CHEST Postgraduate Education Corner

CONTEMPORARY REVIEWS IN SLEEP MEDICINE

Sleep-Related Problems in Common Medical Conditions

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Common medical problems are often associated with abnormalities of sleep. Patients with chronic medical disorders often have fewer hours of sleep and less restorative sleep compared to healthy individuals, and this poor sleep may worsen the subjective symptoms of the disorder. Individuals with lung disease often have disturbed sleep related to oxygen desaturations, coughing, or dyspnea. Both obstructive lung disease and restrictive lung diseases are associated with poor quality sleep. Awakenings from sleep are common in untreated or undertreated asthma, and cause sleep disruption. Gastroesophageal reflux is a major cause of disrupted sleep due to awakenings from heartburn, dyspepsia, acid brash, coughing, or choking. Patients with chronic renal disease commonly have sleep complaints often due to insomnia, insufficient sleep, sleep apnea, or restless legs syndrome. Complaints related to sleep are very common in patients with fibromyalgia and other causes of chronic pain. Sleep disruption increases the sensation of pain and decreases quality of life. Patients with infectious diseases, including acute viral illnesses, HIV-related disease, and Lyme disease, may have significant problems with insomnia and hypersomnolence. Women with menopause have from insomnia, sleep-disordered breathing, restless legs syndrome, or fibromyalgia. Patients with cancer or receiving cancer therapy are often bothered by insomnia or other sleep disturbances that affect quality of life and daytime energy. The objective of this article is to review frequently encountered medical conditions and examine their impact on sleep, and to review frequent sleep-related problems associated with these common medical conditions. ***(CHEST 2009; 135:563–572)***

Key words: cancer; chronic renal failure; COPD; fibromyalgia; gastroesophageal reflux disease; heart failure; HIV-related disease; nocturnal asthma; restrictive lung disease; sleep disorders

Abbreviations: CPAP = continuous positive airway pressure; GERD = gastroesophageal reflux disease; IL = interleukin; OSA = obstructive sleep apnea; REM = rapid eye movement; Sao_2 = arterial oxyhemoglobin saturation; Stage R = rapid eye movement sleep; TNF = tumor necrosis factor

Patients with common medical disorders often complain to their physician about sleep problems, and these patients are often referred to sleep specialists for evaluation and diagnosis. Poor quality sleep or insufficient sleep are associated with fatigue, malaise, and sleepiness. Quality of life is impaired, and subjective symptoms due to the underlying disease seem worse to the patient. If the quality of sleep is improved, subjective symptoms related to the disease may improve. Walsh et al[1] showed in a study of patients with rheumatoid arthritis and poor sleep that improving sleep by the use of a benzodiazepine improved subjective symptoms of joint pain even in the absence of objective improvement. Patients with some medical disorders, such as asthma, may have the most severe symptoms during sleep. Sleep disorders such as obstructive sleep apnea (OSA) have many adverse effects on health and may occur more frequently in certain medical disorders. In this review, the objective will be to review litera-

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ture on sleep-associated problems observed in common medical conditions. Extensive research on the association of sleep-disordered breathing and cardiovascular disease has been reviewed and is not discussed here.[2]

Sleep in Pulmonary Disease

Sleep in COPD

Patients with COPD often have disrupted and fragmented sleep. Patients with COPD have prolonged sleep latency, decreased sleep efficiency, decreased total sleep time, increased wake after sleep onset, decrease in rapid eye movement (REM) sleep (Stage R), and decreased stage N3 sleep (non-REM stage 3 and 4 sleep). Additionally, coughing or dyspnea can be associated with sleep-related arousals.[3] Sleep in patients with COPD is often complicated by hypoxemia. Oxyhemoglobin desaturation frequently occurs during non-REM sleep and worsens significantly during Stage R.[4,5] Hypoxemia may be due to several factors: ventilation-perfusion mismatching, increase in upper airway resistance, unfavorable mechanical position of intercostal muscles and diaphragm due to hyperinflation, relative decrease in oxygen stores, and the position of the baseline arterial oxyhemoglobin saturation (SaO_2) on the oxyhemoglobin dissociation curve (Fig 1).[3]

The degree of nocturnal hypoxemia in COPD is determined primarily by the daytime SaO_2 and daytime $PaCO_2$. Because of the physiology of oxyhemoglobin dissociation, the lower the daytime resting SaO_2, the more likely severe nocturnal desaturations will occur.[6] Reduced hypercapniec ventilatory response and respiratory muscle dysfunction further contribute to desaturation.[7] The coexistence of OSA, termed the *overlap syndrome*, results in more severe oxygen desaturations.[8] Sanders et al[9] analyzed data from nearly 6,000 patients from the Sleep Heart Health Study and observed there was no association between mild COPD and OSA, but that that more severe COPD is associated with more severe desaturations during sleep, and that desaturation is greater in individuals with both COPD and OSA. In contrast, patients with mild airways obstruction in the absence of OSA had minimal alterations in sleep.[9]

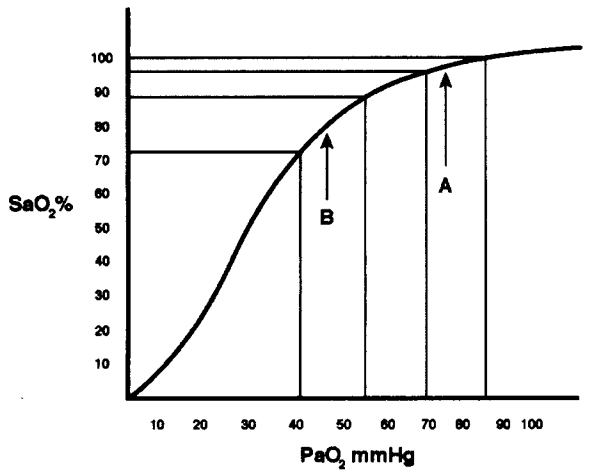

FIGURE 1. Oxyhemoglobin dissociation curve demonstrates the effect of a reduction in PaO_2 in a normal person and a patient with baseline hypoxemia due to lung disease. *A*: An individual who starts with a PaO_2 of approximately 85 mm Hg and decreases to 70 mm Hg, resulting in only a small decrease in SaO_2. *B*: An individual with COPD starts with a PaO_2 of 55 mm Hg at baseline and during sleep has a similar decrease in PaO_2 but has a much larger decrease in SaO_2.

Sleep and Asthma

A characteristic symptom of asthma is nocturnal awakening with dyspnea, cough, or wheeze.[10] Patients with asthma commonly have their lowest peak flow during the night hours.[11] The pathophysiology of nocturnal asthma is complex but is associated with increased parasympathetic activity at night, increased airway inflammation, alteration in glucocorticoid receptors binding, and increased levels of proinflammatory leukotrienes. Evidence shows that a genetic mutation on the β_2-adrenergic receptor, Gly16, is significantly associated with nocturnal asthma.[12] Gastroesophageal reflux is an important contributing cause in many patients. Nocturnal asthma is therefore a complex phenomenon that is related to circadian alterations in airway physiology and inflammation. Treatment with inhaled corticosteriods and long-acting β-agonists is often effective at relieving symptoms in these patients and improving sleep.[13,14]

Sleep and Restrictive Lung Disease

Common interstitial lung diseases are interstitial pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis, and drug-related lung disease. Restrictive lung disease is characterized by a decreased total lung capacity, pulmonary compliance, and diffusing capacity of the lung for carbon monoxide. The ventilatory response to these abnormalities in physiology is rapid, shallow breathing due to vagal stimulation from pulmonary mechanical receptors producing a sensation of dyspnea.

Patients with interstitial lung disease often have fragmented sleep interrupted by frequent arousals. Sleep in these patients is characterized by an increase in arousals, increased stage N1 sleep and stage N2 sleep, and a decrease in stage N3 sleep and Stage R. Hypoxemia often occurs during sleep, as it does with obstructive lung disease, and there are often severe desaturations during Stage R (Fig 2).[15,16]