Microscopic Colitis Foundation

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Fatigue and Microscopic Colitis

by Wayne Persky

As most of us are well aware, fatigue is a common and persistent symptom of microscopic colitis (MC). In fact, fatigue appears to be a common symptom among not only all IBD patients, but patients who have virtually any autoimmune disease. And although no medical trials have been conducted with MC patients with specific regard to the symptom, believe it or not, a study of fatigue associated with MC has been published in a medical Journal, although the study was only an analysis of the results of a survey (Kane, Irvine, Derwa, and Ford, 2018)[1].

The survey involved questions related to various levels of anxiety, depression, and quality of life. And to prove that the researchers didn't understand MC, one of the issues that was included was somatization, which, according to Oxford Languages on Google, means "the production of **recurrent** and multiple medical symptoms with no **discernible** organic cause". In other words, they didn't realize that MC can involve the inflammation of various body organs, thereby causing a multitude of symptoms (similar to a failure to understand this by most medical professionals)

The study involved 129 patients who were diagnosed between 2010 and 2015. 53.5% of them had collagenous colitis (CC), and 38.8% of them had lymphocytic colitis (LC).

Presumably the other 7. 7% of respondents were listed as having simply MC.

As would be expected, the study showed that higher mean fatigue severity scores were associated with abnormal levels of anxiety, depression, and somatization. But surprisingly, patients who were experiencing active MC symptoms, did not report significantly higher fatigue scores. This might suggest that once the disease develops, the emotions of anxiety and depression, and the awareness that a reaction could be triggered at any moment, never significantly recede, even when the disease is in remission. In other words, we're never able to really relax, because we're virtually always aware of the disease, and the risks of its menacing behavior.

According to the Crohn's and Colitis Foundation,

almost 80% of people who have an active IBD, and 50% of those whose IBD is inactive, have a level of fatigue sufficient to significantly affect their daily lives (Crohn's and Colitis Canada, 2019)[2]. They define fatigue as:

- General weakness
- Reduced endurance
- Compromised cognizance and memory

Medical studies of fatigue associated with IBD have been published.

An article in Advances in Therapy (2019), for example, lists some of the primary causes of fatigue associated with IBD (Nocerino, Nguyen, Agrawal, Mone, Lakhani, and Swaminath, 2020)[3]:

Anemia

Anemia can be found in about 68% of hospitalized IBD patients, and about 20% of others. Deficiencies of vitamin B12 and folate (which can cause pernicious anemia), and a few other nutrients, are common with IBD patients primarily because of the malabsorption and diarrhea problems. The researchers included "self-imposed diet restrictions", as a causative factor, but that appears to be just another example of medical bias against patient "self-imposed" diet changes, because they present no evidence to justify that claim. As we are all aware, patients with severe malabsorption and diarrhea problems are unable to absorb the vitamins and other nutrients in their food properly, regardless of their diet.

Concomitant Medications

Occasionally, fatigue may be related to adverse medication side effects. According to the Cleveland Clinic (2021, March 17), medications classified as immunosuppressants are known to have various side effects, including fatigue. Also, medications that alter the gut microbiome can result in alterations to the gut brain axis that cause fatigue.

Sleep Disturbance

Not only can sleep deprivation cause fatigue (for obvious reasons), but sleep disturbances can lead to worsening IBD symptoms, resulting in additional fatigue associated with increased disease severity.

A meta study shows that IBD patients have a high prevalence of fatigue.

A meta-analysis published in Clinical Gastroenterology and Hepatology in 2022, was based on 20 studies selected from a pool of 4524 studies (D'Silva, et al., 2022)[5]. The analysis showed a pooled fatigue prevalence of 47%. The prevalence varied by the definition of fatigue (28% for chronic fatigue, and 48% for a high fatigue level); and the prevalence also varied by the status of the disease (72% for active disease, and 47% for disease in remission). These values were for Crohn's, and ulcerative colitis patients, of course, but it's very likely that the prevalence of fatigue for MC patients is very similar.

Can fatigue associated with IBD be effectively treated?

Studies have been done to assess treatments focused on IBD associated fatigue, but the effectiveness of most methods appears to be uncertain. A meta-analysis of published studies is available at the Cochrane Database of Systematic Reviews (2020)[6]. According to the review, most of the study evidence is rather weak.

Electroacupuncture

Electroacupuncture may result in significant fatigue reductions, but the evidence and studies are based on sparse data.

Cognitive behavioral therapy

The effectiveness of cognitive behavioral therapy cannot be definitively assessed, because of a very low level of evidence.

Adalimumab (Humira)

Abdalimumab, used every other week, may reduce fatigue in IBD patients, but note that this only applies to patients who are known to respond to adalimumab treatments, and again, the evidence is rather uncertain.

Ferric maltol

Ferric maltol is a prescription treatment for iron deficiency. Using it to treat fatigue associated with IBD appears to be counterproductive. The evidence suggests that treatments with ferric maltol results in an increase in fatigue, rather than a reduction, because after 12 weeks of use, patients in the placebo group had less fatigue than those in the treatment group. But anyone who has tried to do so, knows that trying to increase iron levels is a slow process at best, so it's certainly possible that this trial evidence was based on a trial length that was too short to be effective. Again, the evidence quality was low.

Supporting data appears to be absent.

Therefore, there doesn't appear to be any medical research data to support any IBD-associated fatigue treatment methods. Higher quality research studies are needed — studies designed to specifically target the fatigue associated with IBD. Perhaps the best advice at this point, is for IBD patients to try to get good quality sleep, on a nightly basis, as that tends to resolve a lot of issues associated with IBD symptoms, and quality of life.

What does our own experience suggest?

Our own accumulated experience, as indicated by the posts of a majority of the members of our discussion and support forum, suggests that along with brain fog, fatigue is one of the last symptoms of MC to fade away, and that typically happens long after remission is

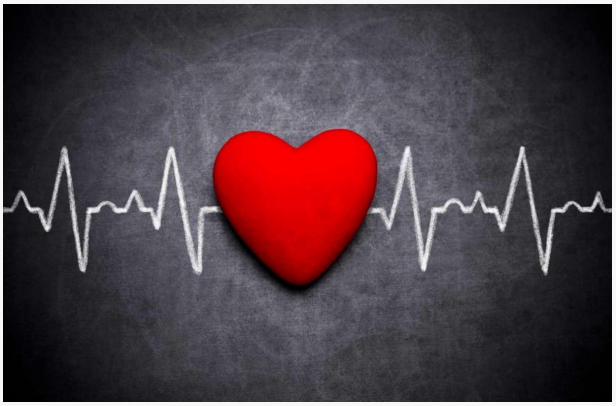
achieved. For most of us, the persistent fatigue seems to resolve approximately a year or two after remission is achieved. There are exceptions, of course, at both extremes, but most of us find that the fatigue is only resolved after significant intestinal healing is accomplished.

Complete healing takes a long time.

Published research shows that the intestinal damage caused by gluten sensitivity requires a significant amount of time for complete intestinal healing[7]. Kids' digestive systems are capable of completely healing in less than two years, but the digestive systems of adults typically require 3 to 5 years for the epithelia of their intestines to return to normal cellular histology. And because healing time depends upon the extent of intestinal damage, and may be age-related, about 10% of older adults often don't completely heal within five years.

Intestinal healing time almost surely affects the resolution of fatigue.

Because complete, or mostly complete, intestinal healing typically takes years, for most adults, persistent fatigue is not likely to be resolved before substantial healing is accomplished. Additionally, because of constraints within the gut-brain axis, fatigue may be dependent upon the state of communications between the brain and the digestive system, further complicating the fatigue recovery process (Carabotti, Scirocco, Maselli, and Severia, 2015)[8].



An ongoing study of IBD associated fatigue implicates cardiovascular issues.

The study is being conducted by researchers at Northwestern Medicine, a nonprofit healthcare system affiliated with Northwestern University Feinberg School of Medicine, in Chicago. They're currently researching the association of lower heart rate variability (HRV) with fatigue in IBD patients. The researchers have noted that while fatigue increases with C-reactive protein (CRP), disease activity, poor quality sleep, and age, for many IBD patients the fatigue continues, even when the disease is in remission (Doyle, 2023, April 25)[9].

For the study,

adult patients from an outpatient IBD clinic were recruited to wear a Fitbit Inspire 2 wristwatch for 14 days. This recorded their sleep quality, and allowed the researchers to measure the patients' HRV. The investigators found that although the published normal HRV rating is 42, their study cohort had an average HRT rating of 31.79. The article at the link listed in the previous paragraph notes that HRV is a measurement of the normal range of changes in the time between each heartbeat. It's associated with the gut brain axis, by way of the vagus nerve, and research has shown that low HRV can be associated with increased cardiovascular risk, and a higher level of vulnerability to psychological stress (Tiwari, Kumar, Malik, Raj, and Kumar, 2021)[10].

In the study, patients self-reported their fatigue levels, and testing was done to determine

CRP, vitamin B-12, vitamin D, and ferritin levels, initially, and at the end of week 1, and the end of week 2. The results of the study showed no significant differences in fatigue due to either gender, or type of IBD, although it did increase with age, in all cases. So, although MC patients were apparently not included in this study, there is no obvious reason why the results of this study would not apply to MC patients, as well as all other IBD patients.

Is lower HRV a symptom of IBD?

Although this article appears to imply that HRV is an independent cause of fatigue, lower HRV is almost surely a symptom of IBD, rather than an independent cause of fatigue, based on its relatively high prevalence level among IBD patients. That is to say, while it's true that increased fatigue may be caused by lower HRV, fatigue probably wouldn't exist in the first place, if IBD were not present. Although the article doesn't mention whether the researchers recognize that lower HRV may be a symptom of IBD, it does offer a therapeutic option for treating fatigue by treating lower HRV, using a technique known as slow-paced breathing (Sevoz-Couche, and Laborde, 2022)[11].

There's still much research to be done

before any solid conclusions can be drawn from this research, but it provides further evidence that the fatigue associated with IBDs apparently involves numerous responses that may involve multiple body systems. It appears that at the very least, the fatigue associated with IBD apparently involves the digestive system, the brain, the enteric nervous system, and the cardiovascular system.

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