Systemic Hypertension in Sleep Apnea Syndrome*  
Relationship with Sleep Architecture and Breathing Abnormalities  

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To examine the possible relationship between systemic HT and SAS we compared 21 hypertensive (HT+) and 29 normotensive (HT−) patients for morphologic characteristics, sleep disturbances and respiratory events monitored during a full night polysomnography. There was no significant difference between HT+ and HT− patients with respect to age, weight, BMI, sleep stage distribution and disorganization, apnea-hypopnea index (number of episodes per hour of sleep) and duration (minutes per hour of sleep) nor O2 saturation indices: mean nocturnal and minimum O2 saturation. We conclude therefore that HT in SAS patients is not directly related to morphologic characteristics, sleep disturbances and breathing abnormalities.

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SAS = sleep apnea syndrome; TST = total sleep time; ANOVA = analysis of variance; AI = apnea index; HT = hypertension

Several sources of evidence suggest that systemic HT and SAS are related: (1) sleep respiratory disturbances have been observed in 22 to 48 percent of patients with essential HT;1–4 (2) prevalence of HT in patients with SAS is estimated to be between 50 and 90 percent;5–8 (3) cyclic elevation in arterial pressure occurs in association with sleep apnea;9 (4) treatment by tracheostomy or CPAP has been shown to reverse HT in SAS patients.10–11 However, the nature of the relationship between SAS and HT is still controversial.12 Indeed, SAS is more prevalent among the obese,6,11 males,13 and older age groups15 in which HT is also more frequent.16–18 Therefore, the association between HT and SAS may be related to other variables common to both.

Most previous studies have focused on the prevalence of breathing abnormalities in HT patients. To further examine the possible association between them and HT, we therefore studied 50 SAS patients and compared those with and without HT for: (1) age and morphometric characteristics; (2) sleep architecture; and (3) sleep breathing abnormalities.

Population and Methods

Population

The patients were referred to our sleep clinic by general practitioners and the pulmonary outpatient clinic for daytime hypersomnolence associated with snoring. No referral was made on the basis of the presence of HT. Among 65 patients consecutively recorded with a SAS during an eight-month period we selected 50 patients without significant airway obstruction (FEV1>85 percent predicted) or daytime hypoxemia (SaO2>90 percent) to exclude any patient with overlap syndrome.19

Among the 50 selected patients (six females), 29 were normotensive and 21 hypertensive (three females) according to WHO criteria: resting supine systolic pressure >160 mm Hg and/or diastolic >95 mm Hg at three different examinations using an appropriately sized cuff.20 Routine renal and endocrine testing did not identify a cause for HT in any patient. Smoking behavior was similar in both groups: 68 percent in hypertensive and 77 percent in normotensive patients. At the time of the study, 19 of 21 HT patients were receiving antihypertensive treatment: diuretics (2), beta blocking agents (2), central inhibitor (1), calcium channel blockers (2), ACE inhibitors (5) or multiple drugs (7). The duration of treatment ranged from one to 12 years with no clear relationship to the onset of snoring or supposed duration of SAS. The severity of HT also was variable, 12 patients being controlled with one drug, while the remaining were not well controlled even with multiple drugs.

Polysomnographic studies

Patients reported to the sleep laboratory at 8:00 p.m. after a light dinner and were monitored during a single night for at least 8 h in a temperature-controlled and sound-attenuated room. No alcohol, sedative or hypnotic agent was permitted for the day preceding the study. The standard protocol included: EEG (C3/A2 and C4/A1, of the international 10-20 system), genioglossal EMG and eye movements (EOG).21 Nasal and oral airflows were monitored by two separate thermocouples. Respiratory movements were measured by abdominal and thoracic inductance bands (Respirace). Calibration of the Respirace was performed in the awake supine state using the isovolume method and a pneumotachograph.22 Respiratory effort was assessed by diaphragmatic EMG recorded from cutaneous electrodes placed laterally in the seventh and eighth intercostal spaces. Arterial oxygen saturation was measured by a pulse oximeter (Biox 3700) applied to a finger. The ECG was continuously monitored and snoring was recorded from a microphone placed at suprasternal notch. All signals were recorded on a polygraph (Alvar) at a speed of 15 mm/s.

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FIGURE 1. Distribution of age, weight and BMI (weight/height\(^2\)) in the HT− and HT+ patients with SAS.

**EEG analysis**

Sleep stages were defined visually using standard criteria except that stages 3 and 4 were combined. A stage change was considered when a stable change in EEG pattern was observed for at least 1 min of recording. Arousal was identified as full EEG arousal: i.e., EEG pattern consistent with the wakeful state for at least 60-s duration. The following information was thus obtained for each nocturnal recording: sleep stage distribution, number of arousals and stage changes, TST, sleep efficiency (TST/total dark time).

**Breathing Events**

Apnea was defined as a cessation of airflow for at least 10 s. Episodes of apnea were scored as central when not associated with respiratory efforts, obstructive if accompanied by respiratory efforts and mixed when initiated by central apnea and terminated by obstructive. Hypopnea was defined as a reduction of 50 percent or more in respiratory amplitude from the average of ten preceding breaths monitored on the Resitrace sum signal. Sleep apnea syndrome was diagnosed if the number of apneas and hypopneas (A/H index) was greater than 10/h of sleep (patient less than 60 years of age) or 20/h (patients more than 60 years of age). Mean apnea and hypopnea duration per hour was computed as total overnight duration of apneas and hypopneas divided by TST.

Oximetry values used for analysis were: minimum saturation recorded throughout the night, mean nocturnal saturation and percentage of time spent at a saturation below 90 percent.

**Statistical Analysis**

Hypertensive and normotensive groups were compared: (1) by chi-square analysis using quartiles of the overall distribution as class limits for distribution of age and weight and BMI at controlled age; (2) by ANOVA with factors of age and BMI for the apnea-hypopnea index, oximetry data and sleep architecture variables.

A regression analysis between systemic (systolic and diastolic) pressures and apnea-hypopnea index was made by the least squares method. A value of p<0.05 was taken as significant and results are expressed as mean ± SD. Statistical analysis was made with the SPSS-PC package.

**RESULTS**

**Age and Morphometric Data**

Figure 1 shows that age, weight and BMI distributions were similar. Mean age was: 53.6±10 years in HT− and 58±11 in HT+ patients. Most patients were obese (mean weight: 95±18 kg in HT− and 97±16 in HT+ patients) but no patient was monstrously overweight (maximum weight = 142 kg). Mean BMI was 32.5±5.2 in HT− and 33.9±6.3 kg/m\(^2\) in HT+ patients. Weight and BMI distributions were not significantly different between HT+ and HT− groups when controlled for age.

**Sleep architecture**

Total sleep time was not different: 341±94 min in HT− and 323±91 in HT+ patients. Sleep stage distribution is shown in Figure 2. Stages 3 and 4 and REM sleep were reduced while stage 2 sleep is increased. The only significant difference between groups in sleep stage distribution was seen in stage 1
being slightly more elevated in HT− patients. Sleep disruption was shown by the total number of stage changes: 40 ± 13 in HT− and 29 ± 9 in HT+ patients (NS). Efficiency of sleep was greatly decreased in most patients but was not different between groups: 73 ± 21 percent in HT− and 68 ± 19 percent in HT+ patients. The number of arousals was similar in both groups: 10 ± 6 in HT− vs 6 ± 3 in HT+ patients.

Apnea and Oxygen Saturation Indices

Figure 3 shows the mean values of A/H indices (36 ± 25/h in HT− and 28 ± 17 in HT+ patients) with a mean duration of apneic time of 13.3 ± 10 min/h in HT− and 14.3 ± 9.5 in HT+ patients. In all patients, respiratory events were mostly obstructive and mixed (88 ± 5 percent in HT− and 95 ± 4 percent HT+ patients). No significant difference is seen between HT− and HT+ groups.

In the main results of our study comparing SAS patients without airflow obstruction but with and without HT are the following: (1) the distribution of age and morphometric characteristics in SAS is not different between HT+ and HT− patients; (2) the two groups of patients do not differ significantly with respect to sleep disorganization and breathing abnormalities.

In adult snorers, Hoffstein et al. used multiple linear regression and showed that obesity and age were the dominant factors contributing to diastolic pressure, as commonly observed in epidemiologic studies. However, in our patients, no significant difference was observed for age, weight or BMI. Thus, confounding variables alone are therefore not likely to explain the observed hypertension in SAS patients.

Because short- term sleep deprivation impairs the baroreceptor reflex function during sleep in rats, we postulated that the presence of HT might be observed patients with the most severe sleep disorganization. It is also known that blood pressure normally falls at night 5 to 14 percent below values taken when awake and that this fall may not exist in patients with HT. We are not aware of any previous report concerning the effect of sleep disruption on long-term blood pressure in man. However, in our group of patients, sleep disruption was identical in both groups.

Cyclic elevation in arterial pressure occurs in association with sleep apnea. Long-term sleep respiratory abnormalities could induce permanent HT by several potential mechanisms. First, repetitive sympathetic discharges which presumably cause the tachycardia and increased blood pressure at termination of apnea could be responsible for a permanent hypertension, as seen with repetitive infusions of catecholamines in animals. Indeed, elevated urinary catecholamine excretion has been shown in SAS patients.

Second, rapid changes in blood pressure during apnea could be the cause of a dysregulation of the renin angiotensin aldosterone control. Third, baroreflexes and/or voloareflexes may be reset or have a change in sensitivity secondary to repetitive systemic and intrathoracic pressure swings. Fourth, blood viscosity could be increased by polycythemia secondary to hypoxia and lead to HT or mechanical properties of the vascular bed could be modified by repetitive hypertensive burdens. In the snorers of the study by Hoffstein et al., mean nocturnal saturation and A/H index were significantly related to diastolic blood pressure, but the variances explained by these variables were only 1.2 and 1.7 percent of total variance, respectively. Moreover, the absence of significant differences in respiratory abnormalities, ie, apnea index and oximetry indices, between our HT+ and HT− patients does not favor a strong direct relationship between sustained HT and respiratory disturbances. Furthermore, the values of systolic and diastolic blood pressures with patients awake in our HT+ patients were not significantly related to the AI in contrast to the data of Kales et al.

Finally, the effect of antihypertensive therapy on observed respiratory disorders does not appear to be
important, since only two patients received beta-blockers which may increase apnea index in SAS and only one patient received a central inhibitor agent.

In summary, despite the high prevalence of HT in SAS patients, the present data do not explain the presence of HT by older age, higher values of BMI, or worse sleep disorganization or respiratory disturbances than in normotensive SAS patients without associated COPD. Other hypotheses may be considered: (1) HT and SAS may not be causally related and the effect of SAS treatment on HT may be the result of a change in an associated variable; (2) HT and SAS may be the consequences of the same abnormality of autonomic cardiorespiratory nervous control. Further studies are therefore needed to elucidate the possible link between HT and SAS.

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