

# Effects of Chronic Opioid Use on Sleep and Wake

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## KEYWORDS

- Opiates • Daytime sleepiness • Depression • Poor sleep • Sleep-disordered breathing
- Central sleep apnea

## KEY POINTS

- Chronic use of opioids has a multitude of negative effects on daytime function, including hypersomnolence, fatigue and depression, and sleep architecture and sleep-related breathing disorders, with resulting daytime consequences.
- Chronic opioid use is an established risk factor for sleep-disordered breathing, particularly for central sleep apnea.
- It is plausible to assume that patients on chronic opioid therapy may suffer from unrecognized sleep-disordered breathing and associated consequences, including respiratory depression and death.
- Sleep-disordered breathing associated with chronic opioid use is a diagnostic and therapeutic challenge.
- Although studies are limited, new-generation servo ventilators deserve further research and should be offered to patients with sleep-disordered breathing, including central sleep apnea, especially in those who do not respond to conventional modes of therapy, such as continuous positive airway pressure or bilevel positive airway pressure.

## INTRODUCTION

Opioid medications are considered a significant component in the multidisciplinary management of chronic pain. In the past 2 decades, the use of opioid medications has dramatically risen in part due to an increased awareness by health care providers to treat chronic pain more effectively. In addition, patients themselves are encouraged to seek treatment. The release of a sentinel joint statement in 1997 by the American Academy of Pain Medicine and the American Pain Society in a national effort to increase awareness and support the treatment of chronic pain has undoubtedly contributed to the opioid crisis.<sup>1</sup> This effort and among others consequently led to an epidemic

of opioid misuse (ie, without prescription or as directed by provider), abuse, and death related to overdose. A recent national large-scale survey reported that 91.8 million Americans used prescription opioids, 11.5 million misused them, and 1.9 million had opioid use disorder.<sup>2</sup> Cumulative data reported that increased use of opioids has resulted in increased morbidity and mortality, with more than 33,000 deaths due to opioid overdose in 2015.<sup>3,4</sup> Opioid-related deaths are most often from prescription opioid pain relievers and illicit use of synthetic compounds, including heroin and fentanyl.<sup>4</sup> With the support of the Secretary of Health and Human Services, President Donald Trump has declared the opioid crisis a national public health emergency.<sup>4</sup>

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The initial acceptance of opioid use for the relieve of chronic pain more than 20 years ago is now being challenged on efficacy and safety of these prescription practices. There is strong evidence to support short-term use of opioids for chronic pain, but support for long-term opioid use is lacking.<sup>3</sup> There are no studies of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain evaluating long-term ( $\geq 1$  year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were less than or equal to 6 weeks in duration.<sup>5</sup> Long-term use results in reduction or loss of analgesic efficacy due to pharmacologic tolerance or opioid-induced hyperalgesia (ie, worsening pain sensitivity). In the long run, among many other consequences, chronic use of opioids is associated with sleep dysfunction, leading to symptoms of excessive daytime sleepiness, daytime fatigue, depression, and notably, respiratory depression during sleep.

Daytime hypersomnolence, daytime fatigue, depression, copharmacy with benzodiazepines and/or antidepressants, and consequently poor general health quality are common in chronic opioid users. There may be a bidirectional relationship between poor sleep quality, sleep-disordered breathing (SDB), and daytime function. Chronic use of opioids is associated with disrupted sleep architecture and SDB, which encompasses a spectrum of ventilatory derangements, including

hypoventilation, hypoxemia, obstructive and central apneas, periodic breathing, and ataxic or irregular breathing. The authors believe that a complex relationship exists between chronic pain, chronic use of opioids, sleep disorders, and daytime symptoms (Fig. 1).

## OPIOIDS AND DAYTIME FUNCTION

Opioids have adverse effects on sleep and daytime function, effects that could be bidirectional. These effects could be modulated by the presence of chronic pain when present. Excessive daytime sleepiness, fatigue, depression, neurocognitive dysfunction, and poor general health are common in patients using opioids chronically. On the other hand, disrupted sleep architecture and SDB are frequently observed during polysomnography, together interacting in a complex manner (see Fig. 1).

In an early pilot study from Australia, Teichtahl and colleagues<sup>6</sup> assessed sleep and daytime function of 10 young patients (mean age 35 years) in a stable methadone maintenance program (MMP) with 9 control patients matched for age, gender, and body mass index. The methadone dose ranged between 50 mg per day and 120 mg per day. All patients were assessed by a psychologist and a physician. Compared with the control group, patients in the MMP were significantly more depressed based on the Beck

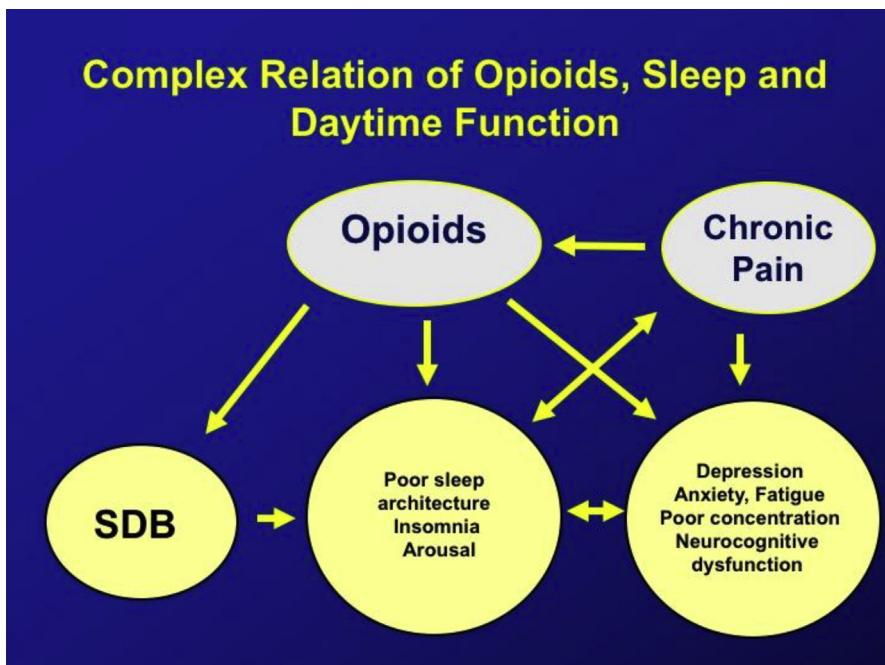


Fig. 1. Bidirectional relationship between opioids, chronic pain, and sleep.

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