SLEEP MEDICINE PEARLS

JCSM
Journal of Clinical Sleep Medicine

pii: jc-00436-14
http://dx.doi.org/10.5664/jcsm.4786

A 27-Year-Old Female on Chronic Opioid Therapy

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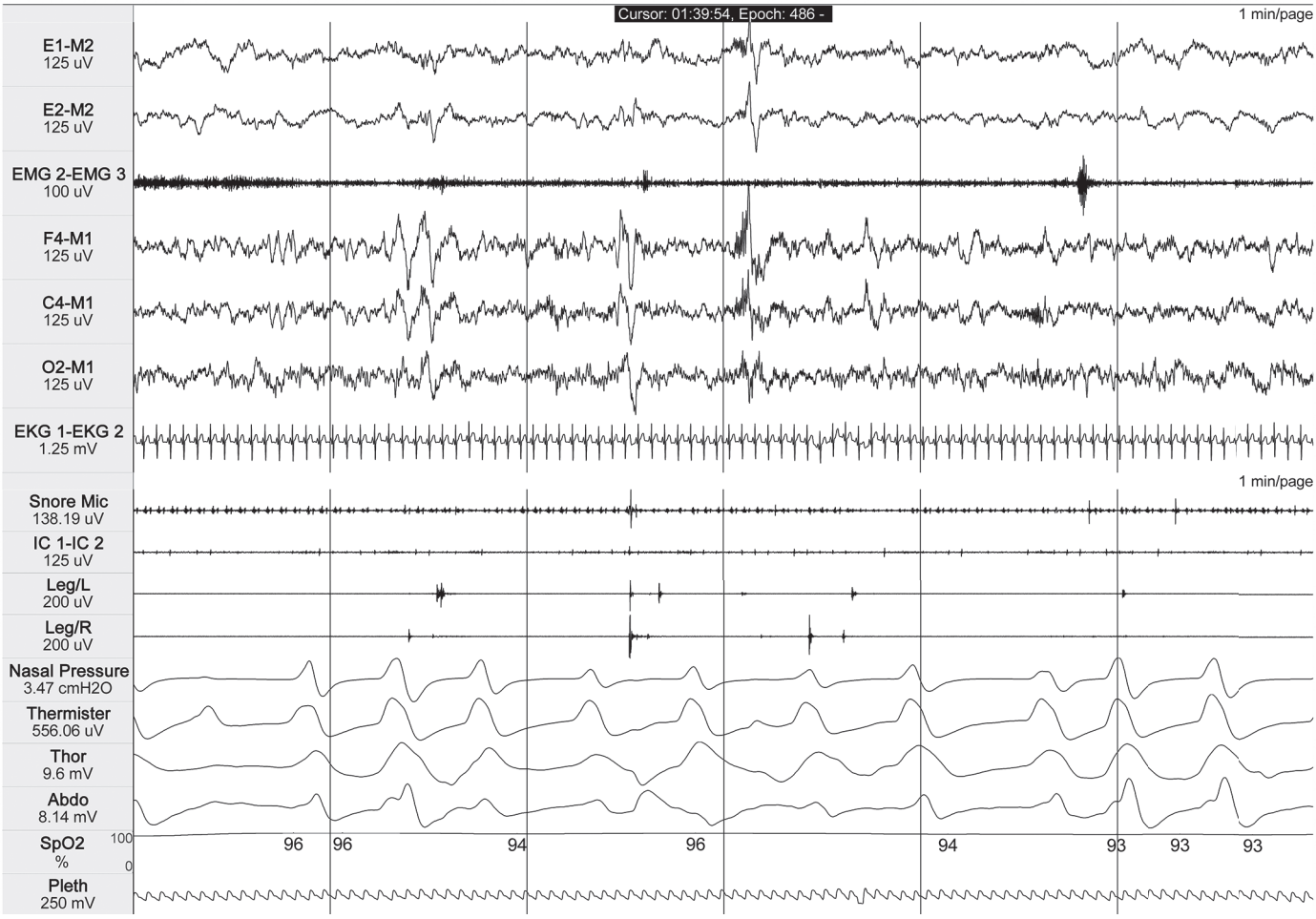
A 27-year-old female was referred to the Sleep Disorders Center at Dartmouth Hitchcock Medical Center for re-evaluation of known obstructive sleep apnea (OSA). Her OSA had been diagnosed by a home sleep test approximately 2 years prior to her presentation. Her apnea-hypopnea index (AHI) on this test was 14 events per hour. She was not on continuous positive airway pressure (CPAP) therapy at the time of her presentation. Her history was notable for snoring, mouth breathing, mouth dryness, some daytime fatigue, and some daytime sleepiness. She would take a 30–60 minute nap around 2–3 times per week. There was no history of involuntary dozing. She scored 10 on the Epworth Sleepiness Scale. She did not drive. She normally got into bed between 8:00 pm and 11:00 pm, and it would take her around 60 minutes to fall asleep. She denied having any nighttime awakenings. She woke up in the morning between 8:00 am and noon and felt refreshed when she would do so. Review of systems was negative for witnessed pauses in breathing during sleep, chest pain, and shortness of breath. Her medical history included a history of type 1 diabetes mellitus, chronic pancreatitis, gastroparesis, and chronic pain. Her surgical history was significant for total pancreatectomy and gastroenterostomy. She had a jejunostomy tube. She was on multiple medications including hydromorphone 12.5 mg every 5 h, sublingual fentanyl spray 800 mcg every 4 h, zolpidem 10 mg at bedtime, trazodone 100 mg at bedtime, lorazepam 1 mg at bedtime, duloxetine 60 mg at bedtime, insulin, and pancreatic enzyme replacement. She denied using any illicit substances. She had never smoked and denied using alcohol. She appeared alert and comfortable during the examination. Her weight was 137 pounds, and she had a BMI of 25.06 kg/m^2. Her respirations were unlabored. Review of her prior records revealed that she had undergone a pharmacological nuclear stress test in October 2012, and her ejection fraction at that time was reported as being 75%.

Suspicion for sleep disordered breathing (SDB) was high and she was advised to undergo an overnight polysomnogram (PSG). The patient stayed in the supine position for the entire duration of the PSG which revealed a severe degree of sleep apnea with an AHI of 71 events per hour. Respiratory events were composed of central apneas, obstructive apneas, and hypopneas, all of which were associated with cyclical oxygen desaturations. During the course of the PSG, at around 1:41 am, the patient took a dose of her sublingual fentanyl spray. A striking change was noted on her PSG after she administered this medication to herself (**Figures 1–3**).

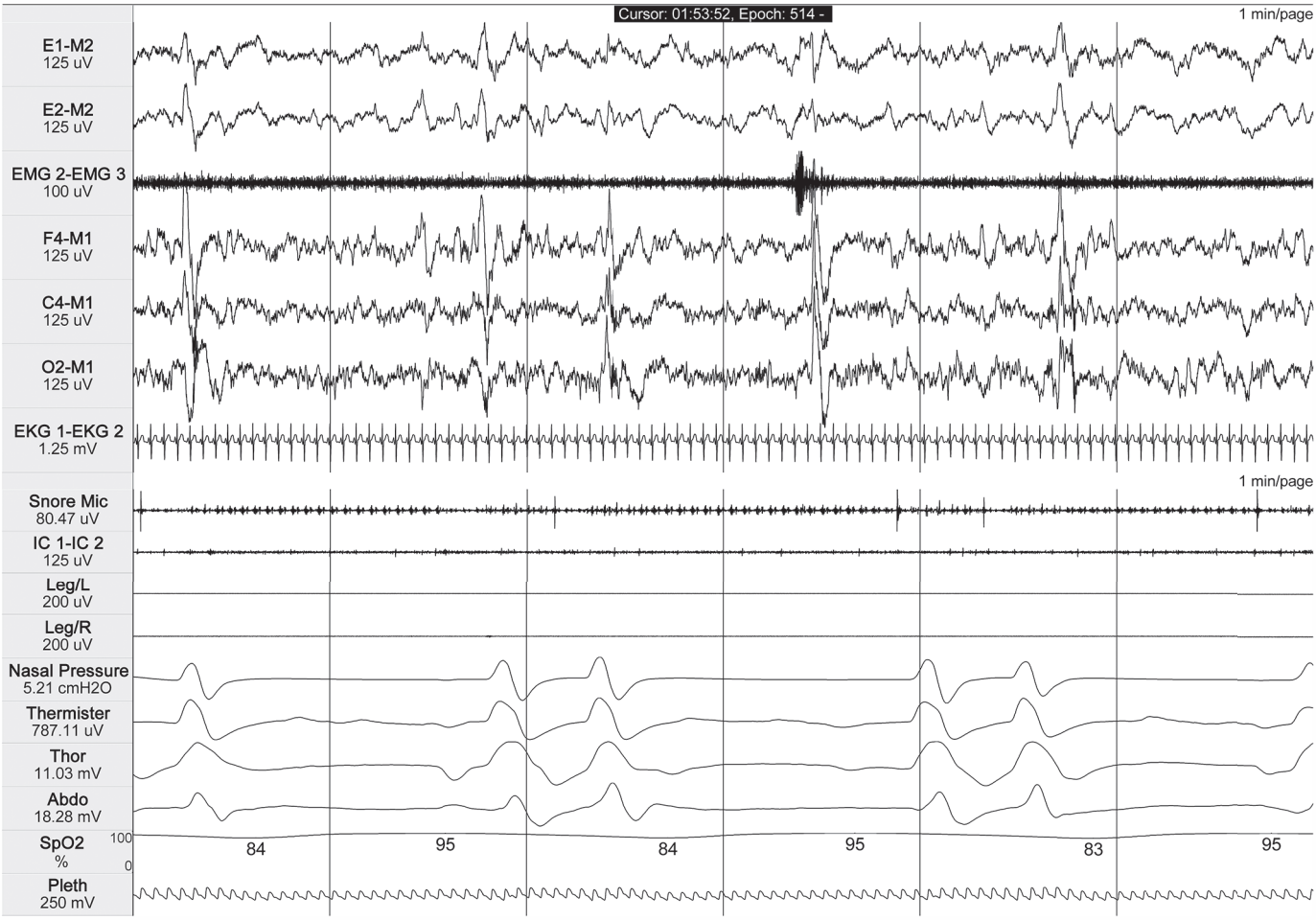
QUESTION: What change was noticed on this patient's PSG after she took a dose of her sublingual fentanyl spray?

Figure 1—One-minute window from overnight polysomnogram.



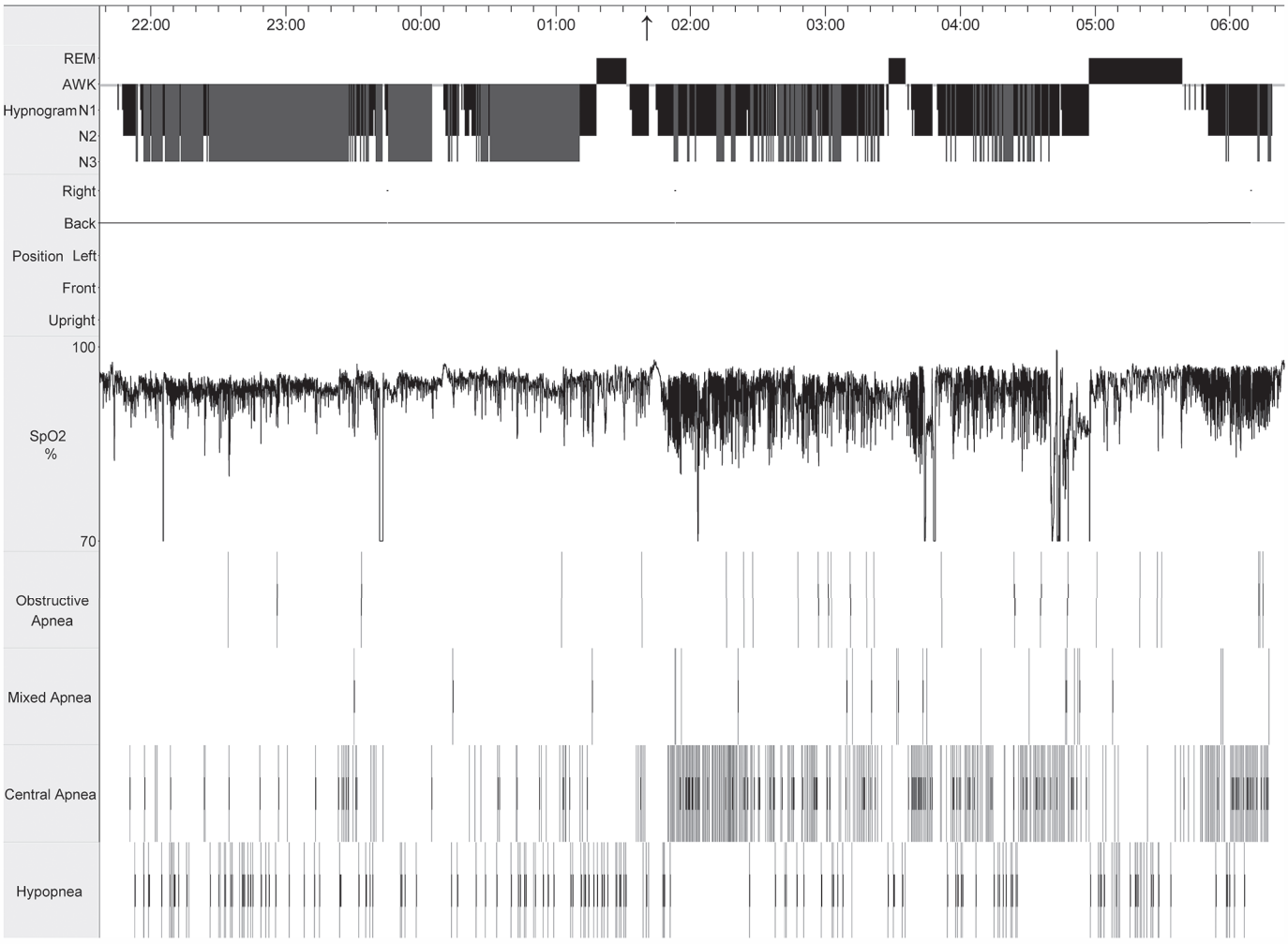
This section is immediately prior to when patient took a dose of her sublingual fentanyl spray. Respiratory rate is around 10 breaths per minute. Oxygen saturation is between 93% and 96%. E1-M2, E2-M2: ocular channels. EMG2-EMG3: chin electromyogram. F4-M1, C4-M1, O2-M1: electroencephalographic channels. EKG1-EKG2: electrocardiogram. IC1-IC2: intercostal leads. Leg/L: left leg electromyogram. Leg/R: right leg electromyogram. Thor: respiratory effort measured by thoracic belt. Abdo: respiratory effort measured by abdominal belt. Pleth: plethysmogram.

Figure 2—One-minute window from overnight polysomnogram.



This section is around 14 minutes after patient took a dose of her sublingual fentanyl spray. Respiratory rate is between 5 and 6 breaths per minute. There are recurrent central apneas associated with cyclical oxygen desaturation. E1-M2, E2-M2: ocular channels. EMG2-EMG3: chin electromyogram. F4-M1, C4-M1, O2-M1: electroencephalographic channels. EKG1-EKG2: electrocardiogram. IC1-IC2: intercostal leads. Leg/L: left leg electromyogram. Leg/R: right leg electromyogram. Thor: respiratory effort measured by thoracic belt. Abdo: respiratory effort measured by abdominal belt. Pleth: plethysmogram.

Figure 3—Summary of sleep stage, body position, oxygen saturation, and respiratory events through the night.



The arrow marks the point around where the patient self-administered a dose of her sublingual fentanyl spray. Note the significant increase in the frequency of central apneas and the severity of oxygen desaturations after this.

ANSWER: There was a significant decrease in the respiratory rate, increase in the frequency of central apneas, and an increase in the severity of oxygen desaturation after this patient took a dose of her sublingual fentanyl spray.

DISCUSSION

This case highlights the fact that single doses of shorter-acting opioid medications, can cause, acute changes in sleep-related respiratory parameters.[1] PSG findings may vary significantly at a given point in time depending on the timing of the opiate administration. In this case, the frequency of central apneas significantly increased after a single dose of opiate. Sleep medicine specialists need to be aware of the timing of opiate medications when interpreting PSG results.

This case also highlights the significantly elevated risk of SDB in patients on chronic opioid therapy.[2–8] Patients on such therapy can have OSA, central sleep apnea (CSA), hypoxemia, hypercapnia, and ataxic breathing which manifests as a variability in the respiratory rate, tidal volume, and duration of the central apneas.[2–9] One study found that 75% of patients on chronic opioid therapy had an AHI ≥ 5 events per hour and 36% had severe sleep apnea (AHI ≥ 30 events/h).[4] Another study found that 70% of patients on chronic opioid therapy had evidence of ataxic breathing.[5] The central apneas seen in patients on opioid medications occur predominantly during NREM sleep rather than REM sleep.[2,9]

Higher doses of opioids and concomitant therapy with benzodiazepines can increase the severity of SDB, and it has been suggested that patients on doses of methadone > 50 mg or on > 150 mg morphine equivalent of other opioids, should be referred for a formal sleep evaluation.[4–6,10] Discontinuation of opioid medications has been reported to lead to a resolution in this form of SDB.[11] Patients with predominantly OSA can be managed with CPAP therapy.[9] However, adaptive servo-ventilation (ASV) is indicated for patients with a predominant component of CSA.[9,12–14]

Prescription opioid use is increasing in the United States and sales of these medications have quadrupled from 1999 to

2010.[15] Prescribers wrote 82.5 prescriptions for opioid pain relievers per 100 persons in the United States in 2012, and there were 16,917 deaths in 2011 related to these medications.[16] SDB in these patients is felt to be one of the risk factors for their increased mortality.[17] Interestingly enough, benzodiazepine use was felt to be a contributing factor in 31% of the above-mentioned deaths.[16]

Providers prescribing opioid medications should have a heightened awareness for the possibility of SDB in their patients on chronic opioid therapy as well as the effects of single doses of shorter-acting opioid medications, and should have a low threshold for referring these patients to a sleep specialist for further evaluation.

SLEEP MEDICINE PEARLS

1. Single doses of shorter-acting opioid medications can cause acute changes in sleep-related respiratory parameters.
2. Patients on chronic opioid therapy are at a significantly high risk for developing sleep disordered breathing.
3. Respiratory abnormalities in patients on chronic opioid therapy can include obstructive sleep apnea, central sleep apnea, hypoxemia, hypercapnia, and ataxic breathing
4. The central apneas seen in patients on opioid medications occur predominantly during NREM sleep rather than REM sleep.

CITATION

Kapoor M, Herrick D. A 27-year-old female on chronic opioid therapy. *J Clin Sleep Med* 2015;11(6):683–687.

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ACKNOWLEDGMENTS

The authors thank Glen Greenough, MD for reviewing this paper and providing technical guidance.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication November, 2014
Submitted in final revised form February, 2015
Accepted for publication February, 2015
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DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.