Sleep and Circadian Hygiene and Inflammatory Bowel Disease

Garth R. Swanson, MD[a,*], Helen J. Burgess, PhD[b]

KEYWORDS

• Advance • Circadian • Delay • Light • Sleep

KEY POINTS

- Inflammatory bowel disease (IBD) is associated with sleep disturbance and possibly some circadian disruption.
- Sleep and circadian disruption can worsen IBD disease course.
- Possible approaches to reduce sleep and circadian disruption in patients are reviewed.
- Large placebo-controlled randomized trials in human patients are needed to fully understand the potential benefits and mechanisms of chronotherapeutic treatments for IBD.

INTRODUCTION

Inflammatory bowel disease (IBD) consists of 2 distinct phenotypic patterns: Crohn disease (CD) and ulcerative colitis (UC), that affects ~1.6 million Americans with as many as 70,000 new cases diagnosed each year.[1] IBD is typically diagnosed at a young age (20s to 30s), has a relapsing and remitting disease course, and has no known cure. This combination of factors leads to a significant health care cost and burden on society that continues to increase as IBD-related hospitalizations cost ~$4 billion annually in the United States.[2] Although a significant portion of patients with IBD will have an aggressive disease course with frequent disease flares, hospitalizations, and surgery, IBD has a highly heterogeneous disease course, and some patients will have mild disease that requires little if any medications.

Disclosure Statement: The authors have nothing to disclose.
H.J. Burgess and G.R. Swanson are supported by grants from the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
[a] Department of Digestive Diseases, Rush University Medical Center, 1725 West Harrison Street, Suite 206, Chicago, IL 60612, USA; [b] Biological Rhythms Research Laboratory, Department of Behavioral Sciences, Rush University Medical Center, 1645 West Jackson Boulevard, Suite 425, Chicago, IL 60612, USA
* Corresponding author.
E-mail address: Garth_R_Swanson@rush.edu

Gastroenterol Clin N Am 46 (2017) 881–893
http://dx.doi.org/10.1016/j.gtc.2017.08.014
gastro.theclinics.com

One group of factors that can have a crucial impact on IBD disease course is environmental stressors. The most well-studied environmental factor that is known to impact IBD course is cigarette smoking. Interestingly, cigarette smoking impacts UC and CD differently because it reduces disease flares in UC and induces disease flares and the risk of surgery in CD.[3] The focus of this review is on sleep and circadian disruption, which have recently received significant interest as important environmental factors that may attribute to disease flare in IBD. This is because both sleep and circadian alterations are capable of impacting key components in IBD disease flares, such as intestinal permeability, translocation of bacterial endotoxins and products, induction of intestinal dysbiosis, and increasing proinflammatory cytokines.[4,5] Here, the authors review the basics of sleep and circadian timing and common forms of circadian disruption that gastroenterologists may see in their clinical patients. A summary of the literature is also provided that examines sleep and circadian disruption in IBD (see **Table 1**). Then, the authors review a range of treatment approaches for circadian disruption, which may be applicable to some patients with IBD.

SLEEP AND CIRCADIAN TIMING

A Basic Overview

The neural circuitry underlying sleep and circadian timing is complex.[6] A key brain center that promotes sleep onset and the consolidation of sleep is the ventrolateral preoptic nucleus.[6] The activity of this brain region is influenced by sleep pressure, which builds up homeostatically as the duration of wakefulness increases. The circadian system interacts with this and other sleep/wake centers to promote the timing of sleep onset and the consolidation of sleep.[6] The central circadian pacemaker (suprachiasmatic nuclei, SCN) also generates and regulates circadian rhythms in the periphery, and those rhythms assist in transmitting the central circadian signal to other systems in the brain and body.[7] Indeed, the central circadian clock has a direct influence on peripheral inflammatory processes[8] and also influences peripheral clocks that exist in almost every cell, tissue, and organ in the body.[9] Both sleep and circadian timing are widely recognized as having a widespread and profound influence on mental and physical health.[10–12]

More than 70% of humans have an endogenous circadian clock with a period greater than 24 hours (on average ~24.2 hours).[13,14] Thus, for most humans, the internal circadian clock takes more than 24 hours to complete one cycle, which results in an endogenous or intrinsic tendency to drift later ("phase delay") each day. This is most commonly seen in the later sleep times that many people adopt on the weekend or on work-free days.[15] To remain in synchrony or "entrained" to the external 24-hour day, and indeed to 9 to 5 society, the circadian clock needs to regularly, if not daily, shift earlier ("phase advance"). The strongest environmental influence on circadian timing is the light-dark (LD) cycle, which is captured by various photoreceptors in the retina and transmitted to the SCN.[16] Light in the evening typically phase delays circadian timing and thus exacerbates the intrinsic tendency to drift later, whereas light in the morning typically phase advances circadian timing and thus can correct for the intrinsic tendency to drift later.[7] The human circadian clock is particularly sensitive to short wavelength or blue light,[17] such as that seen during sunrise and sunset, and also emitted from many electronic devices, such as cell phones and tablets.

The peripheral circadian rhythm often measured to infer the timing of the central circadian clock in humans is the endogenous melatonin rhythm, because the secretion of melatonin from the pineal gland is controlled by the SCN.[18] Specifically, the most reliable marker of circadian timing is the dim light melatonin onset (DLMO),[19] which