Sleep in Rheumatic Diseases and Other Painful Conditions

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Opinion statement

Insufficient sleep is an under-recognized public health problem that is projected to increase in the next decade as the US population ages. Chronic insomnia alone impacts 10% to 15% of adults. Epidemiologic data indicate that pain, fatigue, and mood disturbance are common correlates of persistent insomnia. Rates of most sleep disorders are substantially elevated in rheumatologic diseases, with chronic insomnia impacting at least 50% of patients. Clinicians treating patients with rheumatologic disorders should screen for sleep disorders and possess a basic knowledge of sleep physiology and empirically based intervention approaches. Sleep disturbances occurring within the context of chronic medical illnesses, including rheumatologic diseases, do not typically respond to primary disease and/or pain management interventions. Identification of co-occurring sleep disorders followed by aggressive treatment is recommended and has the potential to improve quality of life, ameliorate pain, and improve psychosocial adaptation to the primary illness. In this report, we briefly highlight that sleep disturbance increases risk for both comorbidities and symptoms associated with rheumatologic diseases, we identify specific sleep disorders commonly encountered in rheumatologic populations, and we discuss pharmacologic and behavioral treatment approaches for the most common sleep disorder observed in rheumatologic conditions, chronic insomnia.

Introduction

Normal human sleep is a multifaceted and dynamic neurophysiologic process that unfolds in a highly organized fashion throughout the night. Polysomnography (PSG) has described sleep as a cyclical interplay of changing states subdivided into five stages: non-rapid eye movement (NREM) stages 1 to 4 and rapid eye movement (REM) sleep. These stages are referred to collectively as sleep architecture. During a typical consolidated sleep period, individuals proceed through four to five NREM-REM cycles. Prominent theories with supporting data suggest that sleep serves to restore and/or conserve energy [1, Class III], is involved in mood regulation [2, Class II], plays a role in neuroplasticity [3, Class II], and consolidates procedural memory [4, Class I]. Although the functions of sleep are not definitively understood, it is known that poor sleep is an independent risk factor for both medical and psychiatric comorbidity, including coronary artery disease [5, Class II], diabetes [6, Class II], widespread pain [7, Class III], and depression [8, Class II]. The disruption or deprivation of sleep is known to negatively change metabolic function [9, Class II], impair immune functioning [10, Class III], increase daytime circulating proinflammatory cytokine levels [11, Class II], and enhance sensitivity to pain [12*, Class I]. Consequently, the aggressive management of insomnia might have prophylactic benefit and has the potential to ameliorate comorbid disease states. Therefore, optimizing sleep is a potentially important objective in the comprehensive management of rheumatic diseases.
INSOMNIA
Clinically significant insomnia is defined as trouble initiating or maintaining sleep, or nonrestorative sleep that causes significant stress or detrimentally impacts daytime function, and persists for a month or more. Prevalence estimates in chronic pain populations range between 50% and 88% [12•, Class I]. Insomnia may be considered a primary disorder when factors that maintain the disturbance are judged to be relatively independent of medical or psychiatric conditions, or it may be considered to be secondary to an underlying disease including other sleep disorders. Chronic insomnia, even when it occurs within the context of medical or psychiatric morbidity, often develops into a complex hybrid disorder. Both disease-related factors, such as pain or anxiety, as well as behavioral factors contribute to symptom presentation and maintenance. As insomnia persists, individuals increasingly engage in maladaptive strategies aimed at coping with their trouble sleeping. Paradoxically, however, these compensatory strategies can aggravate and perpetuate insomnia, irrespective of the underlying disease or chronic illness. Common maladaptive coping efforts that perpetuate insomnia include use of alcohol as a sedative, overuse of stimulants, extending sleep opportunity, keeping irregular sleep-wake cycles, spending excessive time awake in bed, developing the habit of ruminating about the consequences of poor sleep, and so forth. These factors often require independent treatment focus.

Although the neurobiology of insomnia is not yet completely understood, current theories that highlight states of somatic and/or central nervous system hyperarousal that interfere with sleep may represent a final common pathway of the disorder [13, Class I]. Over-activation of stress response systems, particularly the hypothalamic-pituitary-adrenal axis, is associated with insomnia.

OTHER SLEEP DISTURBANCES IN RHEUMATOLOGIC POPULATIONS
Individuals with rheumatic disease often present with a number of sleep difficulties that may or may not be related to the rheumatic disease. There are six primary groups of sleep disturbances, which are outlined in Table 1 [14]. Older adults in general are at increased risk for several sleep disorders, including the following: sleep apnea (ie, repetitive episodes of complete or partial upper airway obstruction during sleep often resulting in hypoxemia and brief arousals; 19.7%), periodic limb movement (PLM) disorder (4% to 11%), and restless legs syndrome (RLS; 9% to 20%; ie, urge to move one's legs, and distressing paresthesias or dysesthesias in legs, which are relieved by movement or externally applied somatosensory input to the affected regions) [17, Class III; 18, Class II; 19, Class III]. The presence of a rheumatologic disease places individuals at increased risk for a sleep disturbance due to various associated risk factors, including persistent pain, older age, obesity, and increased incidence of depression. Pain is the most frequently cited cause of sleep difficulties in rheumatologic diseases [20, Class II]. Certain sleep disruptions have also been associated with particular rheumatic diseases, as highlighted below.

Fibromyalgia
Fibromyalgia (FM), a syndrome characterized by idiopathic widespread pain, has a consistent and well-replicated relationship with sleep disruption. Typically, patients with FM report a pattern of increased nocturnal vigilance, shallow nonrestorative sleep, and sleep maintenance difficulty [21, Class III]. These sleep disturbances and patterns are associated with stiffness, fatigue, and cognitive disturbances in patients with FM [22, Class II]. In FM and other pain conditions, a night of poor sleep typically results in enhanced pain intensity the following day, which is then followed by a poor night's sleep [23, Class II].

Objective polysomnographic anomalies in FM include the intrusion of alpha waves without frank waking into NREM sleep (alpha sleep) [21, Class III], delayed sleep onset [24, Class II], reduced NREM S3 to S4 sleep (slow-wave sleep [SWS]) [25, Class II], increased arousals [22, Class II], reduced REM sleep [25, Class II], and increased wake time after sleep onset (WASO) [25, Class II]. Overall, the mechanisms by which sleep disturbances develop and are associated with the etiology and/or maintenance of FM remain unclear, although recent evidence suggests that sleep fragmentation impairs central pain modulatory processes, which might contribute to diffuse pain sensitivity, and which is a hallmark of the disorder [26, Class II].

Rheumatoid arthritis
Patients with rheumatoid arthritis (RA) display sleep fragmentation—shallow, easily disrupted sleep, with multiple mid-sleep awakenings—as measured by electroencephalogram and by self-report [27, Class II]. Sleep fragmentation has been linked with reports of increased pain and morning stiffness in adults [28, Class II]. Decreased SWS and WASO time have been found to predict pain and disease severity at 6 months [15, Class III]. It is also important to note that patients with RA who have cervical instability may be at increased risk for sleep apnea [29, Class III]. Further, various reports suggest an increased prevalence of RLS in RA [30, Class III]. For example, in one study the prevalence of RLS in RA was found to be 25% and RLS paresthesias were positively associated with RA disease severity [31, Class III]. Although the degree of and cause for comorbidity between RLS and RA is not well established, clinicians should nonetheless assess for the cardinal symptoms of RLS. RLS symptoms follow a circadian pattern, with symptoms usually manifesting in the late evening or nighttime. Patients with RA presenting with symptoms of RLS should also be evaluated for