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Obesity Hypoventilation Syndrome: New Insights

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ABSTRACT

Obesity hypoventilation syndrome (OHS) is an obesity-dependent sleep disorder that has acquired great importance worldwide due to its prevalence and the fact that its features may lead to an increase in morbidity and mortality whilst reducing life quality. This condition is characterised by the presence of chronic hypercapnic respiratory failure not secondary to other causes, alveolar hypoventilation during sleep and with or without apnoeic episodes. In this review, we have gone over new insights about OHS, diagnosis and the role of positive airway pressure, in particular the mechanisms that provide general improvement, physical relief, clinical applications, and management. **(BRN Rev. 2020;6(1):36-49)**

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INTRODUCTION

Over the past few years, studies around the world have shown an alarming increase in obesity rates and the data reveal that this tendency has remained steady. This fact has raised interest in the scientific community deriving in several researches to identify the causes and find solutions to reverse the high obesity rates. The findings have shown diverse causes, being the obesity hypoventilation syndrome (OHS) one that has particularly gained concern in recent times. The most common features of this condition are insufficient ventilation during sleep and abnormal high partial pressure of arterial carbon dioxide ($PaCO_2$) which results in diurnal hypoventilation (this diurnal hypoventilation demonstration is a mandatory condition for diagnosis). These patients have an increase in mortality and morbidity along with a decrease of their life quality[1,2].

In this review, we have examined the new insights about OHS, diagnosis and the role of positive airway pressure (PAP), considering non-invasive ventilation (NIV) and continuous positive airway pressure (CPAP).

DEFINITION AND FEATURES

The obesity hypoventilation syndrome has several synonyms such as hypercapnic sleep apnoea or sleep-associated hypoventilation associated with obesity, and Pickwick´s syndrome; nevertheless, the latter term has gradually become obsolete, as it was confusing when diagnosis analogous conditions exist[1].

The syndrome is characterised by the presence of chronic hypercapnic respiratory failure not secondary to other causes, alveolar hypoventilation during sleep, with or without apnoeic episodes and it is an obesity-dependent disorder[3]. 90% of patients with OHS have concomitant obstructive sleep apnoea (OSA) and all have hypoventilation during sleep, defined as an increase in $PaCO_2$ > 10 mmHg above baseline in wakefulness or with large oxygen desaturation, which are not due to obstructive episodes of apnoea or hypopnoea[4].

EPIDEMIOLOGY, RISK FACTORS AND ASSOCIATES

The exact prevalence of OHS in the general population is unknown, estimates vary significantly across studies, but a conservative estimated prevalence in the United States adult population is projected between 0.15% and 0.3%[5]. The prevalence of OHS in patients referred for suspected OSA is estimated in a range between 10% and 20% and reaches 20%-31% in patients already diagnosed with OSA[4,6,7]. The prevalence of OHS tends to be higher in patients with OSA with extreme obesity[4]; considerable range in prevalence reflects varying patient population across studies[6] and the mean body mass index (BMI) of patients with the lowest prevalence (10%)[8] is 34 kg/m^2 and 59 kg/m^2 from the study with the highest prevalence (31%)[9]. While the relationship/association between OHS and BMI is clear, less is known about the relationship between OHS and OSA in obese patients. Since OSA seems a risk factor to OHS[10,11] it is plausible to think that OSA plays an important role in OHS prevalence in obese patients. The relationship between men and women varies with the series, although it could be close to 1:1[4].

There is a lack of consistent data regarding the factors associated with diurnal hypercapnia in obese patients with OSA. A study conducted in 2009 by Kaw R et al.[10] linked the severity of OSA to individuals diagnosed with apnoea-hypopnoea index (AHI) greater than 65 episodes per hour, recording a BMI above 30 kg/m^2 and greater degree of mechanical restriction of the chest wall.

PATHOPHYSIOLOGY

The three mechanisms that can generate diurnal hypoventilation in obese patients are: impaired respiratory mechanics secondary to obesity; central hypoventilation secondary to leptin resistance, and an altered compensatory response to transient hypoventilation due to apnoea and obstructive hypopnoea[4,12].

In the first mechanism, obesity compromises respiratory function, particularly in supine position which induces hypoventilation by increasing the mechanical load in the system and may result in the weakening of the respiratory muscles[13,14]. The accumulation of fat in the lateral parts of the pharynx intensifies the extra-luminal pressure and modifies the geometry of the upper airway, facilitating total (apnoea) or partial (hypopnoea) collapses[15], which in turn increases the resistance of the upper airway and respiratory work. The main alterations in respiratory mechanics include a decrease in total lung capacity, residual functional capacity, vital capacity, expiratory reserve volume and respiratory system compliance[8,16].

In the second mechanism, leptin is a protein released by adipose tissue whose functions are to reduce appetite and increase energy expenditure[17-19]. This protein is a potent respiratory stimulant[20] and obesity may have central resistance to it. Obese patients have significantly higher leptin levels than lean patients, but this does not reduce appetite, providing indirect evidence of resistance to its effects on the central nervous system[21]. Research in animals has shown that its absence (or lack of effect) could cause hypoventilation[22]. Likewise, leptin has been proposed as an independent predictor of hypercapnia[23,24].

Lastly, in the third mechanism hypoventilation during sleep leads to transient episodes of acute hypercapnia and serum bicarbonate retention. The eucapnic patients with OSA have important compensatory mechanisms to maintain acid-base balance[25,26] so during the day, acute hypercapnia is corrected and excess bicarbonate is excreted[25]. However, patients with OHS show a reduction in ventilation between apnoea periods[27], these abnormalities give rise to persistent nocturnal and diurnal hypercapnia with a reduction in bicarbonate excretion, causing a gradual adaptation of chemoreceptors and the capacity of ventilatory response to CO_2[25] (Fig. 1).

CLINICAL PRESENTATIONS

The diagnosis of OHS is made regularly between the fifth and sixth decades of life, and two clinical presentations commonly observed are the patients who are diagnosed during an acute exacerbation of chronic respiratory failure with acute respiratory acidosis leading to hospital admission (often in the intensive or intermediate care unit) and who remain hypercapnic at hospital discharge or during routine patient evaluation for suspected OSA or dyspnoea[28-32].

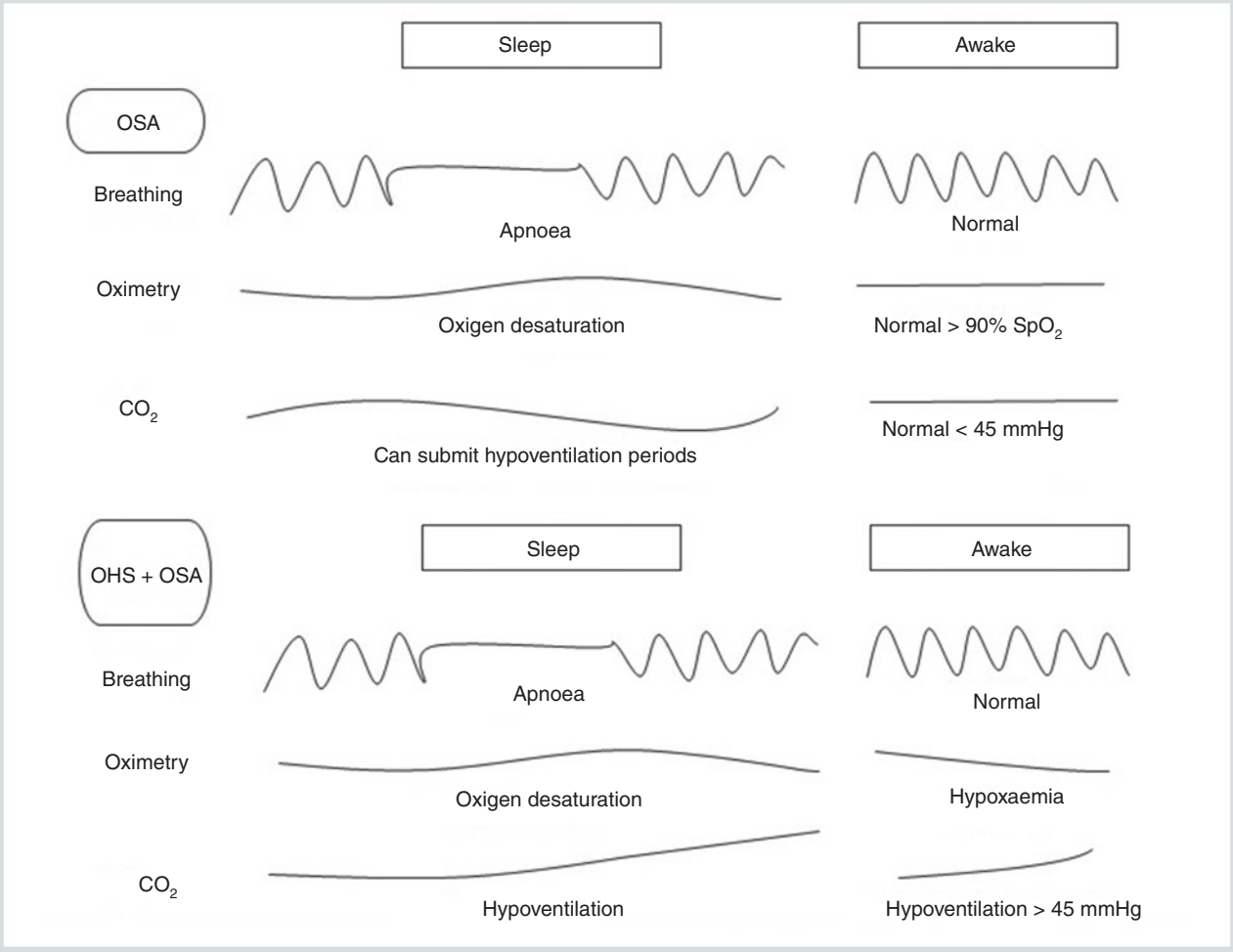

Figure 1. Altered compensatory response to transient hypoventilation due to apnoea and obstructive hypopnoea in OSA and OHS and associated OSA. Eucapnic patients with OSA have apnoea periods associated to arterial hypoxaemia during sleep and may submit hypoventilation periods, these patients have important compensatory mechanisms to maintain an acid-base balance, during the day, acute hypercapnia is corrected, excess bicarbonate is excreted and the oximetry is usually normal; but patients with OHS have a reduction in ventilation between apnoea periods, these alterations give rise to persistent nocturnal and diurnal hypercapnia with a reduction in bicarbonate excretion and may have hypoxaemia during awake.
CO_2: carbon dioxide; OHS: obesity hypoventilation syndrome; OSA: obstructive sleep apnoea; SpO_2: pulse oximetry.

Obesity is mandatory for the diagnosis of OHS (defined as a BMI > 30 kg/m^2) and the patient may have the classical symptoms of OSA, including snoring, presence apnoea, daytime sleepiness, morning headache, nocturia, frequent complaints of dyspnoea and they may also have *cor pulmonale* signs.

On physical examination, obesity is evident, with a neck circumference width of > 38 cm in women and > 40 cm in men, poor visualization of the oropharynx, prominent pulmonary component of second heart noise in cardiac auscultation, and lower limb oedema[30] with some of them having oxygen desaturation.

DIAGNOSIS

The diagnosis of OHS is clinical (Table 1). Complementary studies such as polysomnography may confirm the diagnosis of nocturnal hypoventilation[33] with or without sleep apnoea. It is common to observe an increase in serum bicarbonate as a metabolic compensation secondary to respiratory acidosis which suggests the chronic nature of hypercapnia[30]. Venous serum bicarbonate concentration in blood is an accessible and non-invasive sensitive test that can accurately detect chronic hypercapnia[11,33], being 27 mEq/l the proposed cut-off range.

Arterial hypoxaemia during wakefulness should force the clinician to exclude OHS in patients with OSA[4]. Overall, OSA patients do not present daily arterial hypoxaemia, but OHS patients can present oxygen desaturation during the day. Abnormal arterial oxygen saturation has lower discriminative effects than serum bicarbonate[33].

Spirometry in patients with OHS may be normal, but typically reveal mild-to-moderate restriction secondary to obesity. Peripheral blood biometry may reveal polycythaemia while hypothyroidism should be ruled out in thyroid function tests.

Table 1. Diagnostic criteria of OHS. The complementary findings are not necessary to establish the diagnosis

Clinical diagnostic criteria	A) $PaCO_2$ > 45 mmHg measured by arterial blood gases B) BMI > 30 kg/m^2 C) Exclude other causes of hypoventilation D) Nocturnal hypoventilation with or without sleep apnoea
Complementary	A) Serum bicarbonate level > 27 mEq/L B) Elevated exhaled CO_2 or transcutaneous CO_2 C) Arterial hypoxaemia during wakefulness measured by pulse oximetry

BMI: body mass index; OHS: obesity hypoventilation syndrome; $PaCO_2$: partial pressure of arterial carbon dioxide.

Table 2. Morbidity and mortality in untreated OHS. Patients with untreated OHS can develop various cardio-metabolic complications

Associated morbidity	Heart failure Cor pulmonale Hypertension systemic Coronary heart disease Ischaemic heart disease Pulmonary hypertension Diabetes Dyslipidaemia Metabolic syndrome
Main cause of death	Cardiovascular diseases and acute respiratory problems

OHS: obesity hypoventilation syndrome.

MORBIDITY AND MORTALITY

Patients with untreated OHS can develop various cardio-metabolic complications (Table 2). Compared to equally obese but eucapnic patients, OHS patients have a higher frequency of hypertension, diabetes, and dyslipidaemia[34-36]. Some studies have also reported a high prevalence of pulmonary hypertension, right and left ventricular dysfunctions and left ventricular hypertrophy in patients with OHS[29,37-42].

Untreated OHS is associated with increased mortality, partially related to acute respiratory problems (i.e., acute-on-chronic hypercapnic respiratory failure)[30,43,44] and to cardiovascular morbidity[30]. The reason for higher prevalence of cardio-metabolic comorbidities in patients with OHS is multifactorial. The extent of hypoxaemia and hypercapnia experienced by patients with OHS is much more profound

than that by patients with eucapnic OSA. As such, it leads to a higher prevalence and more severe pulmonary hypertension and metabolic syndrome and a higher risk of other cardiovascular events and mortality compared to eucapnic obese patients[30,45]. Patients with OHS have a higher risk of developing heart failure (odds ratio [OR], 9; 95% confidence interval [CI], 2.3-35), ischaemic heart disease (OR, 9; 95% CI, 1 , 4-57.1) and cor pulmonale (OR, 9; 95% CI, 1.4-57.1)[46]. It is not surprising that the high burden of cardiovascular disease in patients with OHS may lead to a prevalence of pulmonary hypertension ranging from 30% to 88%[28,47,48].

A cross-sectional analysis[48] examined the association between cardiovascular morbidity and OSA severity in patients with OHS, based on tertiles of oxygen desaturation index (ODI). In patients with OHS, the highest OSA severity phenotype was associated with reduced risk of cardiovascular morbidity. Likewise, patients in the highest ODI tertile were younger, predominantly male, with more obesity, more hyper-somnolent, with worse nocturnal and daytime gas exchange status, lower prevalence of arterial hypertension, better exercise tolerance and fewer days hospitalised than patients in the lowest ODI tertile. This study identified two differentiated phenotypes that can also have different outcomes and treatment. Future studies should bring evidence of this knowledge gap.

Several observational studies have reported an all-cause mortality of 24% at 1.5-2 years in untreated OHS patients[49]. Two observational studies including patients with acute-on-chronic hypercapnic respiratory failure reported one-year mortality of 18% (of which patients with a PAP prescription was 55%)[50] and three-year mortality of 31.3% (of which the proportion of patients treated with PAP was unknown)[44]. The main cause of death under PAP therapy is due to cardiovascular disease[51,52], being acute respiratory problems less likely [52].

MANAGEMENT AND TREATMENT

There were no international guidelines for the treatment of OHS until Mokhlesi & Masa[33] conducted the first clinical practice guide of the American Thoracic Society (ATS) for the evaluation and management of OHS in 2019.

The treatment of OHS must be multidisciplinary, including expertise from chest physicians, sleep specialists, cardiologists, nutritionists and/or bariatricians; it should include lifestyle changes, dietetic measures for the, imperative, weight loss, bariatric surgery and PAP treatment, among others (Fig. 2).

Weight loss and surgical treatment

Weight loss is the ideal treatment, as it can improve diurnal respiratory failure, pulmonary hypertension and sleep-disordered breathing[33,53]. The loss of 25 to 30% of actual body weight can lead to the resolution of OHS[33]. Nevertheless, this is often difficult to achieve and to maintain without the use of bariatric surgery[33].

There are, however, limited long-term data on the efficacy of bariatric surgery in OHS[54] and it is not a safe option for some patients with significantly increased perioperative risk[55]. One year after Roux-en-Y bariatric

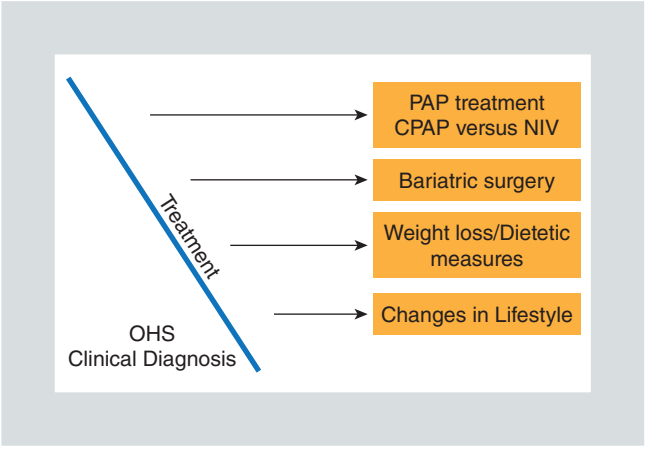

Figure 2. Treatment in OHS. OHS must be treated multidisciplinary, including lifestyle changes (rehabilitation and exercise), dietetic measures and weight loss, bariatric surgery and PAP treatment (CPAP or NIV).
CPAP: continuous positive airway pressure; NIV: non-invasive ventilation; OHS: obesity hypoventilation syndrome; PAP: positive airway pressure.

surgery, partial pressure of oxygen (PaO_2), $PaCO_2$, forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC) improved significantly[54]. The impact of bariatric surgery on improving OSA using the metric of AHI is more variable. In a meta-analysis of 12 studies which included a total of 342 patients, Greenburg et al.[56] showed a decrease in the AHI of 55 to 16 episodes/h in patients with OSA and severe obesity. However, many of these patients remained with moderate or severe OSA (AHI > 15 episodes/h) and therefore continued to require treatment for OSA[56]. In patients with OHS, 14% required PAP treatment after surgical weight loss[55].

As clinicians and patients weigh the risks and benefits of surgical weight loss interventions, it is important to consider that the presence of OSA and the peri-operative extreme weight are independent risk factors associated with peri-operative mortality and adverse events, including venous thromboembolism, surgical re-intervention and prolonged hospital stay[57,58].

Oxygen therapy

Approximately 20% to 30% of patients with OHS have persistent oxygen desaturation episodes during sleep despite adequate PAP therapy[59]. A high concentration of supplemental oxygen without positive pressure therapy can lead to increased hypoventilation and worsening of hypercapnia[60,61].

While oxygen therapy is commonly supplemented to NIV in patients with persistent arterial hypoxaemia, there are no available data about the long-term benefits or clear deleterious effect of this procedure. In a post-hoc analysis in the Pickwick study, 302 sequentially screened OHS patients who were randomly assigned to NIV, CPAP or lifestyle modification were re-analysed[62]. The objective was to assess the medium-term treatment efficacy of adding supplemental oxygen therapy to commonly prescribed treatment modalities in OHS. Outcomes at two months in the NIV subset show supplemental oxygen reduced systolic blood pressure although this could also be explained by a reduction of body weight in this group. In the CPAP group, supplemental oxygen increased the frequency of morning confusion. In the lifestyle modification group, supplemental oxygen increased compensatory metabolic alkalosis and decreased the AHI during sleep. Chronic oxygen therapy produced marginal changes that were insufficient to consider it, globally, as beneficial or deleterious so long-term studies examining outcomes, such as incident cardiovascular morbidity and mortality, are necessary[62].

Pharmacotherapy

Different medications have been investigated to increase the ventilatory impulse in patients with OHS, primarily medroxyprogesterone acetate and acetazolamide, although the available evidence is very limited.

Medroxyprogesterone acetate stimulates breathing at the hypothalamic level[63], although its role in OHS remains uncertain. While one study reported an increase in PaO_2 and a decrease in $PaCO_2$ in patients with OHS treated with this therapeutical approach, a subsequent study did not demonstrate the same benefits[25]. Medroxyprogesterone acetate increases the risk of venous thromboembolism[64], so the administration of the afore-mentioned medication should be limited.

Acetazolamide is a carbonic anhydrase inhibitor that increases minute ventilation by inducing metabolic acidosis through the excretion of bicarbonate in the urine. This medication has been shown to decrease AHI, increase PaO_2 and reduce $PaCO_2$ in patients with OSA. Due to the scarce evidence and its low use, it is not considered or recommended as a usual therapy for patients with OHS. Acetazolamide should not be prescribed as a respiratory stimulant in patients who are not able to normalise or almost normalise their $PaCO_2$ levels with voluntary hyperventilation for one to two minutes[25].

Continuous positive airway pressure and non-invasive ventilation

Positive airway pressure therapy during sleep is the main treatment option for patients with OHS, the most common PAP modalities being NIV and CPAP. The latter prevents upper airway obstructive events but in contrast to NIV, it is not designed to augment ventilation[65]. In patients with OHS and concomitant severe OSA, NIV and CPAP have been shown to be similar in improving daytime symptoms, quality of life, sleep quality, daytime and nocturnal gas exchange status, as well as spirometric and polysomnographic outcomes in medium-term[28,35-39] and long-term[33,52,66] randomised controlled trials (RCTs).

The short-term benefits of PAP include improvement in gas exchange and sleep breathing disorders[2,67] with a response between 50% and 80% of cases, while it can improve gas exchange in a period of 30–90 days[67-71]. This improvement is directly proportional to the hours of PAP use, as each hour decreases $PaCO_2$ by 1.8 mmHg and PaO_2 increases by 3 mmHg.

MECHANISMS OF IMPROVEMENT WITH POSITIVE PRESSURE

The mechanisms by which diurnal hypercapnia improves with PAP are complex and not fully understood. Both CPAP and NIV can influence the following mechanisms: abnormal respiratory mechanics, central responses to hypercapnia and/or neurohormonal dysfunction (leptin resistance) and sleep-disordered breathing.

As far as respiratory mechanics is concerned, NIV can reduce inspiratory muscular activity[72], so that it can efficiently decrease the mechanical load favouring muscular rest and greater muscular efficacy during the day after nocturnal NIV treatment. Continuous positive airway pressure and NIV may decrease the

mechanical load avoiding upper airway repetitive obstructions during sleep.

As for leptin resistance, the levels of serum leptin decrease to normal limits in patients with OSA treated with CPAP[73,74], but it is assumed that apnoeas and hypopnoeas are the cause of the elevated leptin levels rather than being the result of them[22,75]. Leptinaemia also decreases with NIV treatment[76,77] as does daytime hypercapnia, and some studies have shown a correlation between leptinaemia and a reduction in the hypercapnic ventilatory response[78], while another study[77] reported contradictory results, i.e., an increase of leptin with NIV. Therefore, the role of leptin in how NIV treatment achieves improvement is still unclear.

Finally, in regards with sleep-disordered breathing, repetitive obstructive events produce increasing hypercapnia, not resolved with the hyperventilation that occurs at the end of obstructive events. Despite correction of these nocturnal obstructive events with CPAP, daytime $PaCO_2$ does not return to normal in all cases. Several studies have highlighted that the CPAP response may depend on the predominance of nocturnal obstructive events[2,65]. Non-invasive ventilation can prevent obstructive events and reduce hypoventilation during sleep (including rapid eye movement [REM] sleep). Both NIV and CPAP should decrease nocturnal hypercapnia, leading to lower daytime serum bicarbonate and consequently less blunting of the central carbon dioxide response[11].

SCIENTIFIC EVIDENCE

There are several randomised controlled studies that compare different treatments in OHS[67,70]. One of these studies compared the short-term efficacy of NIV and CPAP treatments in 36 patients with OHS selected for their favourable response to a night of CPAP treatment[70]. Following 3 months, the improvements in daytime sleepiness and in clinical and gas exchange parameters were similar between CPAP and NIV groups.

In another trial including 38 patients with mild hypercapnia with NIV compared to a control group treated with conservative measures, the NIV group had a significant reduction in daytime $PaCO_2$, bicarbonate and an increase in pH. Therapy with NIV, as expected, was associated with a great improvement in all sleep variables analysed, sleep architecture, average oxygen saturation, oxygen saturation time less than 90%, apnoea and hypopnoea index, with a positive and significant correlation between average oxygen saturation during sleep and diurnal arterial blood gases. In contrast, no change was observed in any of the metabolic and inflammatory parameters studied, but the follow-up was only one month, so no other conclusions could be drawn[69]. In this study, the patients had a lower BMI and were less hypercapnic than the subjects included in other trials[67,70].

The Pickwick study is to date the largest and most reliable clinical research which addresses the issue of OHS with a sample of 300 individuals using a methodology that compared the data obtained through NIV, CPAP and lifestyle change measures[22]. The Pickwick project has two clinical trials in parallel depending on the existence or absence of severe OSA (AHI ≥ 30). The trial that includes severe OSA has three arms: NIV, CPAP and change in lifestyle for two months (first phase). After this period

of time, the lifestyle change group was re-randomised to NIV or CPAP to continue at least 36 months (second phase). Patients with an AHI < 30 were randomised to NIV or change in lifestyle for at least 36 months (second phase), although an evaluation of results was performed at two months (first phase). The results of the first phase are already available[67]. The first publication included 221 patients with severe OSA randomised to NIV, CPAP and change in lifestyle; $PaCO_2$ improved with each of the three treatments, but the improvement was greater with the use of NIV, with a significant difference in relation to the group of conservative measures. In the CPAP group, the reduction of $PaCO_2$ depended on compliance with the treatment. Thus, NIV and CPAP decreased blood bicarbonate levels but after adjusting baseline data only NIV achieved statistical significance compared to the control group. Sleep variables improved notably with the use of NIV and CPAP, both proving to be equally efficient and with little to no difference between the two; only the NIV group presented increases in the FVC, FEV_1 values and the 6-minute walk test. In another publication of this Pickwick study (the first phase of the trial without severe OSA), 86 patients were randomised and treated for two months with NIV or lifestyle modifications[68]. The NIV group improved significantly $PaCO_2$ and serum bicarbonate levels compared to the control group.

In another RCT, the use of NIV or CPAP was applied for three months to 60 participants. The primary objective was to identify the frequency of treatment failure defined as hospital admission, persistent ventilatory insufficiency or lack of adherence, while secondary objectives included quality of life related to health and drowsiness. A total of 57 patients completed the follow-up without differences in treatment failure between the groups (NIV 14.8% versus CPAP 13.3%; p = 0.87). Of note that adherence to treatment and $PaCO_2$ in wakefulness at three months were similar (NIV 5.3 h/night; CPAP 5.0 h/night; p = 0.62, and $PaCO_2$ in wakefulness at three months of 44.2 and 45.9 mmHg, respectively; p = 0.60). The differences between the groups in the improvement of sleepiness and the quality of life were not significant. Baseline severity of ventilatory failure (based on $PaCO_2$ levels) was the only significant predictor for such insufficiency at three months (OR, 2.3; p = 0.03); no cost-effectiveness or impact on mortality was analysed in this study[71].

Recently, the multicentre, open-label, randomised controlled Pickwick trial at 16 clinical sites in Spain published its long-term results on 97 OHS patients with severe OSA treated with NIV and 107 treated with CPAP. The median follow-up was 5·44 years (interquartile range [IQR] 4·45-6·37) for all patients, 5·37 years (4·36-6·32) in the CPAP group, and 5·55 years (4·53-6·50) in the NIV group. The hospitalisation days per patient-year were 1·63 (standard deviation [SD] 3·74) in the CPAP group and 1·44 (3·07) in the NIV group (adjusted rate ratio 0·78, 95% CI 0·34-1·77; p = 0·561). Changes in other hospital resource utilisation, blood pressure, arterial blood gases, spirometry, quality of life, clinical symptoms and supplemental oxygen therapy remained similar between PAP modalities. Both NIV and CPAP also improved similarly the pulmonary artery pressure and diastolic left ventricular disfunction[79]. Given that CPAP

has lower complexity and cost, CPAP might be the preferred first-line PAP treatment modality[52].

CLINICAL PRACTICE AND FOLLOW-UP

Non-invasive ventilation and CPAP improve gas exchange, respiratory sleep disorders and probably lung function and central respiratory impulse to CO_2. Night-time hypoventilation can be effectively improved, but not in all cases[25,31,80,81], and daytime $PaCO_2$ reduced or restored to normal values[80].

In clinical practice, CPAP should be the initial treatment modality if there is severe OSA, due to its relative simplicity, low cost and efficacy[25,51]. In patients with OHS and non-significant OSA, NIV is preferable, because, when the number of apnoeas is not significant, nocturnal hypoventilation may depend on other mechanisms, such as obesity. In this case, or if the CPAP failed previously, NIV should be preferred[9,11,54,67,81-85] (Fig. 3).

In obese patients with acute hypercapnic respiratory failure or hospitalised patients, NIV should be the first option, due to a likely greater efficacy against hypoventilation, the underlying severity of respiratory failure and also because OSA is probably not the only cause of acute respiratory failure in these patients[86].

Although the duration of treatment with NIV or CPAP is not well established and appears to be undefined, the possibility of withdrawing NIV during short (weekend) or intermediate (vacation) periods in some patients, upon their request, may be recommended.

The improvement in pulmonary gas exchange is observed over a period of 30 to 90 days. Therefore, we could consider a first visit after one week of initiation of NIV, at the first month and then every three or six months, all of them without the need of arterial blood gases, exhaled CO_2 or transcutaneous carbon dioxide control, always depending on the good compliance, tolerance and clinical outcome of each patient. However, we cannot ensure the correct follow-up time, since there are no studies to confirm it[86].

FUTURE CHALLENGES

The prevalence of OHS is expected to increase following global trends in obesity, with significant morbidity associated with this disease. More randomised studies or observational series are required to answer important clinical questions: long-term benefits of PAP (especially in non severe OSA phenotypes), PAP modalities, supplemental oxygen therapy or telemonitorisation tools. In addition, questions formulated in the recent ATS guidelines document[33], whether PAP treatment (empirically or automatically adjusted) has to be initiated immediately after hospital discharge in patients who suffer an acute-on-chronic hypercapnic respiratory failure instead of waiting for the diagnosis confirmation and PAP titration by a sleep study, and if this more severe OHS subgroup needs NIV instead of CPAP, should be solved. A high increase in the knowledge of OHS is expected in the next years, so relevant questions in the subject may be clarified.

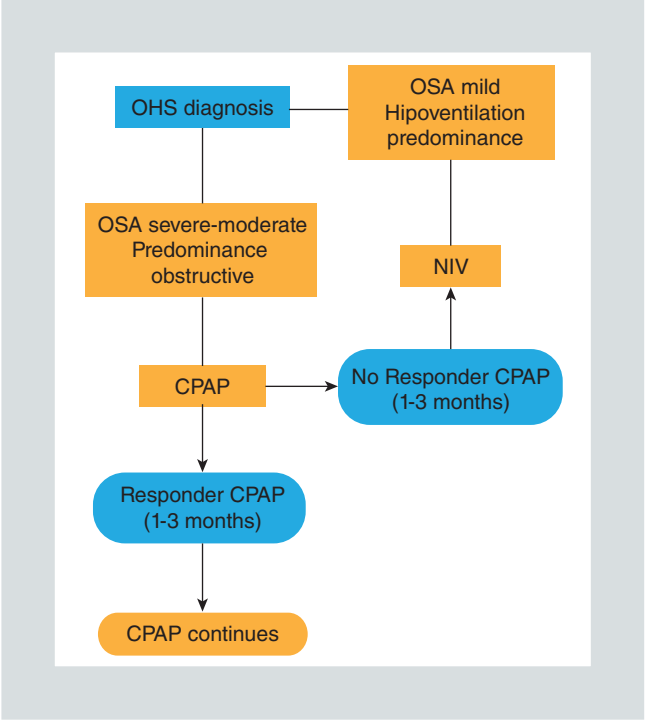

Figure 3. PAP treatment in OHS. CPAP should be the initial modality of treatment if severe OSA is present (predominance obstructive) and if in subsequent evaluations the patient responds with adequate oxygenation and ventilation the CPAP should be continued; if the patient does not respond or if the OHS patient has not significant OSA or has a hypoventilation predominance, NIV should be preferred.
CPAP: continuous positive airway pressure; NIV: non-invasive ventilation; OHS: obesity hypoventilation syndrome; OSA: obstructive sleep apnoea; PAP: positive airway pressure.

CONCLUSIONS

Obesity is a worldwide, increasingly ubiquitous health issue that has triggered the widespread of several related medical conditions, being OHS one that progressively has raised concern among medical professionals. It has a massive impact on the increase of cardio-metabolic complications and its accurate and early diagnosis along with proper treatment are imperative in order to avoid the development of further comorbidity issues and long-term, often life-threatening, complications.

DISCLOSURES

Dr. Ramírez Molina, Dr. Masa Jimenez, and Dr. Gómez de Terreros have nothing to disclose.

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