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Do sleep disorders have an impact on blood pressure?

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“Sleep is that golden chain that ties Health and bodies together”
Thomas Dekker, 1570 - 1632

For many years, virtually every scientific report about the burden of hypertension started out with a statement of this sort: “Hypertension is an important public health challenge worldwide because of its prevalence and concomitant increase in risk of disease1”. This should be no surprise, as hypertension is well established as the risk factor most responsible for global attributable mortality. Indeed, the World Health Organization has reported that 15.9 million of the 55.9 million deaths that occurred worldwide in the year 2000 were due to ischemic heart disease, stroke, hypertensive disease, and other cardiovascular diseases2. Of the 15.9 million cardiovascular deaths, 7.6 million were directly attributable to elevated systolic blood pressure (>115 mm Hg)3, representing 13.6% of total mortality.

Obviously, these data constitute an imperative for the public health establishment worldwide to address this situation. What can we do to reduce the burden of hypertension? Many effective approaches are available to prevent hypertension, to treat it, and to control it!

The epidemiologic risk factors for elevated blood pressure are well recognized: they include genetic factors, environmental factors, and combinations of the two. In the mid-1980s, a few reports highlighted the relationship between sleep apnea —by far one of the most common sleep-disorders—and hypertension. A 1984 publication noted that “Presence of sleep apnea was significantly correlated with higher blood pressure. Patients with the more severe sleep apnea had the higher blood pressure level4”. A 1985 paper concluded, “It is suggested that sleep apnea may play a part in the development of essential hypertension5”. Also in 1985, it was reported that “sleep apnea is associated with systemic hypertension. Treatment of the sleep-disorder breathing resulted in amelioration or remission of high blood pressure6.”

In the years since these early observations, sleep has been “increasingly recognized [as an important] biological function”. Furthermore, “insufficient and poor quality sleep has been linked to neurocognitive impairments, end-organ dysfunction and chronic health conditions, and increased mortality7”. Sleep-disordered breathing, especially sleep apnea, has been found to be very prevalent. The first major study (in 1993)8 reported that among middle-aged people in the United States, sleep apnea prevalence was 4% in men and 2% in women. Another report estimated that between 12 and 18 million American adults have sleep apnea9. Some evidence, albeit mostly anecdotal, indicates that a similar prevalence exists in many countries. It seems logical to conclude, therefore, that abnormal sleep patterns are an issue to be considered in evaluating many, if not all, hypertensive patients.

Key words: Sleep disorders, blood pressure, hypertension.
Evidence exists that (1) sleep-disordered breathing is associated with hypertension, (2) the association is causal, and (3) treating sleep-disordered breathing reduces elevated blood pressure.

(1) The relationship between sleep-disordered breathing and hypertension.

Figure 1a shows the prevalence of hypertension (>140/90 mm Hg) as a function of the apnea-hypopnea index in a cohort of 6,132 subjects over 40 years of age, 52.8% of whom were women. (The apnea-hypopnea index is the average number of apnea and/or hypopnea episodes per hour of sleep. Apnea is a complete cessation of airflow while hypopnea is a decrease in airflow resulting in an oxygen desaturation of 4%). These data demonstrate a direct relationship between the severity of sleep-disordered breathing and the prevalence of hypertension.

(2) The causal effect of sleep-disordered breathing.

A report by Peppard and colleagues also demonstrated the association between hypertension and sleep-disordered breathing, this time in a prospective study involving 709 subjects. These investigators found that the presence of an abnormal apnea-hypopnea index at baseline was predictive of the development of hypertension (>140/90 mm Hg) four years later. Furthermore, the higher the apnea-hypopnea index was, the higher was the odds ratio of developing hypertension (Figure 2). These findings strongly support the causal role of sleep-disordered breathing in the development of hypertension.

(3) Treating sleep-disordered breathing reduces hypertension.

Several studies have addressed what may really be the most important question: if sleep-disordered breathing is a risk factor for hypertension, will treating sleep-disordered breathing reduce, or even eliminate, hypertension? In all of the investigations, the sleep apnea was treated with continuous positive airway pressure, or CPAP. One study, of 19 men who were treated with CPAP for 8 weeks, found a significant reduction in 24-hour ambulatory systolic and diastolic blood pressure among the subset of 14 men for whom CPAP was successful (defined as using the treatment to the required extent and experiencing improvement in daytime symptoms), but no significant blood pressure change in the 5 subjects whose CPAP treatment was unsuccessful.

Another small study compared systolic and diastolic blood pressures in hypertensive and normotensive subjects before and after three months of nasal...
CPAP treatment. A significant decrease in both daytime and nighttime blood pressure occurred in the four hypertensive subjects, but not in the five normotensive ones (see Table).

Because these two studies involved very few patients, it may be premature to draw definitive conclusions from them. Furthermore, a recent study involving 68 subjects failed to confirm their findings. A companion editorial to this last study underscored that these new data should stimulate “extensive trials in order to evaluate the impact of this treatment [CPAP] on blood pressure in obstructive sleep apnea syndrome”

Irrespective of these different results, the totality of evidence suggests that sleep apnea should be actively treated in hypertensive subjects. (1) Obesity and Sleep-disordered Breathing.

As seen in Figures 1b and 2, the influence of sleep-disordered breathing on blood pressure elevation is diminished (though nevertheless still significant) when BMI is taken into account. This finding strongly demonstrates that excess body weight is an important confounding factor in the development of sleep apnea and hypertension.

A report from the National Heart, Lung, and Blood Institute, NIH, estimates that as many as half of people with sleep apnea are overweight. Furthermore, on the basis of several cross-sectional studies, obesity appears to be the most important risk factor for sleep apnea and certainly a prime target for intervention if we are to reduce or eliminate the burden of sleep apnea. The independent association between sleep-disordered breathing and changes in body weight has been evaluated in several studies. One demonstrated that “even modest weight control is likely to be effective in managing sleep-disordered breathing and reducing new occurrence of sleep-disordered breathing.” Figure 3, derived from that study’s data on 945 subjects, shows the estimated percent change in the apnea-hypopnea index for selected decreases or increases in body weight and illustrates the independent association between sleep-disordered breathing and body weight. Another study confirmed this finding, though the association between changes in body weight and changes in the apnea-hypopnea index was not as robust and was stronger for men than for women.

### Table

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Day Time</th>
<th>Night Time</th>
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<td>Before</td>
<td>After</td>
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</tr>
<tr>
<td>Diastolic BP</td>
<td>87.5</td>
<td>85.0 ns</td>
</tr>
</tbody>
</table>

Figure 3. Estimated percent change in the apnea-hypopnea index for selected decrements and increments in percent body weight. Data from reference 17.

A study in a cohort of 3,158 subjects who were 18 to 65 years of age showed that the prevalence of obesity was inversely related to total sleep time. Of course, sleep deprivation does not imply sleep-disordered breathing, but this study underlines the complexity of the relationship. Irrespective, the preponderance of evidence indicates that increased body weight is the most important risk factor of sleep-disordered breathing. (2) Hypertension and Obesity.

Data from various iterations of the National Health and Nutrition Examination Survey (NHANES) have demonstrated that in the general population, the prevalence of hypertension in men and women increases as a function of increasing BMI. Figure 4, based on the results of NHANES III (1988–94), shows that in both men and women hypertension prevalence is twice as great for people with BMI greater than 30 as for those with BMI less than 25. The causal relationship of obesity to hypertension is clearly shown by a study demonstrating that reductions in blood pressure and in risk for hypertension can be achieved via weight loss. Moreover, the association between increased body weight and hypertension is independent of sleep-
disordered breathing just as the relationship between sleep-disordered breathing and hypertension has been shown to be independent of obesity. The purpose of this discussion is not to dwell on the mechanism of these associations. Nonetheless, it would be remiss not to mention that obesity, hypertension, and sleep-disordered-breathing involve closely related, if not common, pathways such as the role of leptin and leptin resistance, the role of hyperglycemia and insulin resistance, and the role of sympathetic activation among other possible factors.

The data presented above demonstrate a number of independent associations. First, a strong association exists between hypertension and sleep-disordered breathing as quantified by the apnea-hypopnea index. Indeed, the fact that hypertension develops over time in subjects with elevated apnea-hypopnea index strongly suggests a causal relationship. This is corroborated by reports showing that treating the sleep-disordered breathing lowers blood pressure. Thus, in view of the prevalence of both hypertension (65 million people in the United States alone in 1999-2000) and sleep-disordered breathing, this association represents a huge public health problem.

Then there is the causal relationship between obesity and hypertension, and the other causal relationship between obesity and sleep-disordered breathing. The interdependence of these three relationships is depicted in Figure 5. This cannot be ignored when considering hypertensive patients, their treatment, and the difficulties that may be encountered in controlling their high blood pressure. Given that a large percentage of patients with sleep-disordered breathing are undiagnosed, one must question how good a job we are doing in treating elevated blood pressure in many of our patients, in the absence of addressing an underlying sleep problem. These issues warrant more investigation, and they should be moved to the forefront of public health concerns, as they very likely bear, at least in part, on the poor control of hypertension that is seen worldwide. Indeed, data from a sample of 16 countries reveal that only 13.8% of all people with hypertension have their blood pressure until proper control, and even among people receiving treatment, only 34.0% have achieved the recommended levels.

This paper began with the question “Do sleep disorders have an impact on blood pressure?”. The answer is definitely yes and, therefore, assessing the presence of sleep disorders and providing appropriate treatment should be part of the diagnosis and treatment of hypertension, especially in patients who have an increased BMI.

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References