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CASE REPORTS

Reversal of Central Sleep Apnea following Discontinuation of Opioids

Matthew J. Davis, M.D.[1]; Marian Livingston, M.D.[2]; Steven M. Scharf, M.D., Ph.D., F.A.A.S.M.[1]

[1]Sleep Disorders Center, Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Maryland Medical Center, Baltimore, MD; [2]Department of Neurology, University of Maryland Medical Center, Baltimore, MD

This case report including polysomnography shows reversal of central sleep apnea after opioid withdrawal. A patient using opioids for pain was diagnosed with central sleep apnea (CSA), but was not compliant with therapy. Five years later he underwent detoxification. Subsequent polysomnography showed no sleep disordered breathing. This is the first report of correction of CSA following opioid withdrawal confirmed by polysomnogram.

Keywords: Central sleep apnea, narcotics, opiates

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Central sleep apnea (CSA) is associated with a number of clinical conditions, including congestive heart failure, brain stem lesions, as well as with opioid use in the absence of other risk factors. A significant association with opioid use was first described by Teichtahl et al. in 2001,[1] then further demonstrated in individuals on long-term methadone maintenance by Wang and Teichtahl.[2] Recently, Alattar and Scharf described a case series of CSA in patients using opioids for chronic pain.[3] Treatment has focused on positive airway pressure (PAP) therapy and ventilatory-assist devices, with varying degrees of success.[4]

REPORT OF CASE

A 35-year-old male presented with complaints of excessive daytime sleepiness. His medical history included major depression, necessitating electroconvulsive therapy and psychiatric hospitalization, hypertension, and severe headaches since childhood. He had failed numerous headache prophylactic medications and ultimately was prescribed opioids. At initial presentation to the sleep clinic, his medications included fentanyl lollipops, fentanyl transdermal patch, hydrocodone, triamterene, fluoxetine, and venlafaxine. He was also using dextroamphetamine/amphetamine and methylphenidate for sleepiness and ramelteon and temazepam to aid sleep initiation. His sleep schedule was suboptimal: bedtime was 02:00; perceived sleep latency was 30 min, with awakenings up to 4 times during the sleep period for various reasons; rise-time was 07:00; and sleep was described as non-refreshing.

The patient complained of excessive sleepiness (Epworth score of 16), mild snoring, and witnessed apneas. Physical exam showed pulse 84, blood pressure 119/79, oxygen saturation 97%, body mass index (BMI) 31.5, and a Mallampati class 2 airway.

Polysomnography was performed (**Table 1**). Respiratory events and sleep architecture were scored according to the 2007 AASM scoring manual.[5] The study was consistent with CSA. After several PAP titrations, the patient was prescribed bilevel PAP at 12 IPAP/8 EPAP with a back-up rate of 12 and 3 liters per minute of oxygen through the machine. The patient said that this allowed him to sleep more continuously but did not improve his daytime sleepiness. Despite these modest improvements in his symptoms, repeated titration studies showed persistent central apneas. It was repeatedly recommended that he discontinue or reduce use of opiates and temazepam as well as the stimulants since these were certainly affecting his sleep pattern. However, the patient stopped using bilevel treatment and was lost to follow-up in the sleep clinic.

The patient continued seeing a neurologist for his headaches and he ultimately agreed to 30-day inpatient narcotic detoxification. This succeeded in eliminating opiates from his regimen, which was confirmed by urine toxicology testing. Approximately 5 years after the initial evaluation, the patient was further evaluated by his neurologist for ongoing headaches. He still complained of some daytime fatigue and depression. Medications included venlafaxine, duloxetine, olanzapine, verapamil, and simvastatin. Epworth score was 10 and BMI was 36.7. Polysomnography was ordered by his neurologist. As seen in **Table 1**, the frequency of disordered breathing events was normal.

DISCUSSION

This patient experienced reversal of severe CSA after discontinuation of opiates. Once withdrawn from opiates, he continued to complain of mild daytime fatigue, though this was modestly improved as indicated by his Epworth score. Clearly, however, this patient had multiple factors influencing his excessive sleepiness, including depression and sedating effects of his medications. Interestingly, this patient's weight actually increased during the period of follow-up—thereby removing a potential confounding factor in the reversal of his disease.

To our knowledge, there has been only one other published case report demonstrating reversal of CSA after withdrawal of

Table 1—Polysomnography results

	Initial PSG	Subsequent PSG following detoxification
Total sleep time (min)	367.5	231.5
Sleep efficiency (%)	90.3	55
Slow wave sleep (% total)	1.4	6.4
REM sleep (% total)	1.1	16.6
Obstructive apnea/hypopneas (#)	37	5
Central apneas (#)	260	3
RDI	50.3	2.9
Minimum oxygen saturation (%)	43	88
T < 90% (min)	15.0	1.4
Arousal index	28.1	5.2

Data from initial and subsequent polysomnograms. PSG, polysomnography; RDI, respiratory disturbance index (apneas plus hypopneas plus respiratory event related arousals per hour of sleep).

opioids. In that case, however, no confirmatory polysomnography was performed.[6] Our case demonstrates the importance of recognizing the role of opioids in the development of sleep disordered breathing, specifically CSA. Previous studies have demonstrated a dose dependent relationship between opioid use and severity of CSA.[7] Possibly, in our patient, the use of high-dose multiple opioid preparations was associated with the observed severe degree of CSA. In this individual, and other selected patients, withdrawal of opioid therapy may be a successful mode of therapy.

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Address correspondence to: Steven M. Scharf, M.D., Ph.D., University of Maryland Sleep Disorders Center, 685 West Baltimore St. MSTF 800, Baltimore, MD 21201-1192; Tel: (410) 706-4771; E-mail: sscharf@medicine.umaryland.edu

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