**HYPERTENSION AND SLEEP**

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**Introduction**

Cardiovascular control is markedly affected by normal sleep with a differential autonomic regulation of the cardiovascular system with the different sleep stages [1]. Blood pressure (BP) and heart rate (HR) decrease throughout non-rapid eye movement (NREM) sleep, particularly during slow-wave sleep (dipping pattern), whereas in REM sleep BP is highly variable and associated with increased wakefulness levels. During the night, normal individuals did not exhibit significant change in cardiac output, and the nocturnal fall in arterial pressure is actually the result of a decrease in total peripheral vascular resistance. Any disturbance in sleep quantity or quality, explained either by sleep habits or sleep disorders, may participate in hypertension development or severity.

In this article, we will successively review the different sleep disorders or sleep habits associated with hypertension and summarize the common pathophysiological intermediary mechanisms explaining the relationship.

**Obstructive sleep apnea syndrome and hypertension**

Obstructive sleep apnea (OSA) is associated with changes in intra thoracic pressures during sleep reflecting variations in respiratory effort, frequent transient arousals, modifications in sleep structure, and intermittent hypoxia. All these factors have an impact on sympathetic activity and may result in long-term sympathetic activation contributing to cardiovascular morbidity. During abnormal respiratory events there is a progressive increase in sympathetic activity and an acute rise in blood pressure, which correlates with the severity of oxygen desaturation. Acoustic respiratory events during sleep are superimposed on chronic adaptations of the cardiovascular system in response to long-term sleep apnea exposure, leading to daytime sustained elevation of sympathetic activity [2]. Obstructive sleep apnea syndrome (OSA) and hypertension are linked in a dose–response fashion. This is true even when taking into account usual confounding factors such as age, alcohol, tobacco consumption, and body mass index (BMI) [3]. Respiratory events and intermittent hypoxia is the main feature leading to sympathetic and renin-angiotensin system (RAS) over-activity and thus to the development of the sustained increase in blood pressure (BP) seen in OSA patients. The endothelial dysfunction evidenced in OSA is also partly explains hypertension, owing to decreased vasodilation and enhanced vasoconstriction, resulting from increased availability of hyperinsulinaemia or other proinflammatory mediators in apneic subjects, especially when overweight, contributes to OSA-induced HT by favouring peripheral vasodilation impairment, endothelial dysfunction, sympathetic hyperactivity, and an increase in renal sodium reabsorption [4]. Hypertension associated with OSA has several characteristics: diastolic and nocturnal predominance and commonly encountered masked hypertension with frequent non-dipper status. Furthermore, as OSA is found in the vast majority of subjects with refractory hypertension, it should be systematically investigated in this situation.

Three meta-analyses derived from 19 randomized controlled trials have demonstrated that continuous positive airway pressure (CPAP), the first-line therapy for moderate to severe OSAS, reduces the 24-h mean BP by approximately −2 mm Hg (pooled estimated effect), Haentjens et al. [5] looked at 12 studies assessing CPAP versus placebo (sham CPAP or pills), including a total of 512 patients. Some of the analyzed studies excluded hypertensive patients whilst others only included hypertensive patients. Furthermore, the presence of an antihypertensive treatment was not constant.

Sleep deprivation studies in normotensive subjects have demonstrated that CPAP treatment. Bazzano LA et al. [6] have investigated in this situation.

**Sleep duration and hypertension**

Sleep duration has decreased in the general population over the last 30 years [8]. In the US, the National Sleep Foundation reported an increase from 12% to 16% of subjects sleeping less than 6 hours on workdays between 1998 and 2005, reflecting voluntary sleep restriction. On the other hand, the prevalence of insomnia complaints was 23% in The Athenogenic Risk in Communities Study (ARIC), a prospective observational cohort involving 13,563 participants aged 45 to 69 years [9]. Two major community-based cohort studies, the Sleep Heart Health Study (SHHS) [10] and the National Health and Nutrition Examination Survey (NHANES) [11] have reported a relation-ship between self-reported short sleep duration and prevalence and incidence of hypertension. Gottlieb et al. [10] have demonstrated from SHHS that short and long habitual sleep duration are both associated with higher prevalence of hypertension when compared with subjects sleeping between 7 and 8 hours per night, after adjustment for possible confounders such as age, sex, race, obesity, apnea–hypopnea index, or lifestyle habits. Short sleep duration was associated with higher prevalence of hypertension in the Korean National Health and Nutrition survey 2001 [12]. Subjects participating in NHANES who had self-reported less than 5 hours of sleep by night demonstrated a higher incidence of hypertension after 8 to 10 years follow-up [11]. This association persisted, even though attenuated, when analyses were adjusted for confounders, body weight in particular.

The relationship between sleep duration and hypertension is age and gender dependent. Adolescents with shorter sleep duration assessed by actigraphy demonstrated higher prevalence of hypertension [13]. Conversely, an association between sleep restriction and incident hypertension was not found in subjects aged between 60 and 86 years of age in the NHANES study [11]. Hypertension was not associated with sleep duration assessed by either self-report or actigraphy in a cross-sectional study of 5058 participants, aged 58 to 98 years of age in the Rotterdam Study [14]. Finally, considering short sleep duration, hypertension was both more prevalent and more incident in women only, in the Whitehall II Study [15].

Short sleep duration and insomnia, although classically related, are different entities. Insomnia entails dissatisfaction with the quality of sleep that can be explained or not by a true reduction in sleep duration. Individuals with short sleep duration do not necessarily suffer from insomnia since they can voluntarily restrict their sleep time. Insomnia is clearly related to psychiatric and psychosomatic disorders, and some insomniac patients have a misperception of their sleep quality. Whether insomnia is associated with increased somatic disorders, cardiovascular in particular, was controversial in the literature. Recently, Ygontzas et al. [16] have demonstrated in a population based study that only insomnia associated with sleep duration < 5 hours (proven by polysomnography) is associated with a five-fold increased risk of hypertension after adjustment for other sleep disorders. Accordingly, in middle-aged subjects of the NHANES, depression was associated with increased incidence of hypertension, but the strength of this link was weakened by 33% after adjust-ment for confounders [17].

Pathophysiological mechanisms underlying short sleep duration and hypertension association.

Sleep deprivation studies in normotensive subjects have demonstrated that BP was increased after nights of sleep restriction [18, 19]. This could mainly be the result of the hypothalamic-pituitary-adrenal axis and elevated sympathetic nervous system activity [19, 20]. Sleep deprivation has also been reported to be associated with systemic inflammation [21], oxidative stress, and endothelial dysfunction — all conditions favouring the appearance of hypertension.

**Restless legs syndrome (RLS), periodic limb movement disorder and hypertension**

RLS is characterized by dysesthesia and leg restlessness occurring predomi-nantly at night during periods of immobility [22]. Unpleasant sensations and the irresistible need to move impair the ability to fall asleep and impair
sleep quality. RLS is associated in 90% of cases with periodic limb movements in sleep (PLMS), which are repetitive flexions of the hips, knees, and ankles during sleep possibly ended by micro arousals. These micro arousals are associated with abrupt increases in blood pressure and sympathetic hyperactivity. PLMS also occur in patients without RLS and are found in 25% of patients undergoing routine polysomnography. Both RLS and PLMS are possibly associated with changes in sleep quantity and/or quality and have been incriminated as causes of hypertension [23].

Among 4000 men aged 18 to 64 years assessed by mail questionnaires, RLS sufferers were more likely to report hypertension after adjustments for age, witnessed apnea, smoking, and alcohol consumption [24]. In a study by Ohayon et al. [25] including 18,980 individuals from 5 European countries, 723 met criteria for RLS and presented with a 2-fold higher risk for elevated blood pressure (21.8 versus 11.1%, respectively, with an OR for hypertension: analyses of the first National Health and Nutrition Examination Survey. Diabetes 1996; 9: 503–505.

References


Conclusion and perspectives

In hypertension, sleep must be taken into account as a relevant life period [1]. Sleep restriction and sleep disorders are both and synergistically associated with increased prevalence and incidence of hypertension. Intervention studies are now needed to assess whether acting to promote voluntary longer sleep duration and/or efficiently to treat sleep disorders could prevent or reverse hypertension.

Figure 1. The common intermediary mechanisms for the link between sleep, sleep disorders, and hypertension. Alterations in sleep quality and sleep disorders are associated with intermediary mechanisms that favour the development of hypertension. Any combination of a pre-existing hypertension, whatever the cause, and sleep disturbances may increase hypertension severity and limit treatment efficacy.

Figure 2. Sympathetic overactivity, endothelial dysfunction, system inflammation, oxidative stress, acute sympathetic surges and non-dipping pattern of blood pressure are common intermediary mechanisms for the link between sleep, sleep disorders, and hypertension. Any combination of a pre-existing hypertension, whatever the cause, and sleep disturbances may increase hypertension severity and limit treatment efficacy.