



REM Related Apnea



Although most patients with obstructive sleep apnea snore and may have witnessed events of stopping breathing throughout the night, patients with REM related obstructive sleep apnea may have a different pattern. They may snore very lightly or even not at all. They may not even have apneic events in sleep stages other than REM sleep. Atonia, or the loss of muscle tone that occurs normally in REM sleep may significantly affect oropharyngeal and other accessory muscles of respiration. The difference in these patients may be an increased level of atonia in the oropharyngeal musculature. These patients may complain of sleep maintenance insomnia where they may have no difficulty falling asleep initially only to awaken two and a half to three hours and then about every hour to hour and a half from that point onward each time they enter their REM sleep cycles and awaken from an apneic event. As the low voltage, mixed frequency EEG of REM sleep are not that different from those of wakefulness, these patients typically wake up wide awake. For this reason, REM related apnea is a common cause of sleep maintenance insomnia.

One polysomnographic analysis of 415 patients determined that 36.4% of patients fulfilled the criteria for REM related apnea, defined as a REM apnea/hypopnea index (AHI) / non-REM AHI ratio >2 . No significant differences were found in Epworth sleepiness scale (ESS) scores and mean sleep latency of the Maintenance of Wakefulness Test (MWT) between groups. A strong male prevalence was found for OSA in the group as a whole, but in this study the incidence of REM OSA was similar in men and women.¹

However, a much larger study involving 2,486 patients referred to a university sleep laboratory with an AHI greater or equal to 5 events per hour performed using the same definition of REM related OSA demonstrated that the prevalence of REM related apnea was 40.8% in women and 21.0% in men. After adjusting for age and obesity, female sex was a significant risk factor for REM related apnea, having an odds ratio of 3.0. Interestingly, the prevalence of REM sleep disordered breathing prevalence waned with increasing age in both sexes, such that

the odds of having REM apnea fell by 26.7% per decade, perhaps secondary to a disproportionate age-dependent rise in the AHI in non-REM sleep. The authors hypothesized that these patterns may reflect age-related decreases in female hormones.²

Another retrospective study of 1,540 OSA patients using the same definition of REM related apnea determined the prevalence of REM related OSA to be 14.4%. This study also determined a higher female prevalence of REM related apnea (24.5 vs 7.9%; $p < 0.001$) and also demonstrated that younger women had a significantly higher prevalence than did older women (27.2 vs 18.6%; $p = 0.008$). These younger women with REM related apnea were more likely to be depressed and significantly more obese than were older women.³

How does REM related apnea occur? Hypoglossal motoneurons, which innervate extrinsic and intrinsic muscles of the tongue, play a key role in maintaining the patency of the upper airway and in the pathophysiology of obstructive sleep apnea syndrome. Excessive atonia of hypoglossal neurons may be the specific mechanism that leads to or exacerbates REM related sleep disordered breathing in selected patients. This has been documented by intracellular recording of hypoglossal

motoneurons during cholinergically induced REM sleep. It has been postulated that there may be a glycinergic premotor inhibitory system acting to suppress hypoglossal motoneurons, which may open new avenues for the treatment of REM related apnea through pharmacological control of respiration-related motoneurons during REM sleep.⁴

What about the cardiac implications of REM related apnea? REM sleep-related bradyarrhythmia syndrome is a cardiac rhythm disorder characterised by asystoles lasting several seconds during REM sleep in otherwise healthy individuals. In contrast to arrhythmias associated with

obstructive sleep apnea, REM sleep-related sinus arrests and atrioventricular (AV) blocks may not necessarily be associated with episodes of apnea or hypopnea. In literature, only few cases have been published, suggesting that the prevalence of this nighttime rhythm disorder is relatively rare. A case report of 2 patients with REM sleep-related sinus arrests and one case of REM sleep-related total AV block. An analysis of heart rate variability has demonstrated a significant lower low-to-high frequency (LF/HF) ratio in slow wave sleep as compared to REM sleep, likely due to the increase in sympathetic activity that occurs during REM sleep. When the same technique was used in 2 patients with REM-related arrhythmias, the shift to an increased LF/HF ratio from slow wave sleep to REM sleep tended to be lower. The authors concluded that these patients may have an increased vagal activity during REM sleep and that the overall dominance of sympathetic activity during REM is present but to a lesser extent and temporarily switches into vagal dominance when the bursts of REMs occur. The authors believe that it is unclear whether these REM sleep-related asystoles require the placement of a pacemaker.⁵

It will be interesting to see how further research elucidates this interesting form of Obstructive Sleep Apnea.

¹ *Chest*. 2005 Nov;128(5):3350-7.

² *Chest*. 2008 Dec;134(6):1156-61. Epub 2008 Sep 23.

³ *Sleep Breath*. 2008 Aug;12(3):259-64. Epub 2007 Dec 11.

⁴ *Neuroscience*. 1999;94(1):11-5.

⁵ *Sleep Breath*. 2007 Sep;11(3):195-9.