Arch Bronconeumol. 2014;50(12):528–534

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Review

Home Ventilation Therapy in Obstructive Sleep Apnea–Hypopnea Syndrome☆

Nicolás González Mangado,* María Fernanda Troncoso Acevedo, Teresa Gómez García

Sección de Neumología, Unidad Multidisciplinar de Sueño, Grupo Español de Sueño, Respiratory Research Group-Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain

ARTICLE INFO

Article history:
Received 20 December 2013
Accepted 4 June 2014
Available online 29 October 2014

Keywords:
Sleep apnea
Sleep apnea–hypopnea syndrome
Continuous positive airway pressure
Ventilatory therapies

ABSTRACT

Obstructive sleep apnea–hypopnea is a highly prevalent disease that is often underdiagnosed at present. It has a significant economic and social welfare impact, accounting for a large part of the resources assigned to home respiratory therapies. As part of the 2014 SEPAR Year of the Chronic Patient and Domiciliary Respiratory Care sponsored by the Spanish Society of Pulmonology and Thoracic Surgery, this article reviews the most recent publications on the indications and controversial issues in the treatment of sleep apnea, the latest evidence for indication of various positive pressure devices, and adjustment modes, ranging from the use of empirical formulae or mathematical estimations to modern auto-CPAP equipment, while not forgetting the gold standard of manual titration. Emphasis is placed on the need for monitoring required by patients to ensure treatment adherence and compliance. Finally, other therapies that are not the object of this article are briefly reviewed.

Terapias ventilatorias domiciliarias en el síndrome de apnea-hipopnea del sueño

Palabras clave:
Apnea del sueño
Síndrome de apnea-hipopnea del sueño
Presión positiva continua en la vía aérea
Terapias ventilatorias

RESUMEN

El síndrome de apnea-hipopnea del sueño es una enfermedad muy prevalente, con tasas altas de infradiagnóstico en el momento actual, que conlleva un elevado impacto sanitario, económico y social, y consume gran parte de los recursos destinados a las terapias respiratorias domiciliarias. Con motivo del Año SEPAR 2014 del paciente crónico y las terapias respiratorias domiciliarias, patrocinado por la Sociedad Española de Neumología y Cirugía Torácica, en este artículo se revisa la literatura más reciente publicada sobre las indicaciones del tratamiento de la apnea del sueño y sus controversias, las últimas evidencias de las indicaciones de los distintos dispositivos de presión positiva, así como los modos de ajuste, desde el uso de fórmulas empíricas o estimaciones matemáticas, a los modernos equipos de auto-CPAP, pasando por la titulación manual como «gold standard». Además, se hace hincapié en la necesidad de seguimiento que los pacientes precisan para asegurar la adherencia y cumplimiento de la terapia. Por último, se comentan someramente otros tratamientos, que no son el objetivo del artículo.

Introduction

Population aging, rising obesity figures, and the growing prevalence of chronic diseases make it necessary to place for greater emphasis on home healthcare. Home respiratory therapy is a treatment option that can improve the quality of life of these patients and control healthcare costs while reducing the number of hospital admissions.

In Spain today, approximately 500 000 patients receive home therapies. According to figures published at the end of 2009,[1] 66% of home respiratory therapies are administered to patients with obstructive sleep apnea–hypopnea syndrome (OSAHS).

There are many reasons why OSAHS has gone from being a simple medical curiosity to become a public health issue over the course of the last 25 years. Firstly, at-risk groups are growing, due to

☆ Please cite this article as: González Mangado N, Troncoso Acevedo MF, Gómez García T. Terapias ventilatorias domiciliarias en el síndrome de apnea-hipopnea del sueño. Arch Bronconeumol. 2014;50:528–534.

* Corresponding author.
E-mail address: ngonzalez@fjd.es (N. González Mangado).

1579-2129/

population aging and widespread obesity; and secondly, advances in technology have contributed new diagnostic and therapeutic tools. However, there is no doubt that the most important change is the understanding that OSAHS, characterized by repeated episodes of partial or complete collapse of the upper airway during sleep, confers a negative survival prognosis by increasing, on the one hand, accident risk, and on the other, cardiovascular morbidity and mortality. Treatment options for patients with OSAHS vary depending on the spectrum of gravity of the disease, ranging from general measures, aimed at reducing upper airway collapse, to the surgical interventions or devices. CPAP, consisting of a turbine that delivers continuous positive pressure to the upper airway via a mask adapted to the patient, is clearly the treatment of choice in OSAHS. The scientific evidence is now indisputable,[2–4] and this approach has been shown to be efficient and cost-effective.[5] Moreover, CPAP treatment reduces the risk of road traffic accidents,[6] appears to reduce high blood pressure in a large percentage of patients[7–12] and reduces the cardiovascular[13–15] and cerebrovascular[14–16] consequences of the disease, as well as its mortality.[14,17–19]

Historical Background

Although the first descriptions of sleep apnea go back to ancient times, awareness of OSAHS began to increase dramatically about 30 years ago. In 330 BC, King Pontus was described as an obese glutton who had difficult remaining awake and had to be woken up with needles. Since then the literature has been full of anecdotal descriptions and medical curiosities, yet it was not until the second half of the 20th century that a precise definition was made of this disease that has affected humans for so long. In 1972, Christian Guilleminault first used the term "sleep apnea syndrome", yet it was not until 1981 that Sullivan first used CPAP in the treatment of this entity.

Ind ications for Positive Pressure Therapy

The objectives of OSAHS treatment are assessed in the short term and in the long term. The aim in the short term is to control disease symptoms, primarily excessive daytime sleepiness, and in the long term to reduce the risks associated with this syndrome.

Various scientific societies have established indications for the prescription of CPAP. These are based on OSAHS severity, determined by the AHI (apnea–hypopnea index), and concomitant symptoms and comorbidities. Indeed, today's clinicians unanimously accept this as the treatment of choice in patients with severe OSAHS with symptoms and associated comorbidities. However, the matter is less clear when the diagnosis is not so severe or there are no symptoms and/or associated comorbidities. As a general guideline, CPAP is indicated on the basis of abnormal AHI.[3,16]

The considerable body of scientific evidence available to date suggests that the indications for CPAP on the basis of OSAHS severity, coexistence of symptoms or comorbidities, and in certain situations or particular groups should be reviewed.

With regard to OSAHS severity, measured by AHI, multiple studies show that an AHI greater than 15 is associated with increased cardiovascular risk, with or without associated symptoms, and that the risk is further aggravated in patients with an AHI greater than 30. A recent analysis of the Sleep Heart Health Study and the Wisconsin Sleep Cohort,[19–21] the largest population cohorts in the United States, suggests that increased AHI may also be considered as an independent cardiovascular risk factor of sleepiness.

There is also proven evidence that patients with severe disease (AHI>30) improve on CPAP, although discrepancies on the efficacy of this technique in mild to moderate disease persist. Simon and Collop[22] recently published a review of the latest advances in obstructive sleep apnea, singling out one study[10] on the efficacy of CPAP in patients with mild to moderate OSAHS that concluded that CPAP improves functional outcome (subjective sleepiness and state of mind) of sleepy patients, despite relatively low adherence. Furthermore, Epworth Sleepiness Scale results of over 10 points were not significantly altered.

With regard to comorbidities, the Spanish Sleep Group has published large multicenter, randomized, controlled studies analyzing the benefit of CPAP in the treatment of systemic hypertension. A study published by Durán-Cantolla et al.[11] found a statistically significant reduction in blood pressure figures in patients with systemic hypertension and obstructive sleep apnea treated with CPAP, although the expected 3 mmHg target (reduction of 2.1 mmHg for systolic and 1.3 mmHg for diastolic pressure) was not reached. Nevertheless, taking into account the prevalence of hypertension and the coexistence of comorbidities, even a minimal reduction of blood pressure with CPAP may be beneficial. Later, the HIPARCO study[23] in patients with moderate to severe OSAHS and hypertension refractory to pharmacological treatment showed that CPAP for 12 weeks reduced mean and diastolic blood pressure and improved nocturnal blood pressure patterns.

The prevalence of obstructive sleep apnea has increased worldwide due to the current obesity epidemic. Drager et al.[24] published a recent review supporting the idea that obstructive sleep apnea exacerbates the cardiometabolic risk in obesity and in metabolic syndrome. According to these authors, current evidence has shown that cardiovascular risk markers, including sympathetic activation, systemic inflammation and endothelial dysfunction, increase significantly in obese patients with OSAHS compared to those without OSAHS. This shows that OSAHS is not simply a phenomenon secondary to obesity. Results from animal models and OSAHS patients show that intermittent hypoxia worsens obesity-related metabolic dysfunction, increasing insulin resistance and non-alcoholic fatty liver. A recent study[25] indicated that effective treatment of OSAHS with CPAP over 3 months significantly reduced several metabolic syndrome components, including blood pressure, triglyceride levels and visceral fat, prompting the authors to conclude that diagnosis and treatment of this disease may reduce the cardiovascular risk of obese patients.

With regard to symptoms, CPAP is clearly the first line of treatment in patients with symptomatic obstructive sleep apnea. However, the indication of CPAP in patients with few or no symptoms is still in dispute. Barbé et al.[12] performed a multicenter, randomized, controlled study to determine the effect of CPAP on the incidence of hypertension and cardiovascular events in 723 non-sleepy patients with moderate and severe OSAHS (AHI>20). They concluded that in non-sleepy OSAHS patients CPAP treatment did not provide a statistically significant reduction in the incidence of hypertension or cardiovascular events compared to standard lifestyle and dietary measures. It should also be pointed out that the study was limited insofar as the sample size could not be accurately calculated due to the lack of previous similar studies. The protective effect of CPAP may also have been overestimated, and significant differences in the association between the treatment and the outcome could possibly have been obtained with a larger sample size and a longer follow-up period. In this respect, when the long-term effect (1 year) of CPAP was analyzed in non-symptomatic hypertensive patients with sleep apnea,[26] CPAP was associated with a small reduction in blood pressure, although this effect was clear only in patients with a treatment compliance of more than 5.6 h/night.

OSAHS studies in certain special populations (women and elderly subjects) deserve special attention.

Many aspects of OSAHS in women remain controversial due on the one hand to lack of data on prevalence,[27] and on the other to ignorance of the consequences and impact of treatment in this population.[28,29] Most studies on the cardiovascular risk of OSAHS and how it improves with CPAP were performed in men. Possible

differences in the typical clinical manifestations and response to treatment between genders have not yet been defined. Campos-Rodríguez et al.[30] analyzed a cohort of women with a diagnosis of OSAHS to investigate whether sleep apnea could be a risk factor for cardiovascular death, and whether CPAP treatment improved that risk. Although the authors point out the limitations of the study (observational, non-randomized, use of two different diagnostic methods), they conclude that severe OSAHS in women is also associated with cardiovascular risk, and that this risk can be reduced with appropriate CPAP treatment.

Likewise, there are remarkably few specific studies on the diagnosis and management of OSAHS in elderly patients. The prevalence of OSAHS in this population is high, and is estimated to be about 15%–20% in subjects over 65 years of age.[31] It is thought that clinical manifestations may differ, or simply, that the neurosensorial problems that appear with age would make them more difficult to detect. Young et al.[32] found that after the age of 50, many patients are unaware whether they snore or suffer apneas, key symptoms in the current algorithm for determining the pretest probability of OSAHS. Treatment efficacy in elderly patients, either in the short or long-term, has not been evaluated in any clinical trial. In a recent study in patients over 65 years of age, Martínez-García et al.[33] found that CPAP was associated with a reduction in cardiovascular death. Until new evidence is available, decision-making will continue to be based on clinical trials performed in young adults.[34] There is no question that studies with a higher level of evidence are needed to clarify the appropriate management of OSAHS in elderly patients. Until such time, the Spanish Sleep Apnea Consensus[35] and recent publications from the Spanish Sleep Group[36] recommend that patients be evaluated on an individual basis and that treatment should not be withheld only on the basis of age.

Lastly, OSAHS is very prevalent in the pediatric population due to a series of pathophysiological processes causing airway dysfunction during sleep. Because of the association between OSAHS and cardiovascular, neurocognitive and metabolic comorbidities from an early age, the consensus document on sleep apnea–hypopnea syndrome in Children[37] and a recent update of the American Pediatrics Academy clinical guidelines[38] call for systematic sleep studies in children with signs and symptoms suggestive of OSAHS. Treatment decisions must be based on polysomnography results, and on symptoms and risk factors. As a rule, first line treatment should be adenotonsillectomy, although there is growing evidence on the benefits of nasal steroids or montelukast in cases of moderate OSAHS.[39] One patient population, consisting of obese children with craniofacial abnormalities or presurgery AHI>20, has significant residual OSAHS despite surgery. In these patients, it is important to confirm that OSAHS has been corrected, and if not, they may be candidates for CPAP or bilevel positive airway pressure (BIPAP).[40] There are also several studies showing the efficacy of nasal CPAP in these patients, although adherence is the greatest obstacle to the effective use of this treatment.[41,42]

Continuous Positive Airway Pressure. Graduation Methods

Optimal pressure for CPAP treatment must be calculated on an individual basis. The very first step, regardless of the choice of pressure regulation method, is to inform and prepare the patient. Training, education and the selection of the appropriate equipment for each patient will determine, to a large extent, treatment tolerance and long-term compliance.

Various methods have been developed for measuring the required level of pressure, such as empirical calculation using mathematical estimates, auto-CPAP titration and polysomnography after CPAP titration.

Titration polysomnography is the best method available and is considered the gold standard in the exact measurement of the CPAP pressure level required for correcting respiratory events (apneas, hypopneas, snoring, arousals and desaturations).[3,43] Its disadvantages lie in the cost and the time required for conducting and analyzing the study.

The use of empirical formulae for simplifying CPAP pressure calculation has been analyzed in many studies. However, there are considerable difficulties involved in developing and validating a common formula for all populations. A PubMed search shows that in recent years several studies with small modifications of the standard formula adapted to various populations[44] have been published in high-impact journals.

Another alternative may be to perform a split-night study. This option, which has economic advantages, may have drawbacks such as insufficient time for appropriate CPAP adjustment and difficulty in adapting to the device, thus affecting the quality of sleep.

Furthermore, correct selection of final pressure is complicated by the fact that some studies have shown that required pressure falls by up to 2 cm H_2O after a period of treatment, once airway edema has been corrected or reduced.[45]

Several publications have documented the possibility of carrying out titration in the patient's home using self-adjusting equipment, known as auto-CPAP.[46,47] One of the most important recent studies is that of Masa et al.[47] in 360 OSAHS patients in whom CPAP was adjusted on the basis of polysomnography, auto-CPAP or mathematical calculations. Higher residual AHI was observed after empirical adjustment, but the difference between the other two methods was not significant.

Comparative studies have been conducted on clinical efficacy and costs, comparing auto-CPAP titration and manual titration in patients with moderate to severe OSAHS with no associated comorbidities. The estimated cost per study night for manual titration was $817, compared to $647 for auto-CPAP in the laboratory, or $132 for auto-CPAP adjustment in the home. An intent-to-treat analysis confirmed the efficacy of auto-CPAP compared to manual titration.[48]

Continuous Positive Airway Pressure. Forms of Administration

Generally, when the appropriate pressure has been established for each patient, home fixed pressure CPAP (no variation between inspiration and expiration) is prescribed. Some devices offer the possibility of slightly reducing the pressure at the start of expiration using different systems (e.g. C-flex, EPR) to improve patient comfort. In certain cases, home auto-CPAP is prescribed.

Home ventilation therapy with auto-CPAP was studied in a review article[49] with a meta-analysis of 24 randomized trials in which efficacy or quality of life in patients on auto-CPAP was compared to other systems with fixed CPAP after adjustment. No significant clinical changes were found between the devices. Considering the higher cost of auto-CPAP devices, this treatment should only be considered in selected cases with wide range of parameters recorded on different nights.[50]

It is important to bear in mind that not all auto-CPAP systems work in the same way, nor do they give the same results. Several auto-CPAP systems are available, but the most widely accepted are those which modify pressure on the basis of the inspiratory flow wave measured by a pneumotachograph and include a pressure transducer for recording pressure, flow, volume and leakage. It is essential to choose the right auto-CPAP system. The main limitations of these devices derive from the algorithm itself, which is often undetermined. In general, to adjust pressure, these devices respond primarily to limited flow and snoring, and as a result

the required pressure is often overestimated. Moreover, when the patient has other comorbidities, such as hypoventilation or cardiovascular disease, along with central events, response cannot be predicted.[51] For these reasons, titration with auto-CPAP should be avoided in complex patients.

Continuous Positive Airway Pressure Compliance

Since CPAP is not a curative treatment, being simply a mechanical pressure effect, it is only effective during use, and therefore must be used continuously. Many studies have shown a correlation between patient adherence and treatment results. Accordingly, as with other therapies in chronic diseases, it is particularly important to supervise and follow-up treatment compliance. In this regard, some studies have attempted to identify or establish profiles of patients with the best compliance, studying variables such as age, sex, educational level, daytime clinical manifestations, apnea severity or CPAP pressure.[52,53] Of all these parameters, perception of improved symptoms has the greatest effect on compliance. Obviously, side effects affect the degree of compliance, but it seems that the situation can be controlled with early identification and correction of any adverse events.

In order to reduce expiratory pressure and thus improve patient comfort, CPAP devices incorporating the C-flex system were created. A metaanalysis[54] and a multicenter study[55] comparing the use of traditional CPAP with the CPAP plus C-flex system were recently published. The new system did not appear to improve compliance except in an intent-to-treat analysis, where a slight improvement was observed in the non-complier group (<4 h use) after CPAP with C-flex was introduced.

One point on which all reviewed studies agree is that to obtain good CPAP compliance, it is essential to improve and ensure patient monitoring and follow-up. As discussed above, patients with greater perceived improvement and well-managed side effects are obviously those with better compliance. Since the pattern of use of the device is established in the first month of treatment (and this can even been used to predict compliance at 3 months), close supervision of patients in this period is crucial. The Spanish Consensus Document on Sleep Apnea[36] recommends regular checks after 1 month and every 3 months during the first year of treatment. This can be done in many different ways, from telephone calls for reinforcement of messages, with or without printed support material, to educational sessions in CPAP schools. These measures will have different objectives depending on the phase of the process. Thus, at the beginning of treatment, the aim is to familiarize the patient with the device and to improve understanding of the disease. During follow-up, the reinforcement sessions are used to resolve problems, adjust parameters, evaluate side effects and prevent dropouts.

All the measures aimed at achieving good treatment compliance raise the same question: what length of daily use is considered good compliance? This issue remains controversial, although there is some consensus with respect to the minimum time of 4 h/night, 70% of nights.[36]

Current technological advances mean that new home CPAP devices can provide read-outs and reliable monitoring of patient adherence. Not only hours of use are recorded, but also mask leakages and residual AHI. Despite the crucial importance of this aspect of follow-up, there are no guidelines for interpreting these compliance data or evaluating the rest of the data provided (e.g., flow signals, mask leakage, etc.). In this respect, a communication was published in 2013 by the American Chest Society[56] that concluded that the hours of use of CPAP can be reliably determined by modern CPAP equipment, but that information on residual events (apnea/hypopnea) and leakages are not so easy to interpret, and the definitions of these parameters varies between CPAP manufacturers.

Other Positive Pressure Modes: Bilevel Pressure

Although most patients benefit from CPAP therapy, it has been known for some time that some have difficulty in tolerating the device, mainly due to the expiration effort needed to overcome the continuous airway pressure, particularly at high pressures. For this reason, Sanders and Kern[57] in 1990 proposed a solution in the form of a BIPAP system. After similar efficacy was demonstrated in the treatment of OSAHS, this system was proposed for use in this patient population, but only as second line treatment due to its higher cost. Furthermore, technological advances in the new CPAP devices with flex system that automatically reduce CPAP pressure at the start of expiration offer a similar alternative at a lower price.

A subgroup of patients that might benefit from a switch to BIPAP are those who require very high continuous CPAP pressures. The latest recommendations from the American Sleep Academy[43] recommend changing to a bilevel device if control is insufficient at a pressure of 15 cm H_2O.

Other indications proposed in recent publications include the use of BIPAP in patients with hypoventilation or associated comorbidities such as chronic respiratory failure as a result of COPD.[58,59] These studies suggest that BIPAP could be useful in older patients, those with significant obesity, COPD or oxygen desaturations greater than those observed in isolated OSAHS.[60]

Pressure adjustment and specific titration recommendations for these devices were published in a Task Force report by the American Sleep Academy published in 2008.[43]

Other Positive Pressure Modes: Adaptive Ventilation

Sleep-disordered breathing (SDB) is yet another comorbidity found in many patients. In clinical practice it is common to see increasingly complex patients with unstable ventilatory control and central apneas in sleep studies that do not improve with CPAP. In many, there is an underlying cardiac cause, primarily heart failure. There is growing scientific evidence to suggest that central apnea syndrome (CAS) with Cheyne–Stokes respiration may be an indicator for higher morbidity and mortality, and effective treatment can improve the clinical course of these patients.[61–63]

Some studies have shown that CPAP reduces AHI, improves left ventricular ejection fraction, and reduces sympathetic activity in heart failure.[64–66] However, the only large randomized prospective study to date has been the Canadian Positive Airway Pressure Study,[67] comparing patients with heart failure and SDB randomly assigned to either CPAP or standard medical care. No major differences in survival before heart transplant were found in this study, and CPAP was ineffective in preventing sleep apnea syndrome in almost half of patients. A post hoc analysis showed that the patient subgroup in whom CPAP reduced AHI to less than 15 events/h had improved prognosis.[68]

Adaptive servo-ventilation (ASV) is a new treatment modality introduced in clinical practice in the last decade to treat central, mixed and complex apneas. ASV delivers pressure support adjusted to the needs of the patient with the aim of stabilizing minute ventilation.

One of the first studies on the short-term effect of AVS, published by Teschler et al.,[69] reported favorable effects for AVS compared to oxygen, CPAP or BIPAP in improving central respiratory sleep disorders.

With regard to the best treatment for CAS, evidence from clinical trials is sparse. In 2011, Aurora et al.[70] published practical guidelines for the treatment of CAS after a review and meta-analysis of

evidence-based studies. These authors recommend (with standard quality of evidence) CPAP for the normalization of AHI in the first-line treatment of CAS with heart failure, with oxygen and AVS as second-line options, since AVS significantly improves left ventricular ejection fraction and AHI. Very little evidence was found for other treatment modalities (BIPAP, acetazolamide, zolpidem, triazolam, etc.) and these are only recommended as an option in some central apnea subtypes. Although other CAS subtypes also appear to respond to CPAP, care must be taken when extrapolating results to other forms of central apnea.

This was followed by another systematic review by Sharma et al.[71] on ASV treatment of SDB in patients with heart failure, which concludes that ASV is more effective than standard treatment for reducing AHI and improving cardiac function and exercise capacity.

ASV may also be useful in the treatment of complex apneas that appear with CPAP treatment, such as opioid-induced CAS, although most of the data suggest that these conditions are transient and self-limiting.[72–74]

Finally, two large multicenter, randomized, controlled trials to confirm the prognostic impact of ASV in the treatment of SDB in heart failure are currently underway (SERVE-HF and ADVENT-HF), and may provide a definitive answer regarding the long-term effect of this treatment.

Other Treatments

Treatment proposals from the range of therapeutic options for OSAHS are neither exclusive nor unique. Indeed, they should be offered to the patient as part of a wide spectrum of possibilities, for use alone or in combination, suitably tailored to each case. In general, the aim of treatment alternatives is to stabilize the airway and prevent it from collapsing.

A series of general measures should be established for all OSAHS patients, including: (1) good sleep hygiene to improve the amount and quality of sleep; (2) control of toxic habits, such alcohol and smoking; (3) avoidance of drugs that undermine the ventilatory response or that might affect sleep architecture; (4) weight loss for all obese and overweight patients, whether diet and exercise or, in the more extreme cases, bariatric surgery[16,36,41]; and (5) postural treatment for positional OSAHS, with the use of a tennis ball in the back: this is the most common recommendation, although compliance is generally low and response partial. The Spanish Sleep Group is currently evaluating vibrating postural devices that may provide better compliance as an alternative for patients who do not tolerate CPAP.

Mandibular advancement devices reduce oropharyngeal obstruction by holding the lower jaw and tongue in a forward position. It is an alternative treatment indicated in patients who snore, non-obese individuals with mild to moderate OSAHS, and those who do not tolerate CPAP.[3,75–77] Recent data suggest that they may also be indicated in patients with severe OSAHS.[78]

The literature on this treatment concludes that the mandibular advancement device, compared to placebo, improves snoring, AHI and subjective sleepiness. Some studies have also shown an improvement in cardiovascular risk and blood pressure.[79,80]

Another consideration is that the numerous mandibular advancement devices available on the market make it difficult to compare efficacy and extrapolate data. Moreover, these devices must be adjusted by experienced professionals (orthodontists and/or maxillofacial surgeons) and their efficacy should be determined in sleep studies.

New intraoral devices based on different principles have produced good results. Negative pressure generators (oral negative pressure therapy, Winx® by Apnicure Inc., Redwood City, CA, US) and nasal systems that aim to emulate CPAP by placing adhesive valves on the nostrils have shown promising preliminary results: prospective studies have yet to be completed.[81]

Lastly, promising 12-month results on stimulation of the pharyngeal dilator muscle (primarily the genioglossus) in 126 selected patients have been published recently by the STAR Trial Group.[82]

Conclusions

OSAHS is a very prevalent yet largely under-diagnosed disease that significantly undermines quality of life. Population aging and rising obesity rates are important co-factors in the foreseeable increase in the prevalence of this syndrome, and consequently its greater social and healthcare impact.

OSAHS has been shown to confer a negative survival prognostic due to accident risk and cardiovascular morbidity and mortality. CPAP therapy in the home is both efficient and effective, controls healthcare costs and reduces hospital admission rates. However, patient adherence to treatment and outcomes are closely correlated. As in other chronic diseases, it is particularly important to supervise and follow-up treatment compliance with support programs based on new resources as telemedicine led by nursing staff and assisted by primary care doctors.

The considerable body of scientific evidence available to date suggests a need to review the indications for CPAP on the basis of OSAHS severity, coexistence of symptoms or comorbidities, and in certain situations or particular groups such as women, children and the elderly, populations that are currently increasing the demand for care.

To conclude, in these changing times of significant advances in technology and communication, OSAHS creates challenges for research in several fields and specialties: these initiatives are needed to improve decision-making in the management of a chronic disease with social and healthcare impact, and are key to improving patient quality of life.

Conflict of Interests

The authors state that they have no conflict of interests.

References

1. Federación española de empresas de tecnología sanitaria. Estudio sobre la eficiencia y los beneficios de las terapias respiratorias domiciliarias. Fenin; 2011.
2. Giles TL, Lasserson TJ, Smith BJ, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database Syst Rev. 2006;3:CD001106.
3. Lloberes P, Durán-Cantolla J, Martínez-García MA, Marín JM, Ferrer A, Corral J, et al. Diagnóstico y tratamiento del síndrome de apneas-hipopneas del sueño. Arch Bronconeumol. 2011;47:143–56.
4. Alfageme I, Acochea J, Calle M, Capote F, Duran-Cantolla J, Gimeno M, et al. Terapias respiratorias. Tratamiento con CPAP. Arch Bronconeumol. 2009;45 Supl 2:1–28.
5. Mar J, Rueda JR, Durán-Cantolla J, Schechter C, Chilcott J. The cost-effectiveness of nCPAP treatment in patients with moderate-to-severe obstructive sleep apnoea. Eur Respir J. 2003;21:515–22.
6. Strohl KP, Brown DB, Collop N, George C, Grunstein R, Han F, et al., ATS Ad Hoc Committee on Sleep Apnea Sleepiness, and Driving Risk in Noncommercial Drivers. An Official American Thoracic Society Clinical Practice Guideline: sleep apnea, sleepiness, and driving risk in noncommercial drivers. An update of a 1994 Statement. Am J Respir Crit Care Med. 2013;187:1259–66.
7. Alajmi M, Mulgrew AT, Fox J, Davidson W, Schulzer M, Mak E, et al. Impact of continuous positive airway pressure therapy on blood pressure in patients with obstructive sleep apnea hypopnea: a meta-analysis of randomized controlled trials. Lung. 2007;185:62–72.
8. Mo L, He Q. Effect of long-term continuous positive airway pressure ventilation on blood pressure in patients with obstructive sleep apnoea hypopnea syndrome: a meta-analysis of clinical trials. Zhonghua Yi Xue Za Zhi. 2007;87:1177–80.
9. Cano-Pumarega I, Durán-Cantolla J, Aizpuru F, Miranda-Serrano E, Rubio R, Martínez-Null C, et al., On behalf of the Spanish Sleep and Breathing Group. Obstructive sleep apnea and systemic hypertension: longitudinal study in the general population: the Vitoria Sleep Cohort. Am J Respir Crit Care Med. 2011;184:1299–304.

10. Weaver TE, Mancini C, Maislin G, Cater J, Staley B, Landis JR, et al. CPAP treatment of sleepy patients with milder OSA: results of the CATNAP randomized clinical trial. Am J Respir Crit Care Med. 2012;186:677–83.
11. Durán-Cantolla J, Aizpuru F, Montserrat JM, Ballester E, Terán-Santos J, Aguirregomoscorta JI, et al., Spanish Sleep and Breathing Group. Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial. BMJ. 2010;341:5991c.
12. Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, et al., Spanish Sleep and Breathing Network. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;307:2161–8.
13. Doherty LS, Kiely JL, Swan V, McNicholas WT. Long-term effects of nasal continuous positive airway pressure therapy on cardiovascular outcomes in sleep apnea syndrome. Chest. 2005;127:2076–84.
14. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea–hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005;365:1046–53.
15. Turgut Celen Y, Peker Y. Cardiovascular consequences of sleep apnea: III. Impact of continuous positive airway pressure treatment. Anadolu Kardiyol Derg. 2010;10:274–80.
16. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5:263–76.
17. Marti S, Sampol G, Muñoz X, Torres F, Roca A, Lloberes P, et al., Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Mortality in severe sleep apnoea/hypopnoea syndrome patients: impact of treatment. Eur Respir J. 2002;20:1511–8.
18. Marshall NS, Wong KK, Liu PY, Cullen SR, Knuiman MW, Grunstein RR. Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep. 2008;31:1079–85.
19. Young T, Finn L, Peppard P, Szklo-Coxe M, Austin D, Nieto FJ, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of Wisconsin Sleep Cohort. Sleep. 2008;31:1071–8.
20. Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, et al. Obstructive sleep apnea–hypopnea and incident stroke: the Sleep Heart Health Study. Am J Respir Crit Care Med. 2010;182:269–77.
21. Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med. 2009;6:e1000132, http://dx.doi.org/10.1371/journal.pmed.1000132.
22. Simon S, Collop N. Latest advances in sleep medicine obstructive sleep apnea. Chest. 2012;142:1645–51.
23. Martínez-García MA, Capote F, Campos-Rodríguez F, Lloberes P, Díaz de Atauri MJ, Somoza M, et al. Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension. The HIPARCO randomized clinical trial. JAMA. 2013;310:2407–15.
24. Drager LF, Togeiro SM, Polotsky VY, Lorenzi-Filho G. Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol. 2013;62:569–76.
25. Sharma SK, Agrawal S, Damodaran D, Sreenivas V, Kadhiravan T, Lakshmy R, et al. CPAP for the metabolic syndrome in patients with obstructive sleep apnea. N Engl J Med. 2011;365:2277–86.
26. Barbé F, Durán-Cantolla J, Capote F, de la Peña M, Chiner E, Masa JF, et al., Spanish Sleep and Breathing Group. Long-term effect of continuous positive airway pressure in hypertensive patients with sleep apnea. Am J Respir Crit Care Med. 2010;181:718–26.
27. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med. 2001;163:608–13.
28. Young T, Finn L, Austin D, Peterson A. Menopausal status and sleep-disordered breathing in the Wisconsin Sleep Cohort study. Am J Respir Crit Care Med. 2003;167:1181–5.
29. Tamanna S, Geraci SA. Major sleep disorders among women: (women's health series). South Med J. 2013;106:470–8.
30. Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I, Almeida-Gonzalez C, Catalan-Serra P, Montserrat JM. Cardiovascular mortality in women with obstructive sleep apnea with or without continuous positive airway pressure treatment: a cohort study. Ann Intern Med. 2012;156:115–22.
31. Martínez-García MA, Durán-Cantolla J, Montserrat JM. Sleep apnea–hypopnea syndrome in the elderly. Arch Bronconeumol. 2010;46:479–88.
32. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2002;162:893–900.
33. Martínez-García MA, Campos-Rodríguez MA, Catalán-Serra P, Soler-Cataluña JJ, Almeida-Gonzalez C, de la Cruz I, et al. Cardiovascular mortality in obstructive sleep apnea in the elderly: role of long-term continuous positive airway pressure treatment: a prospective observational study. Am J Respir Crit Care Med. 2012;186:909–16.
34. Weaver TE, Chasens ER. Continuous positive airway pressure treatment for sleep apnea in older adults. Sleep Med Rev. 2007;11:99–111.
35. Martínez-García MA, Amilibia J, Chiner E, Queipo C, Díaz de Atauri MJ, Carmona-Bernal C, et al. Sleep apnoea in patients of elderly: care activity in Spain (2002–2008). Arch Bronconeumol. 2010;46:502–7.
36. Durán-Cantolla J, Puertas-Cuesta FJ, Pin-Arboledas G, Santa María-Cano J, Grupo Español de Sueño (GES). Documento de consenso nacional sobre el síndrome de apneas-hipopneas del sueño. Arch Bronconeumol. 2005;41:1–110.
37. Alonso-Álvarez ML, Canet T, Cubell-Alarco M, Estivill E, Fernández-Julián E, Gozal D, et al. Documento de consenso del síndrome de apneas hipopneas durante el sueño en niños (versión completa). Arch Bronconeumol. 2011;47 Supl 5:2–18.
38. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, et al., American Academy of Pediatrics. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2012;130:e714–55.
39. Kheirandish-Gozal L, Kim J, Goldbart AD, Gozal D. Novel pharmacological approaches for treatment of obstructive sleep apnea in children. Expert Opin Investig Drugs. 2013;22:71–85.
40. Tan HL, Gozal D, Kheirandish-Gozal L. Obstructive sleep apnea in children: a critical update. Nat Sci Sleep. 2013;5:109–23.
41. Marcus CL, Ward SL, Mallory GB, Rosen CL, Beckerman RC, Weese-Mayer DE, et al. Use of nasal continuous positive airway pressure as treatment of childhood obstructive sleep apnea. J Pediatr. 1995;127:88–94.
42. Marcus CL, Rosen G, Ward SL, Halbower AC, Sterni L, Lutz J, et al. Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea. Pediatrics. 2006;117:e442–51.
43. Kushida CA, Chediak A, Berry RB, Brown LK, Gozal D, Iber C, et al., Positive Airway Pressure Titration Task Force; American Academy of Sleep Medicine. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. J Clin Sleep Med. 2008;4:157–71.
44. Loredo JS, Berry C, Nelesen RA, Dimsdale JE. Prediction of continuous positive airway pressure in obstructive sleep apnea. Sleep Breath. 2007;11:45–51.
45. Sériès F, Marc I, Cormier Y, La Forge J. Required levels of nasal continuous positive airway pressure during treatment of obstructive sleep apnea. Eur Respir J. 1994;7:1776–81.
46. Molina M, Hernández L, Durán J, Farré R, Rubio R, Navajas D, et al. Protocolo para evaluar una CPAP automática. Valoración de la utilidad del Autoset-T para determinar la presión de CPAP óptima en el síndrome de apnea-hipopnea del sueño (SAHS). Arch Bronconeumol. 2003;39:118–25.
47. Masa JF, Jiménez A, Durán J, Capote F, Monasterio C, Mayos M, et al., Cooperative Spanish Group. Alternative methods of titrating continuous positive airway pressure: a large multicenter study. Am J Respir Crit Care Med. 2004;170:1218–24.
48. McArdle N, Singh B, Murphy M, Gain KR, Maguire C, Mutch S, et al. Continuous positive airway pressure titration for obstructive sleep apnoea: automatic versus manual titration. Thorax. 2010;65:606–11.
49. Ip S, D'Ambrosio C, Patel K, Obadan N, Kitsios GD, Chung M, et al. Auto-titrating versus fixed continuous positive airway pressure for the treatment of obstructive sleep apnea: a systematic review with meta-analyses. Syst Rev. 2012;1:20.
50. Xu T, Li T, Wei D, Feng Y, Xian L, Wu H, et al. Effect of automatic versus fixed continuous positive airway pressure for the treatment of obstructive sleep apnea: an up-to-date meta-analysis. Sleep Breath. 2012;16:1017–26.
51. Durán-Cantolla J, Martínez-Null C, Egea Santaolalla C. Tratamiento del síndrome de apneas-hipopneas del sueño (SAHS) con dispositivos mecánicos generadores de presión positiva. CPAP, APAP y ventilación servoasistida. Rev Med Clin Condes. 2013;24:375–95.
52. Kholer M, Smith D, Tippett V, Stradling JR. Predictors of long-term compliance with continuous positive-pressure. Thorax. 2010;65:829–32.
53. Aloia MS. Understanding the problem of poor CPAP adherence. Sleep Med Rev. 2011;15:341–2.
54. Muir JF, Gentina T, Dauvilliers Y, Tamisier R, Sapene M, Escourrou P, et al. Pressure reduction during exhalation in sleep apnea patients treated by continuous positive airway pressure. Chest. 2009;136:490–7.
55. Bakker JP, Marshall NS. Flexible pressure delivery modification of continuous positive airway pressure for obstructive sleep apnea does not improve compliance with therapy: systematic review and meta-analysis. Chest. 2011;139:1322–30.
56. Schwab RJ, Badr SM, Epstein LJ, Gay PC, Gozal D, Kohler M, et al., ATS Subcommittee on CPAP Adherence Tracking Systems. An Official American Thoracic Society Statement: continuous positive airway pressure adherence tracking systems. The optimal monitoring strategies and outcome measures in adults. Am J Respir Crit Care Med. 2013;188:613–20.
57. Sanders MH, Kern NB. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask: physiologic and clinical implications. Chest. 1990;98:317–24.
58. Atwood CW Jr. Progress toward a clearer understanding of the role of bilevel positive airway pressure therapy for obstructive sleep apnea. J Clin Sleep Med. 2013;9:337–8.
59. Brzecka A, Piesiak P, Kosacka M, Jankowska R. Hypoxemia during bilevel positive airway pressure treatment in patients with obstructive sleep apnea syndrome and chronic respiratory insufficiency. Adv Exp Med Biol. 2013;755:117–23.
60. Berry RB, Chediak A, Brown LK, Finder J, Gozal D, Iber C, et al., NPPV Titration Task Force of the American Academy of Sleep Medicine. Best clinical practices for the sleep center adjustment of noninvasive positive pressure ventilation (NPPV) in stable chronic alveolar hypoventilation syndromes. J Clin Sleep Med. 2010;6:491–509.
61. Javaheri S, Shukla R, Zeigler H, Wexler L. Central sleep apnea, right ventricular dysfunction, and low diastolic blood pressure are predictors of mortality in systolic heart failure. J Am Coll Cardiol. 2007;49:2028–34.
62. Brack T, Thüer I, Clarenbach CF, Senn O, Noll G, Russi EW, et al. Daytime Cheyne–Stokes respiration in ambulatory patients with severe congestive heart failure is associated with increased mortality. Chest. 2007;132:1463–71.

63. Naughton MT, Lorenzi-Filho G. Sleep in heart failure. Prog Cardiovasc Dis. 2009;51:339–49.
64. Egea CJ, Aizpuru F, Pinto JÁ, Ayuela JM, Ballester E, Zamarrón C, et al., Spanish Group of Sleep Breathing Disorders. Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: a multicenter study. Sleep Med. 2008;9:660–6.
65. Johnson CB, Beanlands RS, Yoshinaga K, Haddad H, Leech J, de Kemp R, et al. Acute and chronic effects of continuous positive airway pressure therapy on left ventricular systolic and diastolic function in patients with obstructive sleep apnea and congestive heart failure. Can J Cardiol. 2008;24:697–704.
66. Kaneko Y, Floras JS, Usui K, Plante J, Tkacova R, Kubo T, et al. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med. 2003;348:1233–41.
67. Bradley TD, Logan AG, Kimoff RJ, Sériès F, Morrison D, Ferguson K, et al. Continuous positive airway pressure for central sleep apnea and heart failure. N Engl J Med. 2005;353:2025–33.
68. Arzt M, Floras JS, Logan AG, Kimoff RJ, Series F, Morrison D, et al. Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure: a post hoc analysis of the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP). Circulation. 2007;115:3173–80.
69. Teschler H, Döhring J, Wang YM, Berthon-Jones M. Adaptive pressure support servo-ventilation: a novel treatment for Cheyne–Stokes respiration in heart failure. Am J Respir Crit Care Med. 2001;164:614–9.
70. Aurora RN, Chowdhuri S, Ramar K, Bista SR, Casey KR, Lamm CI, et al. The treatment of central sleep apnea syndromes in adults: practice parameters with an evidence-based literature review and meta-analyses. Sleep. 2012;35:17–40.
71. Sharma B, Owens R, Malhotra A. Sleep in congestive heart failure. Med Clin North Am. 2010;94:447–64.
72. Morgenthaler TI, Gay PC, Gordon N, Brown LK. Adaptive servoventilation versus noninvasive positive pressure ventilation for central, mixed, and complex sleep apnea syndromes. Sleep. 2007;30:468–75.
73. Javaheri S, Smith J, Chung E. The prevalence and natural history of complex sleep apnea. J Clin Sleep Med. 2009;5:205–11.
74. Javaheri S, Malik A, Smith J, Chung E. Adaptive pressure support servoventilation: a novel treatment for sleep apnea associated with use of opioids. J Clin Sleep Med. 2008;4:305–10.
75. Morgenthaler TI, Kapen S, Lee-Chiong T, Alessi C, Boehlecke B, Brown T, et al., Standards of Practice Committee; American Academy of Sleep Medicine. Practice parameters for the medical therapy of obstructive sleep apnea. Sleep. 2006;29:1031–5.
76. Randerath WJ, Verbraecken J, Andreas S, Bettega G, Boudewyns A, Hamans E, et al. Non-CPAP therapies in obstructive sleep apnoea. Eur Respir J. 2011;37:1000–28.
77. Manual de procedimientos en CPAP y otros tratamientos para el síndrome de apnea de sueño. Manuales SEPAR de Procedimientos. Editorial RESPIRA; 2014 (In press).
78. Phillips CL, Grunstein RR, Darendeliler MA, Mihailidou AS, Srinivasan VK, Yee BJ, et al. Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. Am J Respir Crit Care Med. 2013;187:879–87.
79. White DP, Shafazand S. Mandibular advancement device vs CPAP in the treatment of obstructive sleep apnea: are they equally effective in short term health outcomes? J Clin Sleep Med. 2013;9:971–2.
80. Iftikhar IH, Hays ER, Iverson MA, Magalang UJ, Maas AK. Effect of oral appliances on blood pressure in obstructive sleep apnea: a systematic review and meta-analysis. J Clin Sleep Med. 2013;9:165–74.
81. Braga CW, Chen Q, Burschtin OE, Rapoport DM, Ayappa I. Changes in lung volume and upper airway using MRI during application of nasal expiratory positive airway pressure in patients with sleep-disordered breathing. J Appl Physiol. 1985;111:1400–9.
82. Strollo PJ Jr, Soose RJ, Maurer JT, de Vries N, Cornelius J, Froymovich O, et al., STAR Trial Group. Upper-airway stimulation for obstructive sleep apnea. N Engl J Med. 2014;370:139–49.