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LETTER TO THE EDITOR

Interaction between inflammatory bowel disease, physical activity, and myokines: Assessment of serum irisin levels

Marwan SM Al-Nimer

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Marwan SM Al-Nimer, Department of Therapeutics and Clinical Pharmacology, College of Medicine, University of Diyala, Baqubah 32001, Iraq

Corresponding author: Marwan SM Al-Nimer, MBChB, MD, PhD, Professor Emerita, Department of Therapeutics and Clinical Pharmacology, College of Medicine, University of Diyala, University Street, Baqubah 32001, Iraq. marwanalnimer@yahoo.com

Abstract

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, showed a wide spectrum of intestinal and extra-intestinal manifestations, which rendered the patients physically inactive and impaired their quality of life. It has been found that physical activity is a non-pharmacological intervention that improves the quality of life for those patients. Irisin is one member of the myokines secreted by muscle contraction during exercise and could be used as an anti-inflammatory biomarker in assessing the physical activity of IBD patients. In addition, experimental studies showed that exogenous irisin significantly decreased the inflammatory markers and the histological changes of the intestinal mucosa observed in experimental colitis. Furthermore, irisin produces changes in the diversity of the microbiota. Therefore, endogenous or exogenous irisin, *via* its anti-inflammatory effects, will improve the health of IBD patients and will limit the barriers to physical activity in patients with IBD.

Key Words: Irisin; Inflammatory bowel disease; Physical activity; Myokines; Prognostic marker

Core Tip: Irisin is a sports hormone secreted with muscle contraction and serves as an anti-inflammatory biomarker as well as attenuating the intestinal microbiota diversity. Low serum levels of irisin were observed in patients with ulcerative colitis, which can be increased with physical activity. Physical activity is useful in patients presented with extra-intestinal manifestations of inflammatory bowel disease (IBD). Exogenous irisin may overcome the barriers of physical activity in IBD, producing beneficial anti-inflammatory effects and attenuating the microbiota diversity.

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TO THE EDITOR

I read with great interest an elegant editorial by Stafie *et al*[1] who commented on the article published in an issue of the *World Journal of Gastroenterology*[2]. Stafie *et al*[1], made a good comment, and they highlighted certain aspects of the barriers to physical activity (PA) in the relapse of inflammatory bowel diseases (IBD). Recent studies showed that PA can be assessed in laboratories by measuring specific markers named myokines. Therefore, it will be useful to fill the gap on the role of PA in IBD by supplementing the commentary with changes in the myokine levels in IBD patients who were doing any PA.

IBD are emerging as a significant global health concern as their incidence continues to rise on a global scale, with detrimental impacts on quality of life[2]. One of the extra-intestinal manifestations of the IBD is musculoskeletal manifestations that occurred as peripheral arthritis, axial spondyloarthritis (ax-SpA), and enthesitis[3]. It has been found that PA significantly and positively impacts the ax-SpA, improving the quality of life[4]. Therefore, PA is a useful non-pharmacological intervention that combats the SpA in IBD, and it is worth trying to look for a biological marker that indicates the benefit of PA in IBD presented with SpA as a comorbidity of extra-intestinal manifestations (EIMs)[3]. It is possible to use the levels of myokines, notably the serum levels of irisin, as a marker for the training or limitation of PA in patients with IBD. Irisin is a member of the myokines derived from the FNDC5 protein, which is produced by myocytes and secreted into the circulation in response to muscle contraction[5]. It is important to know that the irisin levels increased following the exercise, but they did not maintain their higher levels for the long period that followed the exercise[6].

Figure 1 shows the beneficial interactions between the IBD and their EIMs with the production of irisin by PA or using exogenous irisin. Lower serum levels of irisin were significantly observed in patients with ax-SpA presented with sacroilitis and negative HLA-B27 status and who were treated with non-steroidal anti-inflammatory drugs[7]. Exercises trigger the production of irisin, which is sometimes called sport hormone, and play a role in decreasing the inflammation associated with the risk factors of systematic diseases, *e.g.*, non-alcoholic fatty liver disease[8], obesity[9], heart diseases [10,11], *etc.*

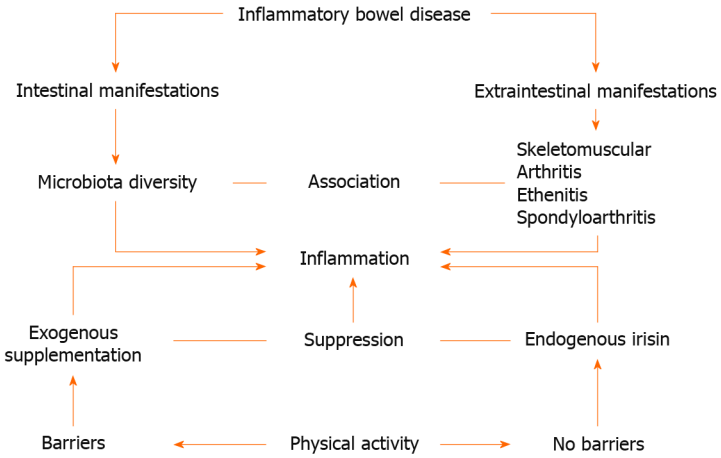

Figure 1 The interactions between irisin, physical activity, and the manifestations of the inflammatory bowel disease.

In an experimental animal model of 2,4,6-trinitrobenzenesulfonic acid colitits fed a high-fat diet, exercised mice showed significantly higher levels of irisin, which is associated with decreased histological changes of the intestinal mucosa, increased colonic blood flow, and attenuation of the plasma levels of inflammatory markers compared with sedentary mice[12]. In an experimental animal model of ulcerative colitis, it has been found that exogenous irisin modulates the intestinal microbiota (by altering the diversity of microorganisms in the stool) and suppresses inflammation in the intestinal mucosa, indicating that irisin has anti-inflammatory properties[13]. It has been suggested that the anti-inflammatory effects of irisin are related to the inhibition of cytotoxicity and apoptosis *via* inhibiting the mitogen-activated protein kinase pathway[14]. The sports activity is a barrier for patients with active Crohn's disease (intestinal manifestations) because it flares up the symptoms[15]. Some authors believe that the barriers to sports medicine are related to psychosocial factors and alterations in the physiological responses to exercise, characterized by a lower sympathetic tone and body temperature[16]. In the scoping review, which included 28 articles, the authors recommended that moderately intense PA is a useful non-pharmacological intervention to improve the quality of life and attenuate the

activity of Crohn's disease[17]. Another scoping review highlighted an important issue about the accuracy of the assessment of the health-related physical fitness status of patients with Crohn's disease due to some limitations in the intensity and type of PA[18]. There is no evidence for using exogenous irisin as an anti-inflammatory medicine in patients with Crohn's disease; therefore, exogenous irisin could be used as a nutriceutical and pharmacological anti-inflammatory medicine[19], as well as a biomarker for certain diseases and PA. In conclusion, PA is a non-pharmacological therapeutic tool in the management of the IBD as it suppressed the inflammation; attenuating the diversity of intestinal microbiota; reliving the symptoms of skeletomuscular complaint. The effects of exogenous irisin, which is still under experimental studies, are similar to the effects of PA and it may substitute the PA in IBD patients with limitations to do exercises.

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FOOTNOTES

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Country of origin: Iraq

ORCID number: Marwan SM Al-Nimer 0000-0002-5336-3353.

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