cmgh
CELLULAR AND MOLECULAR GASTROENTEROLOGY AND HEPATOLOGY

EDITORIAL

Micronutrient Deficiency in Inflammatory Bowel Diseases: Cause or Effect?

Inflammatory bowel diseases (IBDs), encompassing both Crohn's disease (CD) and ulcerative colitis (UC), affect over 3 million individuals in the United States.[1] The pathogenesis of IBD is complex and multifactorial in nature, with contributions from genetic, environmental, and immunological factors. Despite considerable advances in the field, the etiology of IBD still remains elusive. In this regard, recent studies have highlighted the importance of diet (an environmental contributor) in IBD pathogenesis. During IBD, loss of appetite observed in patients or impaired absorption owing to epithelial defects could cause nutrient deficiencies. In fact, deficiency of micronutrients (essential vitamins and minerals) is observed in over half of IBD patients, in which deficits occur more often in CD.[2] Conversely, studies have also demonstrated the potential impact of nutrient deprivation on intestinal epithelial tight junctions, microbial community, and cellular changes (eg, autophagy), which could ultimately contribute to pathogenesis of IBD.[3] However, little is known whether nutritional deficit is a consequence of IBD or if nutritional deficiency could be one of the risk factors in IBD pathogenesis.

Many micronutrients, including vitamins A, B, D, and K, as well as minerals such as iron and zinc, have been recognized to be low in cohorts with IBD.[4] A very recent study demonstrated that fatigue is an important clinical problem observed in patients with IBD.[5] Deficiency of vitamins in B complex, specifically thiamine (B1) and biotin, were suggested to be potential culprits in the development of this symptom.[5] In the current issue of *Cellular and Molecular Gastroenterology and Hepatology*, Skupsky et al[6] provide novel evidence of the role of biotin in UC. Biotin, also known as vitamin B7 or H, is not synthesized in humans; therefore, dietary intake and bacterial synthesis in the gut are its main sources.

In the current study,[6] the authors showed that biotin-deficient diet was able to induce a colitis like phenotype in mice, which was alleviated with biotin supplementation. In addition, dextran sulfate sodium (DSS)–induced colitis mice also showed biotin deficiency along with significantly reduced levels of sodium-dependent multivitamin transporter (SMVT) involved in biotin absorption. Furthermore, supplementation of biotin (1 mM) via oral administration in mice reversed DSS colitis and also induced remission in the same model.[6] Additionally, the authors demonstrated that biotin deficiency resulted in stimulation of the nuclear factor-κB pathway, resulting in colonic inflammation. Also, biotin supplementation during DSS colitis abrogated nuclear factor-κB activation. Interestingly, a significant decrease in SMVT was also observed in UC patients, attesting to the clinical relevance of this study. The authors speculated that supplementation of biotin could be beneficial to IBD patients with flares of acute colitis or to maintain remission. Oral administration of biotin is considered quite safe and does not pose any significant risk with respect to side effects in humans, owing to its water-soluble nature.

The anti-inflammatory activity of biotin has also been recognized in previous studies.[7,8] However, it should be noted that biotin has been identified to skew the T helper cell population, which would likely be more beneficial for UC patients as opposed to CD patients. Thus, more extensive translational studies are needed to establish the optimal benefits of biotin in IBD patients, which could aid in more careful tailoring of the biotin dose based on the type of IBD. In addition, although the authors have correlated the loss of SMVT to biotin deficiency in UC, it should be noted that at pharmacological doses, biotin could also be absorbed via passive diffusion and, hence, loss of SMVT in IBD could be circumvented by using high doses of biotin to alleviate gut inflammation. Additionally, gut dysbiosis could be another factor leading to biotin deficiency in IBD, as certain bacterial species have been shown to heavily utilize biotin, potentially making it unavailable for absorption.[9] Therefore, in future studies, it would be of interest to investigate the role of gut dysbiosis in biotin deficiency in IBD.

In summary, the current work has highlighted the potential therapeutic role of biotin in alleviating UC and has also shed new insights into the implications of micronutrient deficiency in triggering intestinal inflammation. Currently, very little is known about how nutrient deprivation could contribute to IBD. So far, only vitamin D has been linked to IBD pathogenesis. The vitamin A derivative retinoic acid, although widely studied in preclinical models as a therapeutic modality in IBD, has only shown minimal clinical benefit.[10] At present, the understanding is that IBD causes nutrient deficiency and that this may lead to the exacerbation of the condition. However, whether nutrient deprivation is a cause or effect in IBD pathogenesis remains elusive and warrants extensive further investigation.

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Conflicts of interest
The authors disclose no conflicts.

Funding
This work was supported by National Institute of Digestive and Kidney Diseases Grant No. DK92441 (to Pradeep K. Dudeja), Department of Veteran Affairs Grant No. BX 002011 (to Pradeep K. Dudeja), and a VA Senior Research Career Scientist Award (to Pradeep K. Dudeja).


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2352-345X
https://doi.org/10.1016/j.jcmgh.2019.12.009