

Pain-related Sleep Difficulties in Fibromyalgia and Neuropathic Pain

By Pierre Arsenault, PhD, MD

Pierre Arsenault, PhD, MD
Associate Professor,
Department of
Family Medicine,
University of Sherbrooke
Sherbrooke, Quebec

Chronic painful conditions can have a broad-reaching impact on a patient's quality of life (QoL). Physicians should pay particular attention to the deterioration of sleep quantity and/or quality as it is one of the most dramatically affected areas in these patients, which can lead to broader impact on the patients' overall QoL. This review article focuses on sleep difficulties encountered by patients suffering from two common chronic painful conditions: fibromyalgia and neuropathic pain (NeP).

The topics covered include a brief general overview of the two conditions in question, an analysis of the types of sleep difficulties encountered, a discussion of the factors that lead to and exacerbate these difficulties, and the strategies that may be employed to improve sleep in these patients.

FIBROMYALGIA: BRIEF OVERVIEW

Fibromyalgia is a syndrome for which a clear etiology remains elusive, but efforts have been made to define the syndrome clinically. The Canadian Consensus Document on Fibromyalgia (2003) defines it as a history of widespread pain and pain on palpation at 11 or more of 18 defined tender point sites.¹ An epidemiologic study in London, Ontario, showed that the disease prevalence was 4.9% among adult women and 1.6% among adult men.²

In a pooled analysis of four studies involving 100 patients or more, researchers noted that the most commonly reported musculoskeletal symptoms of fibromyalgia were pain in multiple sites (100% of patients), stiffness (76%), "hurt all over" (62%), and swollen feeling in tissues (52%).³⁻⁷ Non-musculoskeletal features included general fatigue (reported by 87% of patients), morning fatigue (75%) and sleep difficulties (72%).

NEUROPATHIC PAIN: BRIEF OVERVIEW

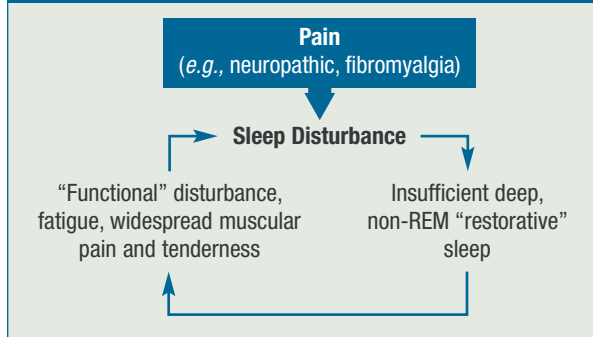
NeP is initiated or caused by a primary lesion or dysfunction of the nervous system,⁸ and is a symptom of an underlying neurologic problem, rather than a condition itself.

It is also associated with a number of comorbidities, which can have additional impact on the individual's pain experience. Psychiatric comorbidities, such as depression and anxiety, are very common among patients with NeP, as are altered sleep patterns.⁸ In a 2001 study of 126 patients with NeP, 10 patients (8%) had an additional pain diagnosis, such as migraine or osteoarthritis, while 34 patients (27%) had an additional chronic disease comorbidity (*e.g.*, cardiovascular disease, asthma). More than half of the patients reported being troubled by symptoms of anxiety, approximately 70% of patients were bothered by symptoms of depression, and almost 90% had sleeping difficulties.⁹

PAIN-RELATED SLEEP DIFFICULTIES

Normal sleep (for adults) consists of seven to nine hours of sleep with approximately 75% to 80% of the time spent in non-rapid eye movement (REM) sleep, and the remaining 20% to 25% in REM sleep.¹⁰ Non-REM sleep is thought to be the period in which bodily restoration and recuperation occur. Any disturbance that affects these parameters (*e.g.*, shorter duration of sleep, disruption of sleep architecture) is considered a sleep difficulty and can lead to—or exacerbate—further health problems.

FIGURE 1 The Vicious Cycle of Pain and Sleep Difficulties¹⁸



While fibromyalgia and NeP are associated with a number of deleterious sequelae, sleep disruption frequently ranks as the most common patient-reported complaint, with sleep difficulties reported by approximately 70% of people with fibromyalgia and 60% of people with NeP.^{7,8} The types of sleep difficulties encountered can vary considerably between individuals and include difficulty falling asleep, tossing and turning, difficulty obtaining deep sleep during the night, waking up frequently during sleep and waking up tired.⁷ Fatigue is also a common complaint in patients suffering from chronic pain and can be centrally mediated, be the result of impaired sleep, or a combination of both.⁷

The exact role that pain plays in sleep disruption is not fully understood, but pain is known to delay sleep onset and fragment sleep architecture.¹¹ Most researchers have also noted a correlation between the intensity of pain and the severity of sleep disturbances.¹² Research has shown that the majority of patients with chronic pain conditions recognize that it is the pain itself that is responsible for their sleep difficulties. These patients may also have additional comorbidities that negatively influence sleep, including restless legs syndrome, periodic limb movement disorder, pulmonary and/or cardiac diseases that cause

cough or shortness of breath, gastroesophageal reflux disease, and psychological distress. Lifestyle choices can also affect sleep quality and quantity; poor sleep hygiene, caffeine or alcohol intake, smoking and lack of physical activity can cause or exacerbate sleep problems.⁷

Pain and sleep difficulties—a classic vicious cycle.

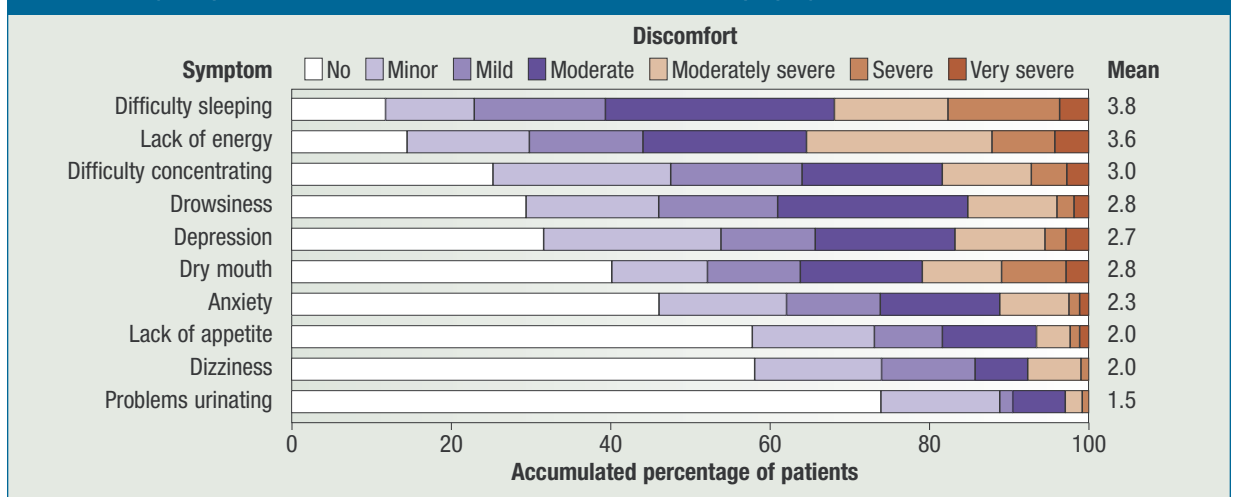
While it is clear that pain can be responsible for a number of sleep difficulties, it is also clear that a lack of sleep can exacerbate pain. Numerous researchers have found that sleep deficits cause an increase in the perception of pain that can be reliably reversed upon restoration of adequate sleep.¹³⁻¹⁷ Dealing with chronic pain requires considerable physical, emotional and cognitive efforts; a lack of sleep substantially impairs these abilities. A longitudinal study in patients with fibromyalgia showed that the intensity of a patient’s pain influences their quality of sleep that night. In turn, the quality of sleep at night influences the intensity of pain the next day—a classic vicious cycle (Figure 1).¹⁸

Severity of sleep difficulties in painful conditions.

The sleep difficulties experienced by chronic pain sufferers can be quite severe. In a 2001 study by Meyer-Rosberg et al, patients with NeP were asked to rate the extent to which they had been bothered by symptoms related to pain and/or side effects during the previous seven days.⁹ A score of one indicated “no discomfort,” while a score of seven indicated “very severe discomfort.” “Difficulty sleeping” was rated the most bothersome symptom, with more than half of the respondents indicating that discomfort was at least moderate (Figure 2).⁹

An analysis of these patients’ health-related QoL (HRQoL) has also demonstrated a significant deleterious effect of NeP on sleep. Using the Nottingham Health Profile (NHP) as one of their standardized measures of HRQoL, Meyer-Rosberg et al found that, compared to the general population, those with NeP exhibited significantly higher (worse) scores on all the measured NHP domains, including sleep and energy (Figure 3).⁹

FIGURE 2 Frequency of the Extent to which Patients are Bothered by Symptoms Related to NeP⁹



MANAGEMENT OF SLEEP DISORDERS IN CHRONIC PAIN CONDITIONS

Sleep hygiene. Patients with sleep difficulties need to receive counseling on proper sleep hygiene. In many cases, this can have a considerable positive impact on helping to overcome sleep difficulties.

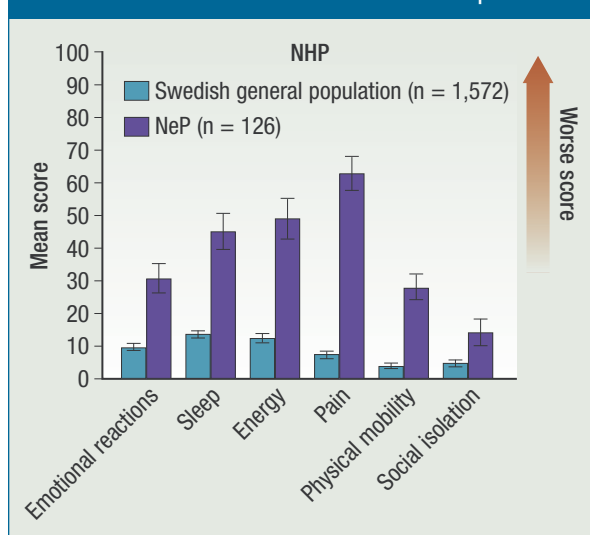
Some of the lifestyle changes that should be encouraged are to get up at the same time every day, even on weekends; to reduce or cut out alcohol, caffeine and nicotine; and to exercise regularly. The sleep environment itself should be as comfortable as possible, not too warm or cold, and with minimal light and noise. Lifestyle choices that should be discouraged include engaging in stimulating activities before bed; engaging in strenuous physical exertion within five hours of bedtime; attempting to go to bed when the patient is not tired; taking naps; drinking alcohol within two hours of bedtime; consuming caffeine within seven hours of bedtime; and smoking within four hours of bedtime.

Sleep-hygiene education has been shown to provide benefit to patients with fibromyalgia and sleep difficulties. In a clinical study published in 2005, patients who received sleep-hygiene education experienced a 20% reduction in nocturnal wake time. Those in the usual-care group experienced only a 3.5% reduction.¹⁹ In this study, the sleep-hygiene education consisted of listening to an audiocassette providing generic sleep education (*i.e.*, descriptions of sleep stages and sleep architecture). A study therapist then provided verbal and written (pamphlet) instructions to limit caffeine and alcohol, engage in regular moderate exercise, have a light bedtime snack and keep the bedroom dark, quiet, and cool.

Cognitive behavioral therapy (CBT) has been shown to be very effective in improving sleep parameters in patients with chronic pain and sleep difficulties. In the same study mentioned above, fibromyalgia patients who received CBT experienced a 50% reduction in nocturnal wake time.¹⁹ The CBT in this study consisted of a standardized audiocassette module designed to correct misconceptions about sleep needs and the effects of aging, circadian rhythms, and sleep loss on sleep/wake functioning. Study therapists then provided verbal and written (pamphlet) stimulus control instructions which encouraged adhering to a standard rising time, exiting bed during extended awakenings, using the bedroom only for sleep and sex, and avoiding daytime naps.

Pharmacotherapy. Although sleep and pain co-exist in a vicious cycle, for patients with fibromyalgia or NeP, it is important to focus on the underlying condition (*i.e.*, the chronic pain). In these particular conditions, controlling the patient's pain becomes the focus of treatment as the underlying condition is non-reversible. However, due to the known relationship between pain and sleep disturbances, the selection of treatment agent(s) can be influenced by the known effects of the various compounds on sleep parameters. Improving sleep parameters may help

FIGURE 3 Nottingham Health Profile (NHP) Mean Scores: Patients with NeP and General Population⁹



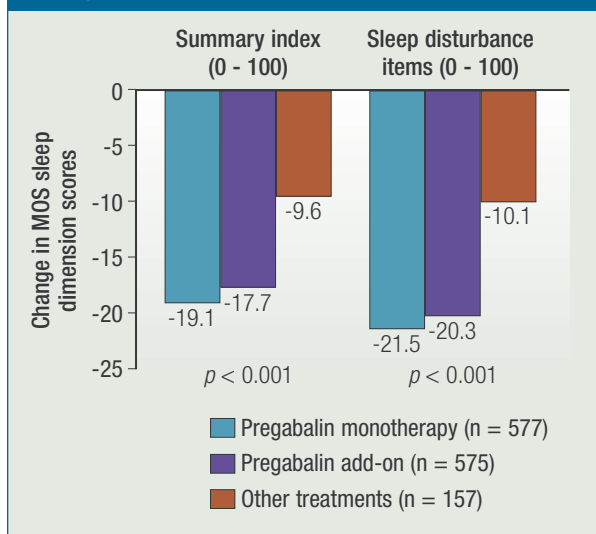
to reduce pain, just as improving pain should help improve sleep parameters. Therefore, agents that improve pain and sleep should be considered as highly desirable choices for the management of these conditions. The data are sparse regarding the effects of many commonly used pain medications on sleep parameters. Some of the more compelling data in this regard have been produced in studies examining the anticonvulsant pregabalin.

Pregabalin is listed among the first-line treatment options for NeP by the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain (2010),²⁰ as well as the Canadian Pain Society (2007).²¹ In addition to efficacy in reducing pain, pregabalin has demonstrated an ability to reduce sleep difficulties and other burdensome symptoms in a number of chronic-pain conditions (*e.g.*, diabetic peripheral neuropathy, post-herpetic neuralgia, spinal cord injury and fibromyalgia).²²

The benefit of pregabalin on patient-reported sleep outcomes is consistent across clinical trials in NeP. In an analysis of 1,354 patients in primary care, patients received pregabalin monotherapy (n = 598), pregabalin as add-on therapy (n = 589) or other pain regimens not including pregabalin (n = 167).²³ The investigators reported that there were significant improvements in pain scores from baseline in each group, but that the improvements were more pronounced in the pregabalin groups. In addition, the beneficial effects on sleep parameters were significantly greater in the pregabalin groups when compared to patients in the non-pregabalin group (Figure 4).²³

Pregabalin has also demonstrated significant benefits on the sleep parameters in patients with fibromyalgia. A recent meta-analysis of clinical trials showed patients with fibromyalgia taking pregabalin had improved sleep disturbance scores, quantity of sleep, sleep adequacy and overall sleep problems.²⁴ Physicians frequently initiate pre-

FIGURE 4 Change in Medical Outcomes Study (MOS) Sleep Questionnaire Scores: Pregabalin vs. Other Therapies for NeP²³



gabalin at low doses and slowly titrate over a few weeks using an asymmetrical dose progression (with higher doses at night) because it helps manage side effects. Some side effects are transient, including dizziness and somnolence. This approach can increase the likelihood of patient compliance and of treatment success.

While pregabalin may have beneficial effects on sleep parameters, other commonly prescribed analgesic medications can potentially exacerbate these problems. Antidepressants with serotonergic and noradrenergic activity are also recommended among first-line options for NeP by the International Association for the Study of Pain, and as a second-line option by the Canadian Pain Society. Duloxetine, one of these agents, has a favorable record of efficacy with respect to reduction in pain scores (in patients with NeP associated with diabetic peripheral neuropathy or fibromyalgia), but is also associated with insomnia as a common adverse effect. In clinical trials, insomnia was reported by up to 10% of patients with NeP and up to 16% of patients with fibromyalgia treated with duloxetine.²⁵ However, in a recent study comparing duloxetine, milnacipran and pregabalin, such differences were not documented in fibromyalgia.²⁶

CONCLUSIONS

Sleep difficulties are one of the major symptoms of chronic painful conditions, including fibromyalgia and NeP. Patients with these conditions are often caught in a vicious cycle in which pain leads to sleep difficulties and sleep difficulties exacerbate pain. When developing a treatment strategy for a patient with a chronic painful condition, improving sleep parameters should be one of the goals of therapy, while contributing to the primary goal of controlling pain. Education regarding optimal lifestyle choices and sleep hygiene should be discussed

with any patients with sleep difficulties. CBT has also been shown to improve sleep parameters.

Finally, when prescribing therapy(ies) to help control pain, one should consider the effect the regimen may have on the patient's sleep parameters. To help break the vicious cycle of pain and sleep difficulties, the agents that promote better sleep (e.g., pregabalin) may be more favorable options than those that do not.

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