Obesity and sleep apnea-hypopnea syndrome

Obesidad y síndrome de apneas-hipopneas del sueño

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Abstract

Obstructive sleep apnea syndrome (OSAS) is caused by the collapse of the upper airway during sleep. Obesity is defined by an excess of corporal fat, which is usually accompanied by an excess of body weight. Obese patients show an increase in cardiovascular mortality which is caused by obesity itself and its association to other cardiovascular risk factors. OSAS is one of the most prevalent and important cardiovascular risk factors associated to obesity. The diagnosis of obstructive sleep apnea syndrome in obese patients is made by polysomnography. OSAS treatment in obesity requires a multidisciplinary approach which includes treatment with modern systems of nasal continuous positive pressure airway (CPAP) therapy and auto-CPAP during sleep, along with lifestyle modification with the aim of achieving weight loss (diet, exercise and behaviour modification). Surgery is sometimes required.

Keywords: obstructive sleep apnea syndrome, obesity, polysomnography, cardiovascular risk, treatment.

Introduction

The sleep apnea-hypopnea syndrome (SAHS) consists of the onset of recurrent limitation events of the airway passage during the sleep as consequence of the anatomic-functional alteration of the upper airway that leads to its collapse, causing reductions of the oxyhemoglobin saturation (SaO₂) and micro-arousals giving place to a non-restoring sleep, excessive somnolence during the day, neuro-psychiatric, respiratory and cardiac disorders. At present, it is named obstructive sleep apnea syndrome (OSAS) in the Anglo-Saxon literature. However, in the national consensus document the use of the SAHS concept is recommended, as it includes a specific reference of the hypopneas, which are considered of increasing importance, both in children and in adults. Moreover, it avoids including the term “obstructive”, which allows including not only these ones, but also the mixed and central ones, many of which are obstructive in origin and they disappear with the application of the continuous positive airway pressure (CPAP). Though the presence of a certain number of apneas and hypopneas during the sleep can be observed almost up to in a forth part of the population, we refer to SAHS when its number is high and causes health problems. The SAHS is a very prevalent disease. It affects 4-6% of the males and 2-4% of the females in an adult middle-aged population, and its prevalence increases with age and with the increase of weight. It has clearly been demonstrated that the SAHS is associated to the worsening of the life quality, morbimortality and traffic accidents.

The obesity constitutes one of the diseases with higher prevalence in occidental countries, and at present, it is considered the most frequent metabolic disease. It might be considered a public health problem, as it causes a reduction of the life expectancy and constitutes the second cause of foreseeable mortality, exceeded only by the consumption of tobacco. At present, the level of obesity is determined by means of an estimation of the body mass index (BMI), that is determined dividing the weight in kilograms per the height in square meters (kg/m²); it is considered...
overweight if the BMI is ≥25 and obesity if the BMI is ≥30. There has been an increase of obesity of 47% between 1987 and 1995 in Spain. This increase has been produced in men and in women, and has affected all the age groups, though it is more relevant in children (in whom the obesity duplicated during the last 10 years) and in elder persons and with a low level of instruction.

**Diagnosis criteria**

The SAHS is characterized by the presence of repeated events of complete obstruction (apneas) or partial events (hypopneas) of the upper airway considering that the soft parts of the throat collapse and are obstructed during the sleep. These obstructions cause an important reduction of the oxygen quantity available in blood and multiple non-conscious arousals, giving place to a non-re- storing sleep, causing an excessive somnolence during the day and tiredness that these patients show.

One of the main hurdles in order to evaluate the magnitude of the SAHS problem in the obese population has been the disparity of criteria to define both the SAHS and the obesity and its different levels, up to the classification proposed by the Spanish Society for the Study of Obesity (SEEDO) during the year 2000 (table 1). The obesity is defined by the excessive accumulation of fats in the organism. The BMI is usually used in order to determine this excess of fat. Except for exceptional situations of lean mass excess, the BMI is a good indicator of the body fat quantity. Another aspect that has to be taken into account when determining some criteria to define the obesity is the distribution pattern of the adipose tissue. It has been demonstrated that the localization of the fat represents a higher risk for the health than the absolute quantity of fat tissue (table 2). The observed variations in the female sex are due to the fact that the risk measures in Spanish women are taken from the values higher than the percentile 90 (Consensus SEEDO 2000). The main definitions of the SAHS are depicted in table 3.

**Obesity and respiratory physiology**

The alterations of the ventilatory function that appear in obese patients might be of mechanistic origin, might affect the gaseous

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**Table 1. Criteria of the SEEDO in order to define the obesity in levels according to the BMI**

<table>
<thead>
<tr>
<th>Ponderal classification</th>
<th>BMI (kg/m²)</th>
</tr>
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<tbody>
<tr>
<td>Insufficient weight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Level 1 overweight</td>
<td>25-26.9</td>
</tr>
<tr>
<td>Level 2 overweight (pre-obesity)</td>
<td>27-29.9</td>
</tr>
<tr>
<td>Level 1 obesity</td>
<td>30-34.9</td>
</tr>
<tr>
<td>Level 2 obesity</td>
<td>35-39.9</td>
</tr>
<tr>
<td>Level 3 obesity (morbid)</td>
<td>40-49.9</td>
</tr>
<tr>
<td>Level 4 obesity (extreme)</td>
<td>≥50</td>
</tr>
</tbody>
</table>

BMI: body mass index.

**Table 2. Risk values according to the distribution of the body fat (SEEDO, 2000)**

<table>
<thead>
<tr>
<th>Men</th>
<th>Women SEEDO</th>
<th>Women European Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index w/h</td>
<td>≥1</td>
<td>≥0.9</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>≥102</td>
<td>≥90</td>
</tr>
</tbody>
</table>

SEEDO: Spanish Society for the Study of Obesity; w/h: waist/hip.

**Table 3. More accepted SAHS definitions**

<table>
<thead>
<tr>
<th>Origin</th>
<th>Definition</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>American Sleep Disorders Association 1990</td>
<td>Recurrent apneas and hypopneas that are associated to a clinical worsening manifested by an increase of the somnolence or alteration of the respiratory and cardiac function</td>
<td>It does not specify how many apneas or hypopneas are needed to cause SAHS</td>
</tr>
<tr>
<td>Spanish Society of Respiratory Pathology</td>
<td>Somnolence picture, neuro-psychiatric, respiratory and cardiac disorders secondary to repeated events of obstruction of the upper airway that cause repeated desaturations of the oxyhemoglobin and temporary arousals causing a non-restoring sleep</td>
<td>It considers the clinical manifestations and does not specify the number of events necessary to constitute the syndrome</td>
</tr>
<tr>
<td>American Academy of the Sleep</td>
<td>1. One RDI ≥5 included the presence of the RERA plus one of the following ones, which cannot be explained by other causes 2. Excessive daily somnolence 3. Two or more of the following: • Asphyxia during the night • Recurrent arousals • Clumsiness at arousal • Fatigue during the day • Concentration difficulties • SAHS = 1 + (2 or 3)</td>
<td>It considers as a whole the RDI and the manifestations. Some consider that the cut point of RDI ≥5 is excessively low, especially in elder patients, and even more if the RAREs are included</td>
</tr>
</tbody>
</table>

RARE: respiratory efforts related to micro-arousals; RDI: respiratory disturbance index; SAHS: sleep apnea-hypopnea syndrome.
interchange or the energetic consumption. The changes observed in the respiratory physiology related to the obesity include the alterations in the ventilatory mechanism, respiratory muscles, regulation of the ventilation and the control of the breathing during the sleep.9

**Ventilatory mechanics**

In obesity, the overload of the mass entails a change of the characteristics of the thoracic cage as it reduces its capacity opposed to the elastic retraction forces of the lung, while an increase of the elastic thorax resistance can be observed over the 70% if the pulmonary capacity. Moreover, the obesity determines an increase of the elastic retraction forces of the lung, probably secondary to an increase of the circulatory plethora. Therefore, there is an increase of the elastic resistances both of the lung and the thoracic cage that condition an increase in the breathing.

**Respiratory muscles**

The obesity might affect the function of the respiratory muscles by different mechanisms. First, it might cause a hypertrophy secondary to the increase of the respiratory work that suggests the mechanic overload. On the other hand, some case has been described regarding to fat infiltration of the inspiratory muscles together with muscular dysfunction. Finally, the changes in the thorax configuration might cause an inadequate length-tension relation and, consequently, a loss of the capacity of generating an adequate inspiratory pressure.10

**Breathing control**

In the obese patients there is a high occlusion pressure (P_{153}), which is a parameter that reflects the central respiratory impulse condition, probably as consequence of the increase of the thorax elastic resistances. This alteration of the respiratory centers in the obesity might be primary or suggest an adaptation mechanism addressed to the prevention of the muscular fatigue.11

**Obesity and SAHS**

The obesity is increasing in all the developed countries (it starts to be named “epidemic of the XXI century”). As it is considered a chronic disease and an independent cardiovascular risk factor, it is assessed as the most frequent and relevant metabolic disease from the health point of view.

The distribution of the body fat has been related to several pathologies and a central body fat predominance has been stated (android or centripetal obesity) in the following ones: SAHS, blood hypertension, diabetes, increase of the plasmatic lipids, cerebrovascular strokes, myocardial infarction, biliary lithiasis, fat liver and some types of cancer (in women, biliary vesicle, breast, ovary and endometrial; in men, prostate and colorectal).12 An increase of the cardiovascular mortality has been observed in several studies, which is duplicated if the BMI is \( \geq 35 \text{ kg/m}^2 \) and triples in patients with morbid obesity (BMI \( \geq 40 \text{ kg/m}^2 \)). The 70% of the subjects who suffer SAHS are obese, and the obesity is the best significant marker of this syndrome. Both parameters are related directly, so when the BMI is \( > 40 \text{ kg/m}^2 \), the presence of SAHS appears in a great percentage of patients. In our series, 2 from 3 morbid obese patients and 2 from 5 women with morbid obesity show SAHS (table 4). The reduction of weight determines the respiratory symptomatic improvement of this patients.13

We find a morphological basis in the association of the SAHS and the obesity, as the obesity determines a sub-mucous fat inflation of the upper airway that conditions a reduction of the caliber and loss of muscular tone that will favor the collapse. On the other hand, the increase of the inspiratory impulse secondary to the high thorax load contributes also to the pressure balance necessary to keep the permeability of the airway during the inspiration.14 In the SAHS pathogenesis of the obese patients, the higher tendency to collapse of the airway that these patients show has a relevant importance.15 The factors that determine it are several. First, the anatomy of the oropharynx in the obese patients has a series of characteristics that make it prone to collapse: the major axis of the airway is longitudinal, making the dilator muscle action of the pharynx; inserted in the same axis, when contracting them they tend more to close than to open it. Moreover, the sectional area of the upper airway is reduced due to the accumulation of fat in the retro palatine region. The reduction of the respiratory reserve volume is also important, favoring a higher tendency to collapse to the airway through the increase of the intraluminal pressure. Finally, the pressure that supposes the increase of surrounding tissues volume by the accumulation of fat, named tissular pressure is added to the rest of the factors that predispose the collapse of the upper airway. The beginning of the sleep entails a reduction of the dilator muscle tone of the pharynx, which, together with the reduction of the pulmonary volume that is produced by the prone position, causes a higher reduction of the upper airway caliber.

**SAHS diagnosis**

The first step to achieve the SAHS diagnosis is the medical suspicion through the performance of a clinical history in which the presence of apneas, unquiet sleep and night somnolence is investigated. Once the pathologies are ruled out which might cause similar symptomatology, a physical exploration shall be performed on which special attention should be taken on the morphological basis in the association of the SAHS and the obesity, as the obesity determines a sub-mucous fat inflation of the upper airway that conditions a reduction of the caliber and loss of muscular tone that will favor the collapse. On the other hand, the increase of the inspiratory impulse secondary to the high thorax load contributes also to the pressure balance necessary to keep the permeability of the airway during the inspiration. In the SAHS pathogenesis of the obese patients, the higher tendency to collapse of the airway that these patients show has a relevant importance. The factors that determine it are several. First, the anatomy of the oropharynx in the obese patients has a series of characteristics that make it prone to collapse: the major axis of the airway is longitudinal, making the dilator muscle action of the pharynx; inserted in the same axis, when contracting them they tend more to close than to open it. Moreover, the sectional area of the upper airway is reduced due to the accumulation of fat, named tissular pressure is added to the rest of the factors that predispose the collapse of the upper airway. The beginning of the sleep entails a reduction of the dilator muscle tone of the pharynx, which, together with the reduction of the pulmonary volume that is produced by the prone position, causes a higher reduction of the upper airway caliber.

**Table 4. SAHS and cardiovascular risk factors in patients with morbid obesity**13

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Men (n=23)</th>
<th>Women (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (BP &gt;140/90 mmHg)</td>
<td>10 (43%)</td>
<td>8 (22%)</td>
</tr>
<tr>
<td>DM (ADA, 1997)</td>
<td>3 (13%)</td>
<td>8 (22%)</td>
</tr>
<tr>
<td>Hydrocarbonated intolerance (ADA, 1997)</td>
<td>7 (30%)</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Hyperlipemia (CT and/or TG &gt;200 mg/dL)</td>
<td>13 (56%)</td>
<td>13 (36%)</td>
</tr>
<tr>
<td>SAHS (&gt;10 desaturations &gt;4%/h)</td>
<td>16 (69%)</td>
<td>14 (39%)</td>
</tr>
</tbody>
</table>

The determination of the BMI, the best prognosis factor as regards to the seriousness of the SAHS, and the measurement of the neck circumference complete the most basic physical exploration. A neck circumference of >43.2 cm in men and of 40.6 in women suppose a risk of SAHS.

Once the clinical suspicion has been determined, the choice diagnosis method is the night polysomnography. It is a record of a series of neuro-physiological, respiratory and cardiac variables that allow us to know the quantity and the quality of the sleep, as well as the repercussions of the apneas and hypopneas during sleep. The study is performed during a night of sleep in which the ventilatory flow and the thorax effort are monitored, which inform us about the presence of hypoventilation, the oxygen arterial saturation in order to determine if the reduction of events of air flow is accompanied by the oxyhemoglobin desaturation, and the brain electrical activity by means of an electroencephalogram, electrooculogram and electromyogram in order to recognize the sleep factors in which such events occur, which are more frequent during the sleep REM phase. Moreover, the snoring presence and the cardiac electrical activity are recorded due to the higher risk of arrhythmias that these patients show secondarily to the increase of the sympathetic tone.

A specially designed unit is needed for the performance of a complete polysomnography study (sleep unit) and the patients should be admitted at hospital at least during one night in order to determine the diagnosis. Several alternatives have been designed in order to facilitate the accessibility to the diagnosis of SAHS, as the portable systems, which in spite of not measuring all the described variables they can be performed at the patient’s house. The set of simplified tests that evaluate the respiratory and cardiac variables are named respiratory polygraphy, and might constitute an alternative to the polysomnography in many patients. The combination of this variant with clinical prediction systems demonstrate hopeful results, though the polysomnography is still the reference pattern and it is the best procedure since the cost-benefit point of view.

The respiratory polygraphy is an acceptable alternative for the diagnosis of SAHS in patients with low probability (rule out SAHS) and a high clinical probability (confirm SAHS). As the obese patients have a high probability of suffering SAHS, the respiratory polygraphy is a good alternative for diagnosis. It is considered that approximately 50-75% of the patients with clinical SAHS suspicion can be treated; therefore a polysomnography per each three respiratory polygraphies would be necessary to tackle this problem.

The presence of an abnormal number of apneas/hypopneas during the sleep associated to symptoms related to the disease determines the SAHS diagnosis and allows quantifying its seriousness. A negative sleep tests (respiratory polygraphy or polysomnography) in the presence of a highly suggestive SAHS clinic indicates the need of undergoing a polysomnography as complete as necessary, included the neuro-physiological, respiratory and cardiac variables.

**SAHS treatment**

A multidisciplinary approach for the treatment of the SAHS in obese patients is required: general measures, pharmacology treatment, CPAP systems and surgery.

**General measures**

It is essential to achieve adequate sleep hygiene. The factors that worsen the SAHS have to be reduced as alcohol, the sedative drugs, the sleep privation and the tobacco; as well as to avoid sleeping in prone position. The postural position in patients in whom the symptoms appear predominantly in prone position is a good alternative within the conservative treatment.

The BMI is the best prognosis factor as regards to the SAHS seriousness, and the reduction of weight is associated to an improvement of the symptomatology, therefore the indication of a hypocaloric diet is essential. The loss of weight leads to a reduction of the SAHS presence and of the morbimortality of these patients.

Some losses of 5-10% of body weight are associated to an improvement of the respiratory symptomatology. The ponderal reduction entails a reduction of the number of apneas and an improvement of the night oxygenation.

The treatment of the obesity requires a multidisciplinary approach that should comprise the diet treatment, physical exercise and the modification of the patient’s habits; occasionally the bariatric surgery is necessary in patients with morbid and extreme obesity. It is recommendable to involve the relatives in the diet changes of the patient in order to favor its adhesion to the diet. In the diet treatment of the obesity and overweight, a moderate energetic restriction should be done, keeping the diet recommendations.

The obese morbid patients who show some concomitant disease besides the SAHS (T2D, blood hypertension, dyslipidemia) are susceptible to receive treatment on very low calorie diets (VLCD) and bariatric surgery, as these pathologies improve with the loss of weight. There is no consensus in the literature regarding to the adequate follow-up time of this type of diets, as this period should be sufficient in order to achieve a remarkable loss of weight, besides modifying relevantly the cardiovascular risk factors and, on the other hand, the malnutrition should be avoided. The VLCD should be used preferably in patients under 65 years of age, as the loss of lean mass in elder persons might be higher during its use.

**Pharmacotherapy**

More than a hundred drugs have been tried: the proprietine and the medroxyprogesterone have been the most studied, though with scarce results. In a recent revision of Smith et al., only the acetazolamide has demonstrated to reduce the apnea-hypopnea index, but on behalf of several secondary effects and without the drug showing a clinical improvement of the patient. Therefore, no drugs are used in the SAHS treatment at present.

**Continuous positive airway pressure systems: CPAP, BiPAP**

The choice treatment in patients with SAHS is the administration of CPAP administered during the sleep. The CPAP is more ef-
cient than the oral devices in order to improve the apneas and the hypopneas. It consists of a nasal mask linked to a turbine that emits air at a determined pressure impeding the obstruction of the upper airway. The treatment proved to be the most efficient in order to suppress the apneas and the hypopneas, it eliminates the symptoms of the disease, normalizes the sleep quality and avoids the potential complications. The treatment with CPAP is usually well tolerated and accepted, and the pressure has to be adjusted to each patient. The CPAP level adjustment should be customized in each patient by means of a polysomnography or a validated auto-CPAP system. The CPAP can be titrated with a self-adjustable equipment at the patient’s home, named self-CPAP. Though there are several systems, the most accepted ones are those that modify the pressure considering the measurement of the inspiratory flow wave. The patients should use the CPAP during more than 4 hours, at least 70% of the nights. This therapeutic guideline is sustained by less than 50% of the patients.

Approximately 50% of the patients show a side effect with CPAP, almost always of mild level and of a temporary nature. The most frequent side effects are the local symptoms (congestion, mucous dryness, and headache), secondary to the high pressure of the supplied air (thorax discomfort, difficulty to get to sleep) and others (claustrophobia, conjunctivitis, etc.). Alternatives as the inspiratory pressure and positive expiratory in the airway (BiPAP) that provides two different pressure levels, or the humidification of used air, are options addressed to improve the therapeutic compliance. The BiPAP is also used in obese patients who require higher air pressures in order to avoid the collapse of the upper airway, which would be intolerable and dangerous in continuous administration.

Mandibular advancement devices
The mandibular advancement devices (MAD) increase the space in the upper airway and constitute an alternative in the SAHS treatment, generally for the non-serious cases and for the patients who do not tolerate or reject the treatment with CPAP. A better tendency to collapse is achieved with these devices through a mechanical effect, offering a stable mandibular position, projecting the tongue and the palate. The best results are achieved with MAD, which allow a gradual advancement progression. They should be indicated and adapted by stomatologists/odontologists with specific training that should coordinate themselves with the sleep units.

Other measurements that are commercialized for the treatment of the snoring and SAHS, as the dilators and the nose drops, have not shown their efficiency.

Surgery of the maxillofacial area
The surgery is indicated in selected cases of SAHS and in some patients who do not tolerate the CPAP. The surgical techniques that are applied at present might be summed up in three groups: a) determination of short-circuit in such stretch (derivative); b) reduction of its content (reducer) and c) broadening of the continent (dilator).

Practical considerations
The sleep apneas-hypopneas syndrome (SAHS) is due mainly to the collapse of the upper airway during the sleep and is associated to the worsening of the life quality, the cardiovascular morbimortality and the traffic accidents.

The obesity and the SAHS are closely related. The prevalence of SAHS is estimated in 2/3 (men) and 2/5 (women) with a BMI higher than 40 kg/m². The reduction of weight determines the respiratory symptomatic improvement of these patients.

The night polysomnography (at hospital) constitutes the reference method for the diagnosis of SAHS, but the respiratory polygraphy at home is an acceptable alternative for the diagnosis of patients with high probability of showing SAHS.

The surgery supposes an alternative for these patients, addressed especially to those who have an added predisposing factor in the upper pharynx, as a hypertrophy of the pharynx pillars, alterations of the tongue or the soft palate and uvula, etc. In these cases, the nose surgery, the adenoidectomy and the uvulo-palatopharyngoplasty are efficacious treatments. There are no prospective studies about the efficiency of the bariatric surgery as therapeutic option for the reduction of weight and the improvement of SAHS, but there are published series of patients intervened with techniques both restrictive and malabsorptive, in which a remarkable improvement of the respiratory condition is objectified.

Conclusions
We are able to conclude that the prevalence of the SAHS increases with the obesity, and the BMI is the best prognosis factor regarding to its seriousness. Once the clinical suspicion is determined, the night polysomnography is the best diagnosis method. The respiratory polygraphy is a good alternative for the diagnosis in the obese patients, due to its high probability of suffering SAHS. The choice treatment in obese patients with SAHS is the administration of CPAP during the sleep.

Declaration of potential conflict of interests
Carlos Morillas states that there are no conflicts of interest as regards to the content of this article.

References


