Sleep
Yet To Be Mapped Waters for Blood Pressure

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See related article, pp 791–796

Much work has focused on the link between sleep apnea and hypertension, and the evidence that suggests an underlying association between these 2 conditions is persuasive. Sleep apnea syndromes encompass 3 related disorders, obstructive sleep apnea, central sleep apnea, and mixed (or complex) sleep apnea. Obstructive sleep apnea is common, readily diagnosed, and more often than not treatable. Obtaining a thorough sleep history from a patient for symptoms of obstructive sleep apnea, including snoring, witnessed apnea, irregular breathing during sleep, restless sleeping often with choking or gasping arousals, excessive sleepiness, frequent traffic accidents, and declines in cognitive function is now viewed as standard practice.

However, obstructive sleep apnea is but one of a number of sleep-related disturbances with the potential for short and more long-term effects on blood pressure (BP). In that regard, emerging evidence suggests a link between restless legs syndrome (RLS)/periodic limb movements in sleep (PLMS) and hypertension. RLS is a neurological disorder characterized by pulsating, tugging, creeping, or other unpleasant sensory feelings in the legs and an uncontrollable and sometimes overwhelming urge to shift leg position. In a typical patient, symptoms occur primarily at night as a person might otherwise be relaxing or when one is resting. Symptoms can be present throughout the day, and severity can accentuate during the nighttime hours with leg movement oftentimes relieving the discomfort. The sensations range in severity from simple discomfort to a painful irritation with the integrity of sleep regularly being disrupted.

Periodic limb movement disorder in sleep is a disorder marked by regular limb movements during sleep. The movements typically involve the lower extremities, but arm and shoulder movements may also take place. Movements span the night and can vary considerably in severity from night to night. The repetitive movements of PLMS are separated by fairly regular intervals of 5 to 90 seconds with limb movements occurring most frequently in light non-rapid eye movement sleep. Although a large majority of individuals with RLS also have PLMS, most people with PLMS do not experience RLS. Both RLS and PLMS are common occurrences in the general population, with most recent data suggesting that ≤10% of the United States population may have RLS.

What appears to be a common theme between RLS and PLMS is that such leg movements are associated with sympathetically mediated elevations in both heart rate and BP. A not unreasonable hypothesis derived from these events is that the repeated overnight changes in BP developing during nighttime RLS and PLMS episodes increase daytime BP based on the cumulative effects of increased nocturnal sympathetic activity.

Thus, it comes as no great surprise that Batool-Anwar et al would find a greater prevalence of hypertension in women presenting with more frequent episodes of RLS. The Nurses’ Health Study II has provided a rich database for cross-sectional studies, such as the one reported on in this issue of the journal. The manner in which these authors assessed this data set occurred with an appropriate understanding of the confounding variables that stood a chance of invalidating their findings.

There were several particularly important findings reported on by these authors. First, there was a discernible relationship between the severity of self-reported RLS severity and an increase in BP, which would make the observed findings internally consistent. Second, an adjustment was made for sleep duration and the association between RLS and hypertension, and although the BP change was attenuated the lesser the length of sleep, nonetheless it remained significant. As the authors rightly point out, this would imply that the effect of RLS on BP was not simply the result of a shortened duration of sleep. Finally, the sensitivity analysis done relative to current antihypertensive users or not found the highest multiple-adjusted odds ratio of 1.84 after excluding antihypertensive therapy use. This would suggest that therapy might have been begun for hypertension even as it was not being viewed as having a recognizable association with RLS.

As always, a study such as this one has both limitations and raises more questions than it was intended to answer. First and foremost, it is a cross-sectional study for which the findings only assessed women. This fact and the knowledge that women develop RLS twice as often as men are both drawbacks as to its generalizability. Also, the magnitude of BP change in millimeters of mercury was very small, even in those with the highest frequency of RLS, such that even the best clinician would not have identified a BP change attributed to RLS. As is the case in general practice, RLS might be
viewed as only one of several factors that could contribute to an elevation in BP. Finally, these findings are observational and cannot in any way be viewed as being mechanistic; thus, no insight can be provided into whether treatment of RLS could in any sort of meaningful way lower BP.9

Hypertension remains widely prevalent in the United States, and despite considerable public health efforts continues to increase as the population both ages and becomes more obese. Innumerable drug therapies exist with a record of proven success in lowering BP, and the skilled hypertension specialist usually can significantly lower BP in a significant number of those patients with poorly controlled hypertension. The artfulness of even the best hypertension specialist comes forth when the role of sleep is considered in a patient’s treatment of hypertension, be it resistant hypertension or otherwise.1

Sleep still remains a very much uncharted domain as to its effect on BP in routine clinical practice. The quantity and quality of sleep, as well as its innate architecture, are fundamental factors in overnight BP values, as well as the particular BP pattern expressed by a patient. There has been a long-standing interest in whether a patient is a dipper or a nondipper in his or her overnight BP pattern; however, despite the wealth of information on the classification of a patient according to his or her dipping status, this characterization remains a simplistic interpretation of overnight BP.10

Embedded in the RLS and/or PMLS patient’s overnight BP pattern are episodic and sometimes chaotic BP changes lasting several minutes relating to the abrupt sympathetic discharge that can occur with or without microarousals characteristic of RLS and/or PLMS (Figure).3 The magnitude of BP changes appears to be greatest when PLMS is associated with microarousals and increase with the duration of the microarousal, while appearing independent of the somatic characteristic of PLMS. This would imply that the intensity of cardiovascular responses might have a closer relationship to the degree of central activation and less attributed to the somatomotor response. There is little information as to what is the set point for activating the sympathetic nervous system with RLS and PLMS. It should be appreciated that it is only recently that RLS is moving toward a quantifiable relationship with hypertension.3

In the foreseeable future, the hypertension specialist and, for that matter, any clinician actively treating hypertension will need to have more than a just passing knowledge of sleep patterns and sleep-related diseases to most effectively treat hypertension and accompanying cardiovascular diseases.

Disclosures

D.S. has been on an advisory board for UCB Pharma. This is not a standing relationship.

References
