Prevalence of Obstructive Sleep Apnea Syndrome in Patients With Sick Sinus Syndrome

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Introduction and objectives. Sleep apnea-hypopnea syndrome (SAHS) has been associated with different cardiovascular diseases. It may even be implicated in the pathophysiology of sick sinus syndrome (SSS). However, the precise relationship between the two syndromes is still unknown. We investigated the prevalence of SAHS in patients diagnosed with SSS.

Patients and methods. Between June 2002 and December 2004, 38 consecutive patients who were diagnosed with SSS by 24-hour Holter monitoring were studied prospectively in our institution. All patients were asked about symptoms of SAHS, and underwent polysomnography out of hospital using a validated monitor.

Results. The patients' mean age was 67 (10) years, 68% were male, and 58% were hypertensive. Holter monitoring demonstrated a maximum heart rate of 87 (6) beats/min, a minimum of 35 (3) beats/min, and a mean of 48 (3) beats/min. Some 24 (63%) patients required pacemaker implantation because of symptomatic SSS. Overall, 39% of patients had symptoms suggestive of SAHS (i.e., an Epworth index or EI>9). Polysomnography showed that only 13% of patients had a normal apnea-hypopnea index (AHI) and that 31.6% (95% CI, 16.8%-46.4%) had SAHS (i.e., AIH>10 and EI>9).

Conclusions. Given that the prevalence of SAHS in the general population is around 3%, our results indicate that it is ten-fold higher in patients with SSS than in the general population. This observation indicates that there may be a relationship between the 2 syndromes.

Key words: *Sick sinus syndrome. Obstructive sleep apnea syndrome. Cardiovascular disease.*

Prevalencia del síndrome de apnea obstructiva del sueño en pacientes con disfunción sinusal

Introducción y objetivos. El síndrome de apnea-hipopnea del sueño (SAHS) ha sido relacionado con varias enfermedades cardiovasculares. Podría incluso estar implicado en la etiopatogenia de la disfunción sinusal (DS), aunque se desconoce la asociación real entre las 2 enfermedades. Pretendemos conocer la prevalencia del SAHS en enfermos diagnosticados de DS.

Pacientes y método. Entre junio de 2002 y diciembre de 2004 se ha estudiado a 38 pacientes consecutivos diagnosticados de DS mediante registro Holter de 24 h. Todos fueron interrogados acerca de si presentaban síntomas relacionados con SAHS y se les hizo una polisomnografía respiratoria con un equipo validado.

Resultados. La edad media de los 38 pacientes fue de 67 ± 10 años, el 68% era varón y el 58%, hipertenso. En el Holter la frecuencia máxima fue de 87 ± 6 lat/min, la mínima de 35 ± 3 lat/min y la media de 48 ± 3 lat/min. El 63% de los pacientes requirió marcapasos por DS sintomática. El 39% tenía somnolencia diurna excesiva (escala de Epworth [ESS] > 9). La polisomnografía demostró que sólo un 13% tenía un índice de apnea-hipopnea/h (IAH) normal y que el 31,6% (intervalo de confianza del 95%, 16,8-46,4) tenía un SAHS (IAH > 10 y ESS > 9).

Conclusiones. Considerando que la prevalencia del SAHS en la población general es de alrededor del 3%, los resultados de nuestro estudio muestran que el SAHS es 10 veces más frecuente en pacientes con DS que en la población general, lo que indica una asociación entre las 2 enfermedades.

Palabras clave: *Disfunción sinusal. Síndrome de apnea/hipopnea del sueño. Enfermedad cardiovascular.*

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INTRODUCTION

Sleep apnea-hypopnea syndrome (SAHS) is characterized by recurrent episodes of partial or total collapse of the upper airway during sleep,[1] leading to the hindrance (hypopnea) or complete obstruction (apnea) of airflow despite efforts to breath. The lack of adequate alveolar ventilation leads to a reduction in

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ABBREVIATIONS

CPAP: continuous positive airway pressure.
SSS: sick sinus syndrome.
ESS: Epworth sleepiness scale.
EF: ejection fraction.
AHI: apnea-hypopnea index.
SAHS: sleep apnea-hypopnea syndrome.

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oxygen saturation and, if the episode is prolonged, to an increase in the arterial partial pressure of CO_2 ($PaCO_2$). These events result in arousals from sleep, which give rise to the daytime symptoms of the disorder: hypersomnia, the sensation that sleep was not refreshing, fatigue, and difficulty in concentrating.

The American Academy of Sleep Medicine (AASM) recently stated that the diagnosis of SAHS requires the detection of obstructive events through the use of a polysomnograph plus the daytime symptoms mentioned above.[2] By this criterion, the prevalence of SAHS in the general adult population is around 3%[3-5]; it is more common in men[5,6] and increases with age.[4,7]

For years it has been suggested that a relationship may exist between SAHS and a number of cardiovascular diseases, including high blood pressure, ischemic heart disease, heart failure, cerebrovascular accidents, and pulmonary hypertension.[8-10] Evidence exists to support a relationship between SAHS and certain supraventricular arrythmias,[11,12] especially atrial fibrillation.[13-15] There is also indirect evidence that it may be related to sick sinus syndrome (SSS). For example, atrial stimulation reduces the number of apnea episodes in patients with SAHS,[16-18] these patients commonly suffer sinus arrest, sinoatrial block and atrial fibrillation (all characteristic of SSS),[19] and non-invasive ventilation treatment with continuous positive airway pressure (CPAP) helps eliminate the bradyarrhythmias they may suffer.[20] In addition, some of the risk factors for SSS and SAHS are the same, e.g., high blood pressure and obesity.

The aim of the present study was to determine the prevalence of SAHS in patients previously diagnosed with SSS. A high prevalence could indicate that SAHS is an etiological factor in SSS. Its early detection and treatment might therefore reduce the prevalence of SSS.

PATIENTS AND METHODS

The study subjects were 38 consecutive patients with SSS, all of whom were enrolled between June 2002 and December 2004. The diagnosis of this condition was established through the detection of chronotropic incompetence, sinoatrial arrests and/or blocks, or 24 h Holter (Cardioscan II® version 10.1) readings indicative

of tachycardia-bradycardia syndrome. All patients kept a diary to record symptoms that might be related to these Holter-detected phenomena. In addition, all underwent an echocardiographic study using a Sequoia® (Acuson) apparatus to assess their ventricular function and to rule out severe ventricular dysfunction. They were then subjected (as out-patients) to a polysomnographic study using a Sibelhome 300® (Sibel, Barcelona) apparatus, and completed a clinical questionnaire on their respiratory symptoms, nocturnal symptoms (snoring, observed apneas, asphyxia, nocturia, etc), medical history, the use of medications, tobacco and alcohol consumption, and anthropometric data. They also answered questions designed to determine their Epworth sleepiness scale (ESS) score. All patients underwent a limited medical examination which included the measuring of blood pressure.

The Sibelhome 300® is a 7-channel digital polygraph whose use has recently been validated. This apparatus records the patient's heart rate, oxygen saturation, body position, abdominal and thoracic movements, snoring, and nasobuccal flow. The results were analyzed manually. Respiratory events were defined according to the criteria of the AASM[2]: apnea, a clear reduction (>50%) in the airflow signal for more than 10 s; hypopnea, a noticeable reduction in the airflow signal (<50%) accompanied by a reduction in oxygen saturation of >3%. For each patient, the total number of episodes of apnea and hypopnea was divided by the duration (hours) of the study to determine the apnea-hypopnea index (AHI), the percentage time that oxygen saturation was <90%, and the mean duration of the apnea/hypopnea episodes. Cut-off points of 10, 20, and 30 were used for the AHI. Sleep apnea-hypopnea syndrome was defined as the combination of an AHI of >10 and an ESS score of ≥9.

Statistical Analysis

A descriptive analysis of the data was performed. Categorical variables were represented as absolute frequencies and percentages. Quantitative variables were represented as means ± the standard deviation (SD). The 95% confidence interval (CI) was calculated for the most significant variables. The Pearson correlation test was used to analyze the linear association between quantitative variables. To determine whether the proportion of patients with SAHS was different to that described for the general population the α coefficient of the z value ($z = P - p / \sqrt{P.Q/n}$) was calculated. Significance was set at $P \leq .05$.

RESULTS

Table 1 shows the main characteristics of the study population. As expected, the mean age of the

TABLE 1. **Population Characteristics (n=38)***

Age, years, mean±SD	66.6±10
Proportion of men, n (%)	26 (68.4)
BMI, mean±SD	28±4
Overweight patients (BMI=25-29), n (%)	14 (36.8)
Obese patients (BMI>30), n (%)	13 (34.2)
Hypertension (SBP≥140 or DBP≥90 mm Hg), n (%)	22 (57.9)
Epworth sleepiness scale, mean±SD	8.0±3.8
Chronic excessive sleepiness (ESS≥9), n (%)	15 (39.5)

SD indicates standard deviation; ESS, Epworth sleepiness scale; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

TABLE 2. **Cardiological Data (n=38)***

FC baseline, beats/min, mean±SD	47.9 (3.3)
Holter data, mean±SD	
Maximum HR, beats/min, mean±SD	86.6±6.3
Minimum HR, beats/min, mean±SD	34.7±3.2
Mean HR, beats/min, ±SD	47.7±3.4
Atrial arrhythmias, n (%)	17 (44.7)
Echocardiography	
EF, n (%)	64.4 (12.8)
Patients with EF<50%, n	0
Patients who received a pacemaker, n (%)	24 (63.2)

*SD indicates standard deviation; HR, heart rate; EF, ejection fraction.

TABLE 3. **Results of the Polysomnographic Study***

Nocturnal Respiratory Disorder (n=38)	Mean±SD	95% CI
AHI	24.9±15.4	20.07-30.33
Obstructive apneas	13.7±11.6	9.89-17.51
Hypopneas	10.8±9.0	7.84-13.76
Central apneas	0.4±0.8	0.14-0.66
Stratification by AHI (n=38)		
Normal (AHI<9.9)	5 (13.2)	0.024-0.239
Mild (AHI, 10-19.9)	12 (31.5)	0.168-0.464
Moderate (AHI, 20-29.9)	9 (23.7)	0.102-0.372
Severe (AHI>30)	12 (31.6)	0.168-0.464
CT90% (n=38)	5.6 ±13	1.33-9.87
Proportion of patients with SAHS (AHI>10+ESS≥9)	12 (31.6%)	16.8-46.4

*SD indicates standard deviation; ESS, Epworth sleepiness scale; CI, confidence interval; AHI, apnea-hypopnea index (per hour); $CT_{90\%}$, mean percentage time with oxygen saturation <90%.

DISCUSSION

The main finding of this study is the high prevalence of sleep-related respiratory problems and SAHS in this population of patients with SSS. Recently, the AASM proposed a consensus definition of SAHS based on an AHI of >5 plus daytime symptoms,[2] the most important being excessive sleepiness. In agreement with this definition, the prevalence of SAHS in the adult population lies between 3.3%[4] and 3.4%,[5] is more common in men (4%) than in women (2%),[3] and increases with age.[5] For this reason, plus the fact that SSS is more prevalent in the elderly (the mean age of the present population was 67 years), it was decided to raise the cut-off for AHI to >10 for the present study. Even with this high cut-off the prevalence of SAHS (AHI>10 and an ESS>9) was 31.6%—almost ten times that seen in the general population. This is not surprising if the results of Gami et al[14] are taken into account. These authors reported that 50% of patients with atrial fibrillation also suffer SAHS. Unfortunately, their study does not report the percentage of patients who also suffered SSS, although it is well known that atrial fibrillation is the most common type of arrhythmia in tachycardia-bradycardia syndrome. In the present study tachycardia-bradycardia syndrome was detected in 45% of the Holter readings; atrial fibrillation was the most common type of tachycardia.

Simantirakis et al[21] also indicate a relationship to exist between SSS and SAHS. These authors reported moderate-severe abnormalities in the heart rate of 47% of the patients they studied (n=23). In addition, they found that after starting treatment for SAHS with CPAP these problems were significantly reduced.

Unfortunately, the present study does not clarify whether SSS facilitates the appearance of obstructive

population was high, as was mean blood pressure, and the majority of patients were men. Table 2 shows the Holter monitoring results; 45% of subjects showed a slow heart rate (fast heart rates caused by atrial arrhythmias were excluded) and suffered atrial arrhythmias (generally atrial fibrillation, which supports the diagnosis of tachycardia-bradycardia syndrome). Table 2 also shows the echocardiography results, which indicate that left ventricular dysfunction was not a problem of the present cohort. The mean ejection fraction (EF) was 64±13%. No patient had an EF of <50%. Twenty four patients (63%) received a definitive pacemaker (mostly in DDD-R mode) due to clinical symptoms associated with SSS. Twenty patients required this procedure soon after having been diagnosed (following the polysomnograph test). The remaining four received their implants due to the appearance of symptoms at some later point.

Finally, Table 3 shows the main results of the polysomnographic study. Only 13.2% of the patients studied had a normal AHI; 31.6% (95% CI, 16.8-46.4) had SAHS. This latter figure is significantly higher (P=.001) than the proportion of people with SAHS in the general population. No significant correlation was found between SAHS and SSS severity. The AHI of the patients who required a pacemaker was no higher than that of those who did not (214±9.9 compared to 26.5±19.2).

apneas or whether SAHS, which generates atrial arrhythmia, ends up causing SSS. The data of Garrigue et al[17,18] on a new treatment for SAHS requiring permanent stimulation of the heart tend to support the first of these possibilities. In their first paper,[17] which involved a study of 15 patients with SAHS, these authors observed episodes of severe sinus bradycardia and even sinus arrests during the polysomnograph test. Later, following atrial stimulation, the patients' obstructive and central apnea problems improved. A hypothesis involving a double mechanism was put forward to explain the improvement in central apnea. In patients with this type of apnea, hypervagotony could be the cause of bradyarrhythmias—therefore permanent atrial stimulation could be of help. In addition, the increase in heart rate caused by electrical stimulation would improve cardiac output, and therefore have a positive effect on the associated pulmonary subedema. However, these authors recognize they have no convincing explanation for the improvement seen in their patients' obstructive apnea. Their work that can be criticized to a certain extent in that their 15 SSS patients also suffered a certain depression in terms of left ventricular function (EF, 54±11%); in fact only 4 patients had a normal EF. In addition, this impairment of ventricular function was worse in the subgroup of patients with central apnea (mean EF, 49%) than in the obstructive apnea subgroup (mean EF, 60%). This is important, not just because there is a close relationship between heart failure and SAHS (as many as 37% of patients with heart failure have SAHS),[22] but because left ventricular dysfunction and the pulmonary subedema it produces are at the root of the typical central apneas seen in Cheyne-Stokes breathing.[23] In the present study, the mean EF was 64±3% and no patient had an EF of <50%. This may have been the reason why the percentage of central apneas (0.4±0.8) observed was practically nil (as is normal in patients with SAHS).

The possibility that SAHS favors the appearance of SSS is supported by the observations of Simantirakis et al[21] This study involved 23 patients, mostly men (somewhat younger than those of the present study with a mean age of 50±11 years), all with moderate-severe SAHS, and all of whom received an insertable Holter for 16 months. The aim was to detect arrhythmias in the first 2 months and, over the next 14, to observe the effect of CPAP treatment on them. Some 47% of these patients showed severe arrhythmia problems over these first 2 months, all of which improved with CPAP until eventually disappearing in the final 6 months of the study

One way or the other, the present study shows a close relationship between SSS and SAHS (which have common risk factors), and the clinical implications are obvious. Further work should determine whether the detection and early treatment of SAHS can prevent the development of SSS, and therefore reduce the incidence of atrial tachycardias and the number of pacemakers that need to be implanted (thus reducing health spending).

Finally, pulmonologists who detect patients with SAHS should think of SSS as a coadjuvant illness, and cardiologists who diagnose SSS should determine whether the patient suffers symptoms indicative of SAHS.

Limitations of the Study

The study had no control group, so a definitive relationship between SSS and SAHS cannot be affirmed; confounding factors may exist that were not taken into account. To confirm the hypothesis that these diseases are linked, further studies with control groups are required. Since this was a preliminary study, follow-up data were not available on changes in the nocturnal respiratory problems of patients who received a pacemaker.

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