associated with an 8% reduction in risk of colorectal cancer [12].

In view of all the above data, vitamin D supplementation might have an important impact on the course of IBD [1,13]. Jørgensen et al. [13] in a randomized double-blind placebo-controlled trialadministered vitamin D at the dose of 1200IU/d to CD patients and after three months they noticed reduced number of disease flares (13% vs. 29% in controls), however, the difference was not statistically significant [13]. Pappa HM et al. [4] in a pediatric group of patients with IBD after supplementation of vitamin D at the dose of 2000IU/d observed a lower level of C-reactive protein and interleukin-6. However, more interventional studies are required to confirm the therapeutic efficacy of vitamin D supplementation in IBD [14]. A target of vitamin D levels between 30 and 50 ng/mL appears to be both safe and have benefits for IBD disease course. Daily vitamin D doses between 1800-10,000IU/d are probably necessary [15].

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