



Sleep and Chronic Obstructive Pulmonary Disease

Tilak K. Verma, MD, MBA

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Sleep impacts ventilation in situations of normal lung function, however, these changes are more prominent in patients with chronic obstructive pulmonary disease (COPD) and can have serious implications. The changes that occur because of the interaction of sleep and COPD can cause significant clinical consequences, but COPD can also exacerbate other sleep disorders.

Normally, minute ventilation and ventilatory responsiveness to carbon dioxide and hypoxia diminish during sleep. Non-rapid eye movement (NREM) sleep is characterized by a 13-15% drop in minute ventilation from wakefulness while rapid eye movement (REM) sleep is characterized by intermittent marked hypoventilation. The hypoxic and hypercapnic ventilatory responses are lower in NREM sleep than wakefulness and even lower in REM sleep. As a result of these changes, the partial pressure of carbon dioxide (PCO2) peaks in REM sleep and there is a small drop in oxyhemoglobin saturation.

COPD is a term for a number of respiratory diseases, including chronic bronchitis and emphysema, that are characterized by airflow limitation that is not fully reversible. As a result of the structural changes, inflammatory responses and changes in airway reactivity from the lung diseases, patients with COPD have larger lung volumes, decreased airflow, ventilation-perfusion mismatch and impairment in gas diffusion.

The usual changes in minute ventilation brought on by sleep are intensified by the presence of COPD. This can result in alveolar hypoventilation and hypoxemia. Studies have shown that minute ventilation during sleep can fall by an average of 35% as a result of a drop in tidal volume. A number of factors contribute to nocturnal oxygen desaturation including alveolar hypoventilation, reduction in functional residual capacity, increase in airway resistance and ventilation-perfusion mismatch. The desaturations are greatest in REM sleep.

Nocturnal hypoxemia due to COPD can have significant cardiovascular and other effects. Patients with COPD have more cardiac dysrhythmias during sleep, particularly ventricular ectopic beats. Nocturnal hypoxemia causes pulmonary arterial pressure to rise and may lead to, or exacerbate, pulmonary hypertension. The intermittent hypoxemia caused by COPD can cause increases in red cell mass leading to polycythemia. Patients with COPD report sleeping more poorly than healthy subjects due to sleep fragmentation related to the desaturation events.

Management of the sleep effects of COPD revolve around treatment of the underlying disorders. Depending on the severity of the disease, management can include bronchodilators, glucocorticoids and supplemental ventilation. Nocturnal hypoxemia should be treated with supplemental oxygen.

Although there is some conflicting data, the consensus of current opinion suggests that supplemental oxygen should be used when there is persistent nocturnal desaturation to a nadir of 88% or below. Overnight pulse oximetry should guide the concentration of oxygen used. Delivery systems such as nasal cannula and oxygen concentrators are easy and convenient to use.

Noninvasive intermittent positive pressure ventilation (NIPPV) via a nasal mask may be successful in improving ventilation in some patients with COPD. In patients who can tolerate the device, NIPPV can improve nocturnal desaturation, hypercapnia and sleep quality. Simultaneous NIPPV and oxygen therapy has been shown to improve PCO2 and quality of life compared to oxygen therapy in randomized trials.

COPD and OSA (Overlap syndrome)

Both COPD and obstructive sleep apnea (OSA) are common disorders. When combined, a situation termed the "overlap syndrome", the two disorders produce major hypoventilation and hypoxemia. The Sleep Heart Health Study, in addition to assessing the cardiovascular consequences of OSA, also reported that COPD and OSA together caused more desaturation and disrupted sleep. Screening studies estimate that as many as 20% of patients with COPD may also have OSA. Similarly, one study reported that around 10% of OSA patients may have undiagnosed COPD.

Clinical situations that should raise suspicion that the two entities coexist include the presence of symptoms out of proportion to the degree of obstructive disease, associated congestive heart failure, both systemic and pulmonary hypertension and daytime hypercapnia and hypoxemia. Obesity hypoventilation, often associated with OSA, can cause greater drops in minute ventilation in patients with (continued on page 2)

Dear Colleague:

In this issue of the Sleep HealthCenters Newsletter, we feature an article by Tilak Verma, MD, the Regional Medical Director of Sleep HealthCenters' Southcoast/Rhode Island Region. Dr. Verma discusses the effect of sleep on Chronic Obstructive Pulmonary Disease (COPD) and the consequences of the interaction between COPD and sleep disorders. In particular, he highlights the overlap syndrome, the condition that results when two common disorders, COPD and obstructive sleep apnea, occur in the same patient.

Sleep HealthCenters held its second Future of Clinical Sleep Medicine forum in September. The forum is designed to bring together local clinicians with research leaders on the cutting edge of clinical sleep medicine. The interactive sessions highlight new advances, identify ways to bring new ideas into clinical practice and generate ideas for future avenues of investigation. In this issue we present a summary of the talk by Ruth Benca, MD, PhD, Director of the Center for Sleep Medicine and Sleep Research at the University of Wisconsin. She presented her views on the sleep laboratory of the future with particular emphasis on her research group's exciting new work with high density EEG polysomnography. This work has the potential to greatly expand the diagnostic scope and utility of polysomnography. In subsequent issues of the Newsletter, we will highlight some of the other topics presented at the Future of Clinical Sleep Medicine forum.

In the CEO Corner, Paul Valentine describes a new Sleep HealthCenters service, the Sleep Health Program. This service is an extension of our current clinical services focused on providing sleep disorders screening, diagnosis and management for companies interested in providing disease prevention and management programs to their employees. Recognition and treatment of sleep disorders can improve performance and long-term health. Sleep HealthCenters has developed a network of partner centers that allows us to provide this service nationwide.

If you have any questions about sleep disorders, our programs or locations, please feel free to contact us.



Sincerely,

Lawrence J. Epstein, MD
Medical Director
Sleep HealthCenters LLC

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Sleep HealthCenters®
Better Sleep. Better Health.



Sleep HealthCenters is a network of sleep medicine centers staffed by experts in the field of sleep medicine. Our integrated care system provides all the services needed to diagnose and treat patients with the entire array of sleep disorders including obstructive sleep apnea, insomnia, narcolepsy and restless legs syndrome.

In this issue of the Sleep HealthCenters Newsletter...

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- ▶ The Sleep Laboratory of the Future
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Massachusetts Affiliations: Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Faulkner Hospital, Hallmark Health, Marlborough Hospital, Massachusetts Eye and Ear Infirmary, McLean Hospital, New England Sinai Hospital, Southcoast Hospitals Group; *New York Affiliations:* Beth Israel Medical Center

Massachusetts Locations: Bedford, Beverly, Boston, Brighton, Framingham, Jamaica Plain, Marlborough, Medford, North Dartmouth, Stoughton, Weymouth, Worcester; *New York Locations:* Manhattan; *Rhode Island Locations:* Cumberland

For more information, please contact us at: 1-877-SLEEPHC (1-877-753-3742) or visit our website at www.sleephealth.com.

Requisition forms are available on our website.



Sleep HealthCenters® Sleep Health Program

Companies large and small are looking for ways to improve their employees' health and wellbeing, and also ways to cut costs associated with employee sleep deprivation and health care costs.

Sleep HealthCenters now offers sleep education workshops to employee groups to teach healthy sleep habits and how to recognize the symptoms of a sleep disorder.

The "Sleep Health Program" screens, diagnoses, treats and provides follow-up care for employees with sleep disorders such as insomnia, restless legs syndrome, sleep apnea and excessive daytime sleepiness.

Read more about the Sleep Health Program in the CEO Corner

(continued from page 1) COPD, producing hypercapnia and hypoxemia. Other clues that point toward the overlap syndrome include the presence of obesity, snoring and daytime headaches in patients with COPD.

The pattern of nocturnal desaturation is different in patients with the overlap syndrome compared to those with only COPD. In patients with both conditions there are frequent desaturations that lead to a broad-band of desaturation rather than the REM-related spike appearance of desaturation seen in COPD only patients.

Role of Polysomnography (PSG)

When OSA is suspected in COPD patients (symptoms of snoring, witnessed respiratory pauses and excessive daytime drowsiness) full channel overnight PSG is the best option for further investigation. The current recommendation is that home sleep testing for the diagnosis of OSA should not be conducted in patients with co-morbid medical conditions such as COPD. These patients are typically excluded from studies on the efficacy of home monitors and thus there is a lack of data with these devices in this population. However, multi-channel home monitoring is likely to have an emerging role as further experience is gained with these devices.

Management of Sleep Disordered Breathing in COPD

Patients with the overlap syndrome can be treated with continuous positive airway pressure (CPAP) for their OSA. While the COPD component does not respond to CPAP, the OSA element can be effectively managed. Management of COPD should also be maximized as described above.

Treatment of the OSA may not resolve the hypoxemia. This can be addressed with the use of either supplemental ventilation or supplemental oxygenation. Supplemental ventilation is typically delivered with a bi-level positive airway pressure device (BPAP). Once the OSA is eliminated with CPAP, the inspira-

tory pressure is raised to increase tidal volume and, thus, minute ventilation. If BPAP does not eliminate hypoxemia, supplemental oxygen can be added through the CPAP device. Again, oxygen should be titrated to maintain oxygen greater than 88%.

COPD and Insomnia

Numerous studies have shown an increased prevalence of insomnia with COPD. These sleep disturbances range from difficulty falling asleep to frequent awakenings and daytime drowsiness. Disrupted sleep arises from a variety of factors including the symptoms of the disease, such as cough and shortness of breath, coexisting depression, physiologic factors such as V/Q mismatch and dampened ventilatory response to hypercapnia and medication effects. Several medications used to treat COPD, such as corticosteroids and theophylline, have been reported to cause problems with sleep.

Management should first focus on maximizing treatment of the underlying breathing disorder. Numerous sedative/hypnotics are available but caution must be exercised in their use because they can cause respiratory depression and worsen sleep induced hypoventilation.

Conclusion

The physiologic derangements caused by COPD are exacerbated with onset of sleep. In particular, REM-related hypoxemia can cause cardiovascular consequences. COPD can also exacerbate sleep disorders such as OSA and insomnia. Management should be directed at treating the underlying respiratory disorder. For persistent hypoxemia, supplemental oxygen may be needed. Because of the frequency of overlap syndrome, patients with COPD should routinely be evaluated for the presence of symptoms of OSA. If present, patients should have a sleep study to look for concurrent OSA. Treatment of OSA is complicated by the presence of COPD with a higher likelihood of residual hypoxemia requiring supplemental ventilation or oxygen.

RESEARCH ACTIVITIES

Sleep HealthCenters is proud to work with some of the premier sleep researchers in the country. The following research studies are currently underway in conjunction with our partners. To take part in a study or for more information, please contact us toll free at 877-SLEEPHC (877-753-3742). For a full listing of our research activities, please log onto our website at www.sleephealth.com.

Do You Snore?

Sleep HealthCenters is looking for people who have never had an overnight sleep study. The purpose of this research study is to see how well devices called portable monitors work for diagnosing Obstructive Sleep Apnea at home. Participants will wear a portable monitor for two consecutive nights at home and will wear a portable monitor during their scheduled overnight sleep study.

If interested, please contact Melissa at Sleep HealthCenters by calling 617-783-1496 x121 or emailing SleepResearch@sleephealth.com.

Tired of Being Tired?

Every morning thousands of people with Obstructive Sleep Apnea and Depression wake up tired. A local clinical research study is underway to see if an investigational drug is effective at reducing daytime sleepiness for people with obstructive sleep apnea and depression. We're looking for people for people who:

- Have daytime sleepiness caused by obstructive sleep apnea
- Use nasal CPAP therapy to treat their apnea
- Are taking prescription medication for depression
- Are between 18 and 65 years old

If you want to learn more, please contact Melissa at Sleep HealthCenters by calling 617-783-1496 x121 or emailing SleepResearch@sleephealth.com.

CASE STUDY

WR is a 66 year old gentleman who sought pulmonary evaluation for symptoms of shortness of breath, cough and wheezing of five years duration. The cough was productive of a moderate quantity of white sputum. Shortness of breath occurred on exertion such as climbing a flight of stairs. He became more winded while carrying groceries. Wheezing was episodic and worsened with respiratory infections. There were no complaints of chest pain or discomfort. He had intermittent nasal congestion and sneezing that occurred seasonally. He was a one to two pack per day smoker who had smoked since his teenage years. He had worked in a textile mill in various locations such as spinning and weaving. His father had been a smoker and died with emphysema. In addition, he also complained of fatigue and daytime sleepiness due to poor sleep. His sleep was fragmented with multiple awakenings at night and he had been told he snored loudly.

Examination revealed an obese male, 66 inches tall and weighing 200 lbs. Blood pressure was 140/88, heart rate 90 beats/minute and respiratory rate of 20 to 22 breaths/minute. ENT examination was notable for a mild deviation of the septum, some clear nasal secretions, a small chin and a deep and low soft palate with wide and prominent uvula. Lung examination revealed distant and diminished breath sounds with a prolonged expiratory phase, scattered ronchi and few expiratory wheezes. Cardiac rhythm was regular, P2 was accentuated. Abdomen was soft, protuberant and obese without pulsatile masses or bruits. Ankles were edematous. There was no clubbing.

Lab investigations revealed a normal CBC and renal function was notable for slight elevation of the bicarbonate. Chest x-ray showed some hyperinflation. EKG revealed reduced limb lead voltage and delay in R wave progression. PFTs showed a FEV1 of 1.8 liters, increase in the residual volume and reduction in the diffusing capacity. ABG: pH 7.35, PCO2 55, PO2 66, oxygen saturation 95% on room air.

He was diagnosed with chronic obstructive pulmonary disease and started on short acting bronchodilators and a long acting cholinergic bronchodilator. He was encouraged to stop smoking, screened for alpha 1 antitrypsin and received an influenza and pneumococcal vaccine. To improve function he was enrolled in pulmonary rehabilitation.

His sleep complaints were investigated with an overnight sleep study. A split night study was performed with the diagnostic portion revealing OSA with an AHI of 22.2/hour but he had severe desaturations during REM sleep with a nadir of 75%. CPAP was titrated to 12cm with significant reduction in the AHI. His saturations improved but by the end of the night remained between 88-91% while asleep despite the elimination of all obstruction.

His shortness of breath has improved on medication. He uses CPAP nightly and participates intermittently in the maintenance phase of pulmonary rehabilitation that includes weight management. His sleep is more continuous and his sleepiness is greatly reduced. A follow-up overnight oximetry on CPAP demonstrated oxyhemoglobin saturation remaining above 88% and he has not required supplemental oxygen.

THE SLEEP LABORATORY OF THE FUTURE

Sleep HealthCenters' second Future of Clinical Sleep Medicine Forum (FOCSM) was held on September 18, 2008, in Boston, Massachusetts. This forum is designed to bring together sleep clinicians and sleep scientists on the cutting edge of clinical sleep medicine to share their visions of where the field is going. In this issue of our newsletter, we present one of the topics. Other FOCSM topics will be discussed in future newsletters.

Ruth Benca, MD, PhD, is the director of the Center for Sleep Medicine and Sleep Research at the University of Wisconsin Hospital and Clinical Professor of Psychiatry at the University of Wisconsin.

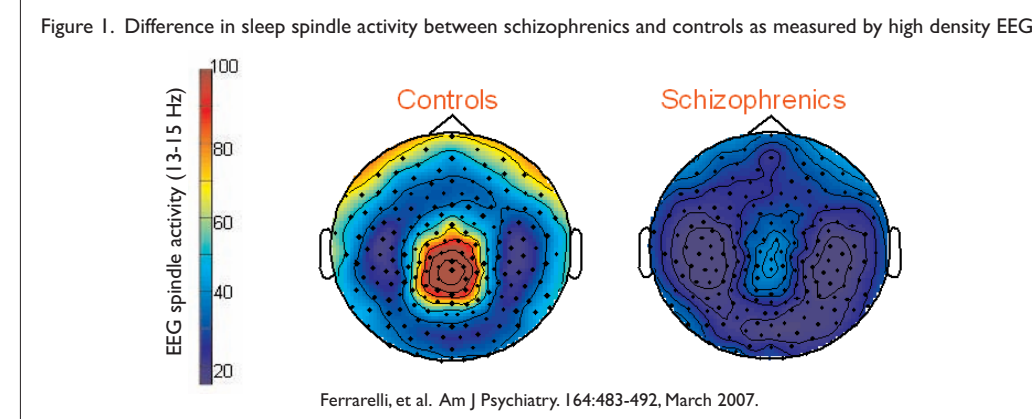
The sleep medicine environment has changed dramatically but what happens in sleep laboratories has not. Most sleep centers test predominantly for sleep apnea, relatively few patients are seen in clinic and there has been little change in the way sleep studies are conducted. However, insurance providers are becoming more restrictive in the types of tests they will cover and the amount of reimbursement they will pay, the use of home sleep testing is increasing and there have been significant technological advances in the machines for recording sleep.

The standard data reported from a sleep study are "one-dimensional", reporting only sleep stages, sleep latencies and significant events such as changes in respiration or leg movements. EEG analysis assumes that activity in one area of the scalp represents the activity of the entire brain. At the same time, sleep recording equipment is smaller, more portable and capable of gathering and analyzing large amounts of data including brain activity, respiratory patterns and cardiovascular patterns. Laboratory based sleep testing needs to offer increased value in comparison to

portable monitoring that merely detects sleep disordered breathing.

High density, 256-lead, EEG polysomnography, developed by Giulio Tononi and colleagues at the University of Wisconsin, provides information on brain activity in multiple dimensions, both spatial and temporal. High density EEG allows measurement of the change in power density by region across the night and allows characterization of the origin and spread of individual waves. This type of topographic analysis is stable within individuals across nights and the patterns can represent a larger variety of disorders. Individual waves, such as slow waves or spindles, can be tracked from origin through propagation. See Figure 1. Scoring sleep using this methodology could make epoch-based scoring obsolete.

Recent studies suggest using high density EEG could expand the functionality of sleep testing. A study by Ferrarelli, et al, has shown sleep spindle activity measured by high density EEG is reduced in schizophrenia and full night patterns can differentiate between



CEO CORNER

Paul S. Valentine
President and
Chief Executive Officer

We are excited to announce a new sleep disorders screening service for companies nationwide. The "Sleep Health Program" screens, diagnoses, treats and provides follow-up care for employees with sleep disorders such as insomnia, restless legs syndrome, sleep apnea and excessive daytime sleepiness. Companies large and small are looking for ways to improve their employees' health and wellbeing, and also ways to cut costs associated with employee sleep deprivation and health care costs.

Sleep HealthCenters now offers sleep education workshops to employee groups to teach healthy sleep habits and how to recognize the symptoms of a sleep disorder. By participating in the Sleep Health Program, employees are offered the chance to answer questions about their sleep health. Any employee

considered to be "at risk" of a sleep disorder can visit one of our 15 sleep centers in MA, RI and NY or in one of our partner centers across the nation. We assign each employee a Sleep Specialist, board certified in sleep medicine, and a case manager (nurse practitioner or respiratory therapist) to oversee their care.

After a thorough evaluation with their Sleep Specialist, employees may have a diagnostic test either in a sleep lab or in their own home using the latest at-home diagnostic technology. Depending on the diagnosis, treatment may involve PAP devices, cognitive behavioral therapy, medication or other solutions recommended by our specialists. The case manager and employee continue to work together and record improvements in quality of life (QoL), symptoms, and co-morbid conditions over time. The goal for each employee is to take control of their sleep health and successfully manage their sleep disorder. The entire program is managed centrally from our headquarters in Massachusetts to ensure all patients receive a standardized quality of care and that the sponsoring company can be provided feedback about participation rates.

schizophrenic and normal control subjects. Sleep testing may become a diagnostic tool for the diagnosis of schizophrenia. The patterns of slow-wave and spindle activity during sleep is changed following a stroke and can be used to locate residual damage and monitor recovery.

These studies suggest that high density EEG brain imaging could become important for diagnosing and managing neuropsychiatric disorders and determining brain function in other sleep disorders. This would significantly expand the role of the sleep laboratory and the utility of sleep testing.

The sleep laboratory of the future will likely utilize home sleep testing to increase access to sleep diagnostic services. Improved physiological monitoring in laboratory-based studies, such as high density EEG brain imaging, will broaden the application of sleep testing to other areas of medicine including psychiatry, neurology, cardiology and pulmonology.

We have launched the Sleep Health Program in the trucking industry, offering education, fatigue management and clinical services to commercial motor vehicle drivers. We know that approximately one in three truck drivers suffers from undiagnosed sleep apnea, leaving them at increased risk of cardiovascular disease and automobile accidents. Because of this risk, the Federal Motor Carrier Safety Administration is currently reviewing recommendations to implement mandatory testing for sleep apnea in any commercial driver with a body mass index of 33 or greater. By reaching out to commercial motor vehicle drivers before any legislative changes occur, we can help them become safer drivers immediately and give them a future advantage by documenting the successful management of their disorder.

For more information about the Sleep Health Program, visit us at www.sleephealth.com.

