The Association of Obstructive Sleep Apnea and Chronic Pain
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Overview

Obstructive sleep apnea (OSA) is associated with numerous comorbid conditions. In many, a causative relationship has either been well established or strongly associated. As the knowledge of sleep-disordered breathing and its consequences continues to grow, so does the list of associated or consequential conditions. This article is part 2 of a 5-part series exploring more recently identified consequences of OSA.

Introduction

Chronic pain has become the most common reason for outpatient medical visits.[1] Treatment of chronic pain syndromes and the habitual use of opioids have dramatically increased in the past 2 decades. Between 1990 and 1996, the long-term use of oxycodone increased by 23%, hydromorphone use increased by 19%, morphine use increased by 59%, and the use of fentanyl increased 1168%.[2-4] This dramatic rise in habitual narcotic use has continued, and the long-term use of opioids more than doubled from 2000-2008.[2-4]

A bidirectional relationship exists between pain and sleep disturbances. Pain fragments sleep continuity, impairs sleep quality, and disrupts normal sleep architecture. Reciprocally, poor quality or insufficient quality of sleep may decrease the pain threshold, impair recovery from injuries, or further exacerbate the pain response. Painful stimuli produce microarousals, which disrupt sleep continuity and alter normal sleep. Chronic pain is associated with increased high frequency EEG activity and a decrease in slow frequency EEG activity. Furthermore, chronic pain is associated with the appearance of alpha waves superimposed on slower EEG frequencies, or "alpha-delta" sleep.[5,6] In short, pain produces a state of shallow sleep while disrupting restorative slow-wave sleep.

An estimated 28 million Americans have sleep complaints due to chronic pain syndromes. Among patients with chronic pain, more than 50% experience sleep disturbances. Some reports say as many as 70%-88% patients with chronic pain report sleep trouble.[6,7] Sleep disturbance shows an independent and linear correlation with pain severity, even after controlling for health measures and sleep habits.

Sleep complaints portend worse outcomes among those with chronic pain. Compared with patients who have no sleep complaints, patients with chronic pain and insomnia report poorer quality-of-life indices and have increased healthcare utilization.

In patients with fibromyalgia, complaints of poor sleep quality and fatigue are more prominent than pain.[8,9] Similar to other conditions, sleep quality and the pain response share a reciprocal cause-and-effect relationship. Among patients with fibromyalgia, a poor night's sleep predicts more pain the next day, and more pain predicts greater sleep impairment that night.[8] Patients with fibromyalgia frequently experience nonrestorative sleep and alpha-wave intrusions are commonly observed during polysomnography. The prevalence of insomnia, restless legs syndrome (RLS), and hypersomnia are higher among patients with fibromyalgia than within the general population.[9] Similarly, OSA is significantly more common, with observed rates of 46%-80% reported among patients with fibromyalgia.[9]

Effect of Narcotics on Respiratory Physiology

Narcotics, and in particular opioids, have several effects on respiratory physiology, which are more pronounced during sleep. They decrease central respiratory patterns, respiratory rate, and tidal volume. They also increase airway resistance and decrease the patency of the upper airways. This may lead to ineffective ventilation and upper airway obstruction in susceptible individuals.
These agents can produce irregularities in normal breathing patterns. Irregular respiratory pauses and gasping may lead to erratic breathing and significant variability in respiratory rate and effort. This atactic, or Biot breathing, is observed in the majority of patients with long-term opiate use.\textsuperscript{[10]}

**Narcotic Use and Sleep-Disordered Breathing**

The incidence of sleep-disordered breathing after both short- and long-term opioid use is well established, but also somewhat controversial. Several studies have shown a marked increase in sleep-disordered breathing with both acute and chronic use of narcotics, regardless of the agent used, dose, duration of therapy, or individual risk factors for OSA. In contrast, other reports have failed to observe increased rates of sleep-disordered breathing in patients using opioids.

For example, whereas no significant increase in OSA was seen in a study of 50 consecutive patients receiving long-term methadone therapy compared with controls,\textsuperscript{[11]} another study of 71 patients with long-term methadone use diagnosed OSA in 35\% of patients.\textsuperscript{[12]} Of note, these individuals were evaluated because of sleep complaints. Given the variability in the published literature, it is likely that the emergence of OSA does result from narcotic use, but it is significantly more probable in susceptible individuals.

The form of sleep-disordered breathing associated with chronic opioid use is equally controversial. Although central sleep apnea (CSA) is classically associated with opioid use, it appears that OSA is more commonly encountered.\textsuperscript{[10,12]} Earlier reports found a predominance of CSA, whereas more recent studies have shown OSA is significantly more common among patients receiving long-term opioid therapy.

This transition is not due to any identifiable changes in the demographic characteristics of the included participants. It may reflect an evolution in the practice of pain management, with newer agents, different delivery systems, and higher doses being used. Or, it may be that obstruction has always been the predominant respiratory event and this transition merely reflects the advancement of the field of sleep medicine and sophistication of polysomnographic equipment, which allow a more accurate assessment of sleep and sleep disorders. Regardless, both breathing patterns are commonly observed, and it is important to differentiate the 2 because this may alter treatment and treatment strategies.

Among patients receiving acute oral narcotics, OSA is observed in 35.2\% and CSA in only 14.1\%. In a study assessing methadone maintenance patients with subjective sleep complaints, OSA was significantly more common than CSA.\textsuperscript{[12]} Similarly, OSA was diagnosed in 35\%-57\% of patients managed in long-term pain clinics.\textsuperscript{[13]} In an observational controlled trial of nonobese long-term opioid users, the majority of patients were found to have sleep-disordered breathing, with a mean apnea/hypopnea index of 43.9 ± 1.2. Most apneas were obstructive and not central events.\textsuperscript{[13]}

Famey and colleagues\textsuperscript{[14]} explored the occurrence of sleep disordered breathing in a population of young, non-obese, long-term opioid users. The demographic characteristics of this cohort were not typical for a high prevalence of OSA. The mean age was 31.8 ± 12.3 years, the mean body mass index was 24.9 ± 5.9 kg/m\(^2\), and 60\% were women. Nonetheless, at least mild OSA was present in 63\%. Furthermore, moderate OSA was observed in 16\%, and 17\% had severe sleep apnea. Nocturnal hypoxia was also common was more significant than would be expected for the degree of sleep apnea noted. An oxygen saturation below 90\% for 10\% or more of the total sleep time was noted in 38.6\% of the cohort.\textsuperscript{[14]}

**Treatment of Opioid-Induced Sleep-Disordered Breathing**

The treatment of opioid-induced sleep disordered breathing is similar to that for other etiologies of OSA and CSA, with positive airway pressure (PAP) being the most efficacious therapeutic option. Improvement, or even resolution, of sleep-disordered breathing after cessation of medication has been frequently reported. Both oral appliances and uvulopalatopharyngoplasty (UPPP) have also been shown to be beneficial in these individuals. However, unlike in
other patients with sleep apnea, apneas may be more refractory to PAP therapy among those with opioid-induced OSA.

The common coexistence of central events may require further management. Although CSA may resolve or diminish with continuous PAP (CPAP), persistent events often require bilevel PAP (BiPAP) or adaptive servoventilation (ASV).

Guilleminault and colleagues\textsuperscript{[13]} found that despite adequate titration with CPAP or BiPAP, nocturnal awakenings and central apneas persisted in the majority of patients. They observed a residual apnea/hypopnea index of 13.8 ± 2.8 among their cohort. The predominance of residual events were central in nature. The authors concluded that BiPAP with a back-up rate was most effective for resolving these events. In a similar study, Farney and colleagues\textsuperscript{[15]} determined that both BiPAP with back-up rate and ASV were superior to CPAP in the treatment of sleep disordered breathing associated with long-term opioid therapy.\textsuperscript{[15]}

Similar to other forms of CSA, both BiPAP and ASV are more effective in ablating respiratory events and normalizing objective sleep measures than CPAP. However, no studies have compared long-term outcomes among these different treatment options.

Conclusions

Chronic pain and disrupted sleep are commonly associated, and they share a clear cause-and-effect relationship. Pain fragments sleep, and poor sleep worsens the pain response. The prevalence of sleep disorders and the number of patients experiencing chronic pain continue to increase. Finally, pain and sleep disorders are among the most common reason for medical care. It is important to understand these conditions and appreciate the intimate relationship they share.

It seems clear that long-term narcotic use causes, precipitates, or exacerbates sleep-disordered breathing; as the use of these agents continues to grow, so will the number of individuals with opioid-induced apnea. Prompt recognition and appropriate treatment will probably improve outcomes and quality of life. It may also reduce overall healthcare utilization and aid in controlling pain.

References


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