Sleep Apnea Year 2006: Review of Publications in *Archivos de Bronconeumología*

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Introduction

Sleep apnea-hypopnea syndrome (SAHS) is characterized by recurrent episodes of upper airway collapse, which may be complete (apnea) or partial (hypopnea). The direct consequences of upper airway collapse are falls in oxygen saturation levels and arousals, which are, in turn, responsible for excessive daytime sleepiness and neurological and psychiatric disorders.\(^1,2\) The prevalence of SAHS has been estimated to be about 4% to 6% in men and 2% to 4% in women.\(^3,4\) Underdiagnosis of SAHS is a universal problem; in Spain, it is estimated that fewer than 10% of cases are diagnosed, and, consequently, treated.\(^5\)

SAHS is usually diagnosed by polysomnography, although portable respiratory polygraphs may be used for selected patients.\(^5,7-9\) Several studies have demonstrated an association between sleep apnea and high blood pressure, cardiovascular and cerebrovascular disease,\(^15-18\) and traffic accidents.\(^19-22\) Continuous positive airway pressure (CPAP) is considered the treatment of choice for SAHS cases with the most pronounced symptoms,\(^23,24\) as it has been shown to improve clinical symptoms (especially daytime sleepiness), quality of life, and the apnea-hypopnea index (AHI).\(^25-29\) and also to reduce traffic accidents.\(^30\) the frequency of cardiovascular events, and even mortality.\(^18\) For all the reasons mentioned, SAHS is considered to be a public health problem of the first order.\(^8,31\)

Sleep Apnea Year

In 2001 the board of directors of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) agreed to implement a program of activities over the period of a year, under the umbrella of what are known as SEPAR Years, sponsored by the Spanish Lung Foundation. The first SEPAR Year was COPD Year in 2002,\(^32-34\) followed by Asthma Year in 2003,\(^35,36\) Pneumonia Year in 2004,\(^37\) Lung Cancer Year in 2005,\(^38\) and finally, Sleep Apnea Year in 2006. SEPAR Years are organized around informative activities referring to a key public health issue and targeted at both the general public and the health care authorities. The target populations for Sleep Apnea Year were the general public, primary care physicians, occupational medicine professionals, driving license testing bodies, consumer organizations, and public health authorities.

The strategic lines along which information and activities were developed were as follows: \(a\) communicating clinical, diagnostic and therapeutic aspects of SAHS of interest to patients, families, and nonspecialist health care staff; \(b\) raising awareness of the issue of road and workplace accidents, and also of the cardiovascular complications associated with SAHS; \(c\) highlighting diagnostic delays, the high prevalence of SAHS, and underdiagnosis; \(d\) drawing attention to sleep apnea in children and possible prevention factors; \(e\) providing information on the relationship between SAHS and obesity, and issuing recommendations on healthy eating patterns; and \(f\) defending the right to a good night’s sleep, and warning of the negative effects of poor sleep patterns on quality of life.

Sleep Apnea Year: Organization and Activities

Sleep Apnea Year was organized by a specially created central committee and 11 regional subcommittees which undertook the following activities:

1. **Cooperation agreements.** The number of cooperating organizations (Figure) totalled 50, 29 of which were private bodies and 31 of which were public institutions. Of the institutions, particularly worthy of mention, apart from the Spanish Ministry of Health and Consumer Affairs and the road traffic safety body (Dirección General de Tráfico, or DGT), was the involvement of most of the regional governments via their health departments. Two private companies, Flex and Carburos Médica, were the main funding sources for the project.

2. **Consensus statement.** Under the supervision of Dr Joaquín Durán, representatives of 17 societies and institutions drew up a statement, now the standard guide for SAHS in the Spanish language.\(^9\)

3. **Marquee/traveling exhibition.** A large marquee measuring 5 meters long, 9 meters wide and 3 meters tall
was commissioned for a traveling exhibition that visited 23 Spanish cities and towns. The marquee housed the following units: a) a film projection area for informative videos; b) SEPAR, DGT, Ministry of Health and Consumer Affairs, Flex, and Carburos Médica stands from which informative leaflets were distributed and sleep apnea questionnaires were administered; c) a spirometry area and a reconstructed sleep laboratory equipped with diagnostic and treatment devices; and d) 4 plasma screens displaying complementary information on an ongoing basis.

4. Information brochure. A sleep apnea brochure containing information directed at the general public was distributed both from the marquee and—through the health departments of the regional governments—from health care centers all over Spain. Over a million copies of the brochure were printed.

5. Training course for primary care physicians. The course, consisting of 3 training seminars (1 given by a primary care physician) and a practical CPAP workshop, was offered in 60 cities and towns in Spain.

6. SAHS diagnostic resources and delays. A special Sleep Apnea Year study on SAHS was published in Archivos de Bronconeumología (see the section “Publications on other aspects of SAHS” below).

7. Sleep apnea and road accidents. A number of activities were implemented in cooperation with the DGT, as follows: the purchase of radio slots and scientific society journal insertions, the publication of articles on Sleep Apnea Year in the DGT road safety magazine Tráfico, and the printing and distribution of an information leaflet on drowsiness at the wheel. In addition, during the traffic safety campaign put in motion for the long weekend coinciding with Constitution Day (6 December), half a million information leaflets were distributed (estimated to have been read by around 1.5 million people).

8. Sleep apnea book. A book in Spanish on controlling sleep apnea (Controlando la apnea del sueño) was written by the SEPAR Nursing Assembly with the aim of providing the general public with direct, simple, and graphic information on sleep apnea. Some 20 000 copies of the book were distributed from the marquee.

9. Scheduled news releases to the media. With a view to maintaining media interest in sleep apnea, a number of news items on subjects of strategic interest were prepared in advance for monthly release to the media.

10. Website. A website (www.apnea2006.org), with links to the sponsors, was created to provide detailed information on Sleep Apnea Year.

Publications in Archivos de Bronconeumología

Having summarized Sleep Apnea Year activities, this article will now focus on reviewing and commenting on articles published in Archivos de Bronconeumología between January 2006 and February 2008, with a view to determining the scientific focus of sleep apnea publications during and after Sleep Apnea Year. A search was conducted, for the period indicated, by inserting the search string Sleep apnea and Arch Bronconeumol in the PubMed search engine. The authors analyzed each publication to ensure that they genuinely dealt with the subject of sleep apnea, with the result that 2 articles were excluded. In order to place the information resulting from this first search in perspective, publications on sleep apnea for 2 identical time blocks before 2006 (January 2000 to February 2002 and January 2003 to February 2005) were retrieved using the same search and selection strategy; in this case, 4 retrieved articles were excluded.

Table 1 reveals that the overall number of publications on SAHS increased; furthermore, in terms of article type, the number of original research articles published increased to the point where these represented 84% of the total for the period that reflected Sleep Apnea Year. Table 2, which categorizes SAHS publications by topic, shows that articles on diagnosis and treatment were consistently the most frequent; there was also an apparent falling trend in the number of clinical studies in contrast with a rising trend in the number of studies analyzing the repercussions of SAHS.

Publications January 2006 to February 2008

SAHS epidemiology. Obesity is a growing source of concern in developed countries. Although obesity is a clear risk factor for SAHS in adults, there is no clear evidence of this association in children, and cases have even been reported in children failing to thrive.\textsuperscript{39} The aim of a study...
by Sardón et al\textsuperscript{40} was to determine whether there was any association between SAHS and obesity in a cohort of children aged 2 to 14 years, referred on the basis of a clinical suspicion of SAHS. An in-hospital respiratory polygraphy was carried out on 400 children (mean age, 5 years), 65\% of whom were boys. An SAHS diagnosis (AHI $\geq 3$) was established for 74.5\% (298) of these patients, and no association between obesity and AHI was demonstrated. A limitation of this study was the fact that respiratory polygraphy rather than polysomnography was used as the diagnostic tool. Respiratory polygraphy is not standardized for use with children, although there is evidence supporting its use as a screening test.\textsuperscript{43,44} Consequently, the statistical analysis conducted to determine the association between SAHS and obesity only included cases with a positive diagnosis in the linear regression analysis, resulting in lower statistical power than would have been the case had the analysis included both positive and negative polysomnography diagnoses. The study nonetheless raises questions about the association between SAHS and obesity in children, and points to the need for further research with a different design for confirmation.

The fact that the general public and primary care physicians are now more knowledgeable about SAHS has led to a significant increase in the number of referrals to respiratory medicine specialists. Pellicer Císcar\textsuperscript{42} compared quantitative and qualitative changes in the health care demands made on the respiratory medicine department of a regional hospital for 2 periods 10 years apart: 1992-1993 and 2002-2003. An analysis of patient characteristics revealed that the reason for referral that experienced most growth between the periods was a suspicion of sleep apnea—to the point where this became the most frequent reason for consultation in 2002-2003. It would be interesting for further studies to be conducted with the same aim of determining the proportion of SAHS referrals among all visits to pulmonology specialists.

**Clinical aspects of SAHS.** In view of the fact that the demand for sleep studies is growing, and given that SAHS manifests itself differently in adults and children,\textsuperscript{43} the study by Llombart et al\textsuperscript{44} aimed to evaluate the characteristics of childhood SAHS and to determine whether there were any differences in symptoms, severity, or treatment between children with tonsillar hypertrophy and children with concomitant conditions that increased the risk of SAHS. The cases of 58 children, 42 with tonsillar hypertrophy and 16 with additional conditions favoring SAHS, were reviewed retrospectively. Although the study was descriptive and retrospective, it was interesting from the point of view of observing the differences in clinical manifestations between children and adults. Children with SAHS in this study suffered from recurrent infections, failure to thrive, hyperactivity, and neurological and psychiatric manifestations, whereas sleepiness and obesity were very infrequent. Obesity, however, was more common in the group with additional conditions favoring SAHS, as were craniofacial abnormalities and longer periods of nocturnal desaturation. This group also more frequently required combined treatment with CPAP and surgery.

The Functional Outcomes of Sleep Questionnaire (FOSQ) is a test specifically designed to evaluate quality of life in individuals who experience sleep disorders.\textsuperscript{45} A Spanish language version has been validated,\textsuperscript{46} but the reference values for diseased and healthy populations are unknown, and, although it is widely used, its usefulness in terms of specifically evaluating the impact of sleepiness on patients with SAHS has not been determined. A study by Vidal et al\textsuperscript{47} evaluated 31 patients

<table>
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<th>TABLE 1</th>
<th>Articles on Sleep Apnea Published in Archivos de Bronconeumología, Categorized According to Publication Type*</th>
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<tbody>
<tr>
<td>Original research articles</td>
<td>10 (77%)</td>
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<tr>
<td>Editorials</td>
<td>–</td>
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<tr>
<td>Special articles</td>
<td>–</td>
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<tr>
<td>Reviews</td>
<td>2 (15%)</td>
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<tr>
<td>SEPAR recommendations</td>
<td>–</td>
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<tr>
<td>Case reports</td>
<td>–</td>
</tr>
<tr>
<td>Letters to the editor</td>
<td>1 (8%)</td>
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<tr>
<td>Recommendations and guidelines</td>
<td>–</td>
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<tr>
<td>Articles in supplements</td>
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<td>Total</td>
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<th>TABLE 2</th>
<th>Articles on Sleep Apnea Published in Archivos de Bronconeumología, Categorized According to Topic</th>
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<tr>
<td><strong>January 2000 to February 2002</strong></td>
<td><strong>January 2003 to February 2005</strong></td>
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<tr>
<td>Epidemiology</td>
<td>1 (7.7%)</td>
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<tr>
<td>Pathogenesis</td>
<td>1 (7.7%)</td>
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<tr>
<td>Clinical signs</td>
<td>2 (15%)</td>
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<tr>
<td>and symptoms</td>
<td>–</td>
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<tr>
<td>Diagnosis</td>
<td>4 (31%)</td>
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<tr>
<td>Repercussions</td>
<td>–</td>
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<tr>
<td>Treatment</td>
<td>4 (31%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>1 (7.7%)</td>
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<td>Total</td>
<td>13</td>
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with SAHS and 31 apparently healthy subjects. In addition to obtaining reference values, the study demonstrated that the FOSQ, compared to the Epworth Sleepiness Scale, is a good instrument for evaluating the impact of sleepiness on activities of daily living, and, consequently, would be of practical use in assessing response to treatment. Like other quality-of-life scales for SAHS, the fact that the FOSQ is time-consuming to administer limits its usefulness in routine clinical practice. It would therefore be useful to have available a validated test—for example, an analog scale or similar—that required less time to administer.

**SAHS diagnosis.** Split-night polysomnography is widely used, particularly in countries like the United States where respiratory polygraphy and auto-titrating CPAP are not routinely used and where insurance companies do not reimburse the cost of such tests. A study by Ciftci et al evaluated polysomnography recordings for 45 patients with SAHS (AHI ≥ 5) by dividing the recording period into 2 parts: the first 3 hours and the remaining hours. The aim was to determine whether the characteristics of the first 3 hours of polysomnography recording were similar to both the second part of the recording and the entire recording (that is, the first and second parts together). The amount of deep sleep differed (with more deep sleep in the first 3 hours), as did the amount of rapid eye-movement (REM) sleep (with more REM sleep in the second period), but there were no differences in the AHI. It could safely be concluded, therefore, that the first 3 hours of a recording will reflect respiratory changes that occur throughout the entire night. Furthermore, given that the second part of the recording has been shown to be similar to the first 3 hours, there would be no reason not to perform CPAP titration in this second period. These results are consistent with those obtained in other studies in which CPAP titrated in the first part of the night was used effectively during the second half of the polysomnographic period. It would be interesting for future studies to determine whether respiratory polygraphy with self-titrating CPAP in the patient’s home results in a better cost/effectiveness ratio than split-night polysomnography.

Pulse oximetry is a recording technique that has traditionally been widely used in SAHS diagnosis, but which is now no longer recommended because specificity is high but sensitivity is low. Most pulse oximetry studies have been performed at altitudes below 2000 meters. However, as a consequence of a shift in the position of the oxygen-hemoglobin dissociation curve, a reduction in $\text{PaO}_2$ may lead, in theory, to small ventilation changes that cause oxygen desaturation. There is growing interest in simplified single-channel diagnostic systems, such as oximetry with subsequent self-titrating CPAP or airflow measured by a nasal prong. A study by Torre-Bouscoulet et al. performed in Mexico City, 2240 meters above sea level, compared 2 nonrandomized groups of patients with suspected SAHS. The first group, consisting of 38 patients, underwent conventional polysomnography, with airflow measured by a nasal prong. The second group, consisting of 30 patients also with suspected SAHS, was studied using a single-channel nasal airflow system (ApneaLink, ResMed Corp, Poway, California, USA) and pulse oximetry (not incorporated in the ApneaLink device). Hypopnea during polysomnography was defined as a decrease in airflow associated with desaturation or arousal; hypopnea was defined only as a decrease in airflow when using the ApneaLink device. In the analysis of the desaturation index detected by pulse oximetry, the readings obtained for the 2 devices (polysomnograph vs the ApneaLink device) were processed separately; for both groups, the only criterion was desaturation. There was good agreement between the AHIs detected by both polysomnography and the ApneaLink, and the desaturation indices detected by pulse oximetry. Also assessed, considering several cutoffs, was the diagnostic yield, and sensitivity was observed to be greater than specificity. Further studies are needed to demonstrate whether the diagnostic efficacy of pulse oximetry systems is greater at this altitude than at sea level.

The growing demand for sleep studies is leading to delays in access to diagnostic services. As polysomnography is both costly and time-consuming, however, there is a need to explore the use of simpler diagnostic systems. The portable respiratory polygraph, which has 4 to 6 recording channels (a Level III system according to the American Academy of Sleep Medicine), has been shown to be effective in supervised hospital settings. A number of studies of home use of respiratory polygraphy have been conducted. However, there have been many methodological differences in terms of the devices studied and their airflow measurement systems, logistical setups for providing home equipment, and definitions of apnea and AHI cutoff points; furthermore, both automated and manual analyses were conducted, and few of the studies included a cost/benefit analysis. It is therefore difficult to say that the level of available evidence is high. Alonso et al performed a study aimed at evaluating the diagnostic reliability and cost of using a respiratory polygraph (Edentrace II, Edentec Corp, Eden Prairie, Minnesota, USA) that measured flow through a thermistor compared to using conventional polysomnography. Recordings were made in the home setting, where suitably trained nurses assisted patients in fitting the equipment. Included in the study were 45 patients with suspicion of SAHS. Taking an AHI ≥10 as the basis for diagnosis, the polysomnography indicated SAHS prevalence to be 46.6%. The most efficient respiratory disturbance index (RDI) cutoff for the respiratory polygraph was 11.6, and the most sensitive and most specific cutoffs were 7.2 and 13.7, respectively. Bearing in mind that the pretest probability of presenting SAHS was 46.6%, diagnostic probabilities would be calculated as follows: if respiratory polygraphy yielded an RDI <7.2 (the sensitive cutoff), then the posttest likelihood of presenting SAHS would fall to 13.6%, whereas if respiratory polygraphy yielded an RDI ≥13.7 (the specific cutoff), then the posttest probability of presenting SAHS would be 92.8%. The cost per person was estimated to be €147 for respiratory polygraphy and €179 for polysomnography.

The study by Jurado Gámez et al. which evaluated 52 patients, had an aim and methods similar to those of
the previous study. The respiratory polygraph (Compumedic Series-P Screener, Compumedic Sleep Ltd, Abbotsford, Australia) recorded airflow using a thermistor and nasal pressure sensor. Patient selection was, on the face of it, similar to that of the study by Alonso et al\(^5\)(clinical suspicion of SAHS), although, for the same polysomnography cutoff point (AHI \(\geq 10\)), prevalence was 90%; this high prevalence places limitations on the evaluation of diagnostic efficacy parameters (specificity and predictive values). With a cutoff point of AHI \(\geq 10\) for both polysomnography and respiratory polygraphy, sensitivity was 87%. In the study by Alonso et al, pretest sensitivity was 90% for the sensitive cutoff, and 61% for the specific cutoff. The best area under the receiver operating characteristic curve was for an AHI cutoff of 5.6 in respiratory polygraphy in the study by Jurado Gámez and coworkers, whereas a cutoff of 11.6 was found to offer the best area under the curve in the study by Alonso and coworkers. Although the same parameters were not used to calculate cost in the 2 studies, both found that respiratory polygraphy was less costly than polysomnography (€153 for respiratory polygraphy and €255 for polysomnography in the study by Jurado Gámez and coworkers).

Although these 2 studies indicate that home respiratory polygraphy is both diagnostically effective and cost efficient, they also vary greatly in terms of results, for which reason multicenter studies based on larger samples are necessary. Another issue worth investigating is whether cost savings could be made in logistical aspects, that is, in delivering the system and explaining its use. Two logistical approaches are typical in Spain.\(^5\) One alternative is for patients come to the hospital during the day, collect the respiratory polygraph, and obtain the information they need to set it up at home. The second approach is for specialist staff (from the hospital, or, more frequently, from a CPAP supplier) to take the equipment to the patient’s home and explain its use; in this, case, the patient sets up the equipment for overnight recording, or, alternatively, the supplier’s staff (as was the case in the 2 studies described above).

Underdiagnosis of SAHS is a serious problem. As mentioned, around 90% of patients with SAHS are estimated to go undiagnosed and untreated. A number of approaches to resolving this problem have been proposed. An example can be found in the information campaigns targeted at the general public, health authorities, and primary care physicians (as organized during the SEPAR Sleep Apnea Year). In regard to primary care physicians, the efficacy of a specific training plan has not been studied in depth, although an article by Martínez-García et al\(^5\) touches on this issue. A group of 16 primary care physicians from the same health care area were provided with additional information on SAHS in 2 seminar-workshops; they were also issued with a protocolized referral form, and enabled to directly contact a hospital sleep unit. Another group of 21 primary care physicians from the same area who received no information served as the control group. Data were collected for both groups before and after the training period, that is, between January and June 2005 and between January and June 2006. The trained physicians made significantly more referrals and the level of agreement between data recorded by these physicians and the specialists was greater. Although the study was limited by the fact that it was conducted in a small health care area, its results would seem to indicate that increasing the scientific motivation of primary care physicians would reduce the rate of underdiagnosis of SAHS and improve referral quality.

The high prevalence of SAHS, its serious repercussions, questions of treatment efficacy, and underdiagnosis have all led to an increase in the demand for sleep studies, and this demand, in turn, has led to longer waiting lists. The situation with regard to SAHS diagnosis needs to be understood so that specialists and health care authorities (who, ultimately, are responsible for resolving the problem) have the information necessary to adapt resources to needs. Several studies evaluating SAHS diagnosis have been performed in Spain.\(^6,56-58\) The most recent study, conducted during Sleep Apnea Year, was based on a survey of 780 hospitals listed in the catalogue of the Ministry of Health and Consumer Affairs.\(^5\) Only 29% of the 780 hospitals evaluated patients with suspected SAHS. The mean wait time for a consultation was 61 days, the mean wait time for respiratory polygraphy was 224 days, and the mean number of respiratory polygraphs per 100,000 inhabitants was 0.99 (compared to a recommendation of 3 devices). The mean wait time for polysomnography was 166 days, and the mean number of polysomnography beds per 100,000 inhabitants was 0.49 (compared to a recommendation of 1 bed). Finally, only 18% and 33% of the centers offering respiratory polygraphy and polysomnography, respectively, employed a technician for daytime readings—which undoubtedly accounted for poor optimization in terms of equipment use. The authors of this study concluded that resources were very inadequate, leading to waiting lists that were unacceptably long. Although it is acknowledged that the SAHS diagnostic situation has improved with respect to past decades, the fact is that much remains to be done, and health care authorities urgently need to dedicate more resources to this public health problem.

Repercussions of SAHS. The association between congestive heart failure and SAHS is well established.\(^59\) The gold standard for diagnosing heart failure is catheterization, although noninvasive methods, such as echocardiography, radioactive isotope imaging, and carbon dioxide (CO\(_2\)) rebreathing are also used. In a study of patients with SAHS, Alonso-Fernández et al\(^60\) evaluated cardiac output measurement using both the equilibrium and exponential CO\(_2\) rebreathing techniques, comparing variability and reproducibility with reference to left ventricular function as assessed by echocardiography. Cardiac output evaluated by the CO\(_2\) rebreathing techniques correlated—although only moderately—with systolic ventricular function as recorded by echocardiography. Of the 2 rebreathing techniques, the equilibrium technique proved to be less variable and more reproducible. This study indicates that in determining cardiac output in patients with SAHS, CO\(_2\) rebreathing techniques do not appear to be a viable alternative to estimating ventricular function by echocardiography.
Around half of all patients receiving treatment for hypertension continue to have high blood pressures, and in 10%, hypertension persists despite treatment with a combination of drugs.61 Although some studies have associated difficult-to-control hypertension with an increased number of apneic events,62,63 it should be noted that the definition of the problem varied between them. Martínez-García et al64 studied 49 patients in order to analyze the relationship between apneic events and difficult-to-control hypertension, understood as blood pressure remaining high despite treatment with 3 or more antihypertensive agents. Day- and nighttime systolic blood pressure measured by a 24-hour ambulatory monitoring device was significantly higher in the 14 patients with severe SAHS (AHI ≥30), compared to the 15 patients with mild SAHS (AHI between 10 and 29), and compared to the 20 patients without SAHS (AHI <10). Although no differences were observed in nighttime diastolic pressure, the daytime values differed in patients with severe and moderate SAHS. Likewise, patients with severe SAHS took more antihypertensive agents. After adjustments were made for age and sex, a significant positive correlation between both systolic and diastolic pressure and body mass index (BMI) was observed in patients without SAHS; no correlation was found with the AHI, however. Patients with both mild and severe SAHS showed significant positive correlations with the BMI and AHI, again after adjustments for age and sex. Regression analysis revealed both the AHI and BMI to be independently associated factors, although the AHI had a higher predictive value. This study confirms the high prevalence of SAHS in patients with difficult-to-control hypertension, pointing to 2 prediction factors, namely, obesity and SAHS. Further studies need to investigate the possible existence of a causal relationship by analyzing whether treatment with CPAP would improve control over blood pressure when the BMI remains unchanged.

Hyperuricemia is frequently observed in patients with SAHS and is almost certainly associated with obesity.65 although it could be a marker of tissue hypoxia.66 Hyperuricemia has been associated with SAHS on the basis of nighttime urinary excretion levels of uric acid,67,68 and, for this reason, Ruiz et al69 posed the question as to whether uricemia could be a biological marker of SAHS. These authors retrospectively analyzed a sample of 1135 subjects suspected to have SAHS and on whom respiratory polygraphy (n=819) or polysomnography (n=316) had been performed. The study demonstrated an association between uricemia and the number of apneic events and desaturations. Nevertheless, when adjusted to take account of confounding factors (mainly BMI), the association was found to be spurious, indicating that since uricemia is not an independently associated factor it has no predictive value. Since other studies have reported that nighttime urinary excretion of uric acid falls in patients with SAHS treated with CPAP,66,68 it is likely that the hypoxemia caused by SAHS raises uric acid levels, but that obesity produces a greater effect.

The episodes of hypoxia followed by reoxygenation resulting from apneas and hypopneas may release an excess of free radicals, to the point where antioxidant capacity is overstretched, thereby giving rise to oxidative stress.70 This oxidative stress may, in turn, lead to endothelial dysfunction and the development of cardiovascular conditions. Some studies have reported that oxidative stress markers fall once patients with SAHS begin to receive CPAP treatment.71 Hernández et al72 decided to test this hypothesis on a sample of 36 patients with SAHS who were candidates for CPAP treatment and on 10 apparently healthy individuals used as controls. The oxidative stress marker chosen for the study was malondialdehyde, a byproduct of lipid peroxidation. After a mean follow-up of 3 months, it was observed that, after taking into account confounding factors, the oxidative stress marker in patients treated with CPAP fell significantly, whereas there was no change in the control subjects. This study confirms, in a larger sample, findings from an earlier study and highlights the cardiovascular risk of patients with SAHS.

SAHS treatment. There is a growing demand for positive-pressure treatment administered through nasal masks for patients with SAHS or with conditions requiring treatment with noninvasive ventilation.73-77 Since the same circuit is used for inhalation and exhalation, it is very important to avoid CO2 rebreathing by ensuring ongoing renewal of air in the mask. An orifice or window in the mask enables air to be expelled without negatively affecting pressure.78 The aim of the study by Mediano et al79 was to analyze end-tidal CO2 fraction (FETCO2) for the prototype of a new Spanish-made mask compared to 2 commercial models: Profile Lite and ComfortClassic (Respironics Inc, Pittsburgh, Pennsylvania, USA). Included in the study were 11 apparently healthy volunteers, 12 patients with severe SAHS, and 12 patients with hypercapnia but apparently without SAHS. FETCO2 was measured after 3 minutes of treatment with CPAP at pressures of 4, 5, 6, 8, 10, 15, and 20 cm H2O. For the sample as a whole and for the same mask pressure, the prototype had a lower FETCO2 than the 2 commercial masks. When the sample was broken down according to the 3 subgroups, the FETCO2 concentration was lower, from a CPAP pressure level of 4 cm H2O in the patients with hypercapnia, and from 8 cm H2O in the healthy subjects and in the patients with SAHS. This study highlights the need for more information on residual CO2 levels in masks used in routine clinical practice, so as to support decision making about the most suitable masks to use—most especially for patients with hypercapnia who are candidates for treatment with CPAP or noninvasive ventilation. Information on residual CO2 levels should, moreover, be included in the description of technical characteristics for commercially used masks.

Patients with central sleep apneas represent fewer than 10% of all patients studied for suspicion of nighttime apneas.80 This syndrome can present in patients with high or normal daytime PaCO2 and may be either idiopathic or secondary. Llombart et al81 reported the case of a patient with normal PaCO2, central apneas, chronic renal failure, and hyperparathyroidism. Following a parathyroidectomy and the commencement of regular dialysis, the number of central events fell substantially. Residual central apneas
also responded to treatment with CPAP—contrasting with a failed attempt at CPAP treatment prior to surgery and dialysis. These authors also commented on the potential causes of the syndrome in this case.

Access to SAHS diagnostic services is a universal problem,60,62 further aggravated in developing countries by difficulties in obtaining funding for both diagnosis and treatment. In their study, Torre Bouscoul et al63 analyzed 2 factors: the frequency with which treatment was started by patients for whom treatment with CPAP was indicated, and the degree to which patients adhered to treatment. The study took place in a Mexico City referral hospital that generally attends to patients with no public health insurance coverage. Only 45% of Mexicans, in fact, have public health insurance, and insurance cover for treatment with CPAP is not universal. Included in the study were 304 patients who had been recommended for treatment with CPAP; these patients were required to obtain their own equipment. Treatment was started by 55% of the patients; 28% of these patients obtained the equipment free of charge (from a charity or through public health insurance) and the remaining 72% purchased or rented the equipment. Comparing those who initiated treatment to those who failed to do so, the former were covered by public health insurance, had higher RDIs, and were also more likely to have severe SAHS (RDI ≥30 and Epworth Sleepiness Scale > 10). The study did not evaluate whether obtaining the equipment free of charge was a predictive factor; however, given that most of the subjects with public health insurance did not have to pay for the equipment (65%), obtaining the equipment free of charge seems to imply that benefiting from such insurance was a relevant factor. Unlike what happens in developed countries, the Epworth Sleepiness Scale was not a predictor of initiating treatment or adherence. In brief, although this study does not address all doubts about SAHS in developing countries (where public health insurance cover is limited), it would appear that the availability of free treatment and having severe SAHS for which treatment is essential (irrespective of the degree of daytime sleepiness) may be the best predictors of the acquisition of equipment and the commencement of treatment.

**Other aspects of SAHS.** In an article by De Granda Orive and Jareño Esteban,84 59 studies published in 2006 in Archivos de Bronconeumología were reviewed and commented. Four articles on sleep disorders60,64,69,72 were discussed in this review article.

An article by Alonso Álvarez et al85 reviewed SAHS in children. There is growing interest in this topic, and pediatric associations recommend active screening given that prevalence is estimated as being between 1% and 3%.86 Less is known about the disease in children and diagnostic criteria have not been standardized in this population. Very clear differences between pediatric and adult SAHS have been observed, and upper airway abnormalities, (tonsillar hypertrophy in particular), appear to be more frequent in the pathogenesis for children. Nonetheless, the fact that children without SAHS can also present with the same degree of tonsillar hypertrophy as children with SAHS is evidence that other conditioning factors, possibly genetic in origin, may play a part.87 Symptoms in children are also different, with a predominance of nighttime symptoms (snoring, noisy breathing, visible apneas, night sweats, odd sleeping positions with an overextended neck, etc) rather than daytime symptoms (behavior disorders, hyperactivity, poor school performance, stunted growth, etc). Pediatric SAHS is diagnosed by polysomnography, and the time for an apneic event to be considered as such is shorter than for adults, given that even small hypoventilations can cause desaturation. It is not clear what cutoff point for apnea or apnea-hypopnea can be considered abnormal,88 nor what treatment should be administered for mild and moderate cases of SAHS. For severe cases of pediatric SAHS, the first-line treatment is surgery.

**REFERENCES**


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