OBESITY- HYPOVENTILATION SYNDROME - A NEGLECTED PROBLEM?

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Abstract

Obesity-hypoventilation syndrome (OHS) is the most severe complication of obesity, being burdened by numerous cardiovascular complications and an increase in the mortality rate. Late recognition of this syndrome is common.

Approaching the patient with suspicion or confirmed with OHS requires a multidisciplinary team. Positive pressure treatment remains the first line therapy, with the highest efficiency. Weight loss should be recommended in all patients. Apparently, bariatric surgery is superior to lifestyle changes.

Early detection and prompt treatment are of paramount importance to minimize adverse effects, which has necessitated consideration of this article.

Keywords: obesity-hypoventilation syndrome, obesity, cardiovascular complications, weight loss.

Abstract

Sindromul de obezitate-hipoventilație (OHS) este cea mai severă complicație a obezității, fiind împovărat de numeroase complicații cardiovasculare și determinând creșterea ratei mortalității. Recunoașterea tardivă a acestui sindrom este frecventă.

Abordarea pacientului cu suspiciune de OHS sau OHS confirmată necesită o echipă multidisciplinară. Tratamentul cu presiune pozitivă rămâne prima linie de terapie, cu cea mai mare eficiență. Pierderea în greutate trebuie recomandată la toți pacienții. Aparent, chirurgia bariatrică este superioară modificărilor stilului de viață.

Detectarea timpurie și tratamentul prompt sunt de o importanță capitală pentru a minimiza efectele adverse, ceea ce ne-a determinat să abordăm această temă.

Cuvinte cheie: sindrom de obezitate-hipoventilație, obezitate, complicații cardiovasculare, scădere în greutate.

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Introduction

The description of respiratory complications of obesity dates back a long time^(1, 2), initially defining obese patients who associated excessive daytime sleepiness, secondary polycythemia, pulmonary hypertension, and chronic pulmonary heart disease. Nocturnal monitoring of these patients made it possible to describe obstructive sleep apnea syndrome; however, it was observed that some of these patients also had diurnal hypoventilation⁽³⁾.

Academy of Sleep Medicine defines obesity hypoventilation syndrome (OHS) by the presence of alveolar hypoventilation (awake $pCO_2 > 45\text{mmHg}$), in an obese individual ($BMI \geq 30\text{kg/m}^2$), in the absence of other causes that could explain alveolar hypoventilation⁽⁴⁾.

Most patients associate obstructive sleep apnea syndrome (OSAS), but 10% of patients with OHS have only nocturnal hypoventilation, accentuated during REM sleep. This aspect necessitates a night sleep study (preferably polysomno-graphy) to be able to diagnose correctly and to be able to individualize the therapy. Some authors have suggested the use of serum HCO_3^- values in venous blood for the diagnosis of OHS, using a value $\geq 27\text{ mEq/l}$, suggestive for chronic respiratory acidosis secondary to hypoventilation⁽⁵⁾.

OHS is the most severe complication of obesity, being burdened by numerous cardiovascular complications and an increase in the mortality rate⁽⁶⁾. Early detection and prompt treatment are of paramount importance to minimize adverse effects, which has necessitated consideration of this article.

Epidemiology

The prevalence of OHS in the general population is not known, but it most likely follows the growing trend of obesity. The CDC estimates in the US that 38.9% of the population is obese and 7.6% have a $BMI \geq 40\text{ kg/m}^2$ ⁽⁷⁾. Patients with OHS tend to be more obese ($BMI \geq 35\text{ kg/m}^2$), to associate more severe sleep apnea syndrome (apnea-hypopnea index $AHI \geq 30/\text{h}$) and to show more frequent signs and symptoms of chronic pulmonary heart disease compared to patients who have only OSAS. It is estimated that up to 50% of those with $BMI \geq 40\text{ kg/m}^2$ associate OHS, and among patients who go to sleep centers for suspected sleep apnea syndrome, OHS is found in 17% of patients, so it can be estimated a prevalence of OHS in the general population of 0.6%⁽⁸⁾.

Among patients undergoing bariatric surgery, up to 65% of them has OHS⁽⁹⁾. For hospitalized patients with $BMI \geq 35\text{ kg/m}^2$, regardless of the reason, OHS was identified

in 31% of them, and in patients with BMI ≥ 50 kg/m² OHS was identified in 48% of patients. Of concern in this study was the late recognition of OHS and the appropriate initiation of therapy in only 13% of patients. In another study, it was estimated that 8% of hospitalizations in an ICU with chronic hypercapnic respiratory failure met the diagnostic criteria for OHS and 75% of them were erroneously labeled as chronic obstructive pulmonary disease, even in absence of respiratory function tests⁽¹⁰⁾.

Risk factors for OHS

Obesity, especially morbid obesity with a BMI >50 kg/m², is the main risk factor for OHS. However, not all severely obese patients have OHS. Risk factors for OHS in obese patients are not well described but may include the presence of central obesity (increased waist/hip ratio), decreased lung function secondary to obesity, reduced muscle strength of inspiratory muscles, the presence of severe obstructive sleep apnea syndrome⁽¹¹⁾. Male gender is not a risk factor for OHS compared to sleep apnea syndrome⁽¹²⁾.

Staging of hypoventilation obesity syndrome

Two tests are required for the diagnosis of OHS: a sleep study (necessary to confirm the presence of OSAS) and measurement of awake arterial blood gas. This may delay the diagnosis of OHS, as measurement of arterial blood gases is not a standard maneuver in medical services, and evidence of hypercapnia is usually attributed to other lung diseases, most often COPD⁽¹³⁾. Thus, tests are needed to simplify the diagnosis of OHS.

The most often proposed parameter is serum HCO₃, a value of <27 mEq/L practically excludes the presence of hypercapnia. Daytime and nighttime hypoxemia cannot currently be used in the diagnosis of OHS, as the present studies are not uniform, and a correct analysis cannot be performed. To establish the diagnosis OHS, it is recommended to measure PCO₂ in patients who have a high suspicion of OHS, and in those with low or moderate probability, serum bicarbonate can be dosed; a value <27 mEq/L excludes OHS, and for a value $27 \geq$ mEq/L is necessary to measure arterial PCO₂ to confirm the diagnosis⁽¹⁴⁾.

Taskforce of the European Respiratory Society proposed a staging of OHS depending on the value of HCO₃, the presence of OSAS and cardiovascular and metabolic comorbidities. Obese patients who have OSAS but do not have hypercapnia are considered stage 0. Stage I are patients who have nocturnal alveolar hypoventilation (evidenced by increased pCO₂ during sleep) but have normal pCO₂ and HCO₃ being awake. Stage II are patients with normal awake pCO₂ but HCO₃ >27 mEq/L. Stage III are patients who have diurnal hypercapnia. Stage IV are patients who have diurnal hypercapnia and cardiovascular and metabolic comorbidities⁽¹⁵⁾.

OHS pathogenesis

The pathogenesis of OHS is not very well described, but it most likely occurs due to the interaction of several factors. Most often cited are the presence of OSAS, excessive production of CO₂ by excess adipose tissue, decreased activity of the respiratory center (ventilatory drive) and altered pulmonary mechanics secondary to obesity⁽¹⁶⁾. OSAS is the main contributing factor to OHS.

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OSAS is present in 90% of OHS cases, and treatment of OSA, using positive pressure, causes the remission of hypercapnia in most patients. Patients with OSAS who are hypercapnic tend to have a higher AHI, be more obese, and have a decrease in lung function⁽¹⁷⁾.

During respiratory obstructive episodes there is a reduction or even cessation of ventilation, but with an increased metabolic production of CO₂ and an increase in respiratory effort due to upper airway obstruction encountered in OSAS. Patients who remain eucapnic manage, by compensatory increase in alveolar ventilation, to eliminate CO₂ during periods of resumption of respiration. For this aspect, a normal function of the respiratory center and a good respiratory mechanics are necessary. In patients with OHS, ventilation during non-apnea periods is less than in those with eucapnia, which will cause excessive, episodic accumulation of CO₂; this will decrease the elimination of HCO₃ in the kidneys to compensate for the decrease in pH. If the excess HCO₃ is not properly eliminated by the renal system during awake, there will be a chronic retention of HCO₃, which will cause a further decrease in the ventilatory response to CO₂ accumulation^(18,19).

Impairment of respiratory function is supported by abnormal spirometry in obese hypercapnic patients, due to fat deposition in the chest and abdominal wall, reducing chest

distensibility. This will lead to a reduction in total lung capacity, reserve expiratory volume and functional residual capacity. Also, the respiratory pattern encountered in patients with OHS (low current volumes, increased respiratory rate) causes the collapse of the small airways, which will increase the resistance in the airways and increase the respiratory effort⁽²⁰⁾. Decreased ventilation, decreased pulmonary distensibility, respiratory pattern - causes alteration of the ventilation/perfusion ratio and the appearance of hypoxemia.

Alteration of ventilation drive is probably the central element of OHS pathogenesis. Obese hypercapnic patients are not able to adapt ventilation to the level of CO₂, probably by a decrease in the chemosensitivity of the respiratory center to CO₂⁽²¹⁾. Leptin, produced by adipose tissue, has the role of regulating appetite, the rate of basal metabolism and stimulating ventilation. Experimental induction of leptin deficiency in mice results in a phenotype similar to OHS, and leptin administration will determine the correction of hypercapnia^(22,23).

Clinical manifestations

The typical OHS patient is an obese patient with diurnal hypersomnolence. In 90% of cases, patients with OHS associate OSAS, and 70% have severe OSAS with AHI >30/h.

Those associated with OSAS show suggestive symptoms, with noisy snoring, apnea noticed by the entourage, daytime fatigue, impaired concentration and memory, short and thick neck. Most patients with OHS, due to the late recognition of this pathology, usually present when they have significant complications: severe hypoxic hypercapnic respiratory failure (chronic form, or acute on chronic form, needing emergency hospitalization), pulmonary hypertension, chronic pulmonary heart disease. The occurrence of right heart failure causes exertional dyspnea, hepatomegaly, leg edema and jugular turgor. Secondary polycythemia (clinical - facial plethora) may also occur⁽²⁴⁾.

Diagnostic

The first step in establishing the diagnosis of OHS is a high clinical suspicion. In the Marius Nasta Somnology Laboratory, the suspicion of OHS is raised in an obese patient, diagnosed with severe OSAS, especially those with an AHI>50/h, or obese patients who have diurnal hypoxemia unexplained by another pathology, or if during nocturnal oximetry there is a SO_2 min <80% (nadir of SO_2), or who has exertional dyspnea that cannot be explained by another pathology or shows signs and symptoms of PH or right heart failure. We recommend the following investigations in these patients:

- Arterial blood gases (performed in an awake patient, without additional O_2) for the value of PCO_2 and pO_2 .
- Tests necessary to exclude other causes of hypoventilation - spirometry with bronchodilator test (COPD, severe interstitial lung disease), chest X-Ray (restrictive chest disease, severe interstitial lung disease), thyroid hormone dosing. A detailed history of chronic

treatment is also needed, as chronic sedative use can induce hypoventilation.

- Sleep study - we usually use polygraphy being easier and cheaper. The ideal recommendation, however, remains polysomnography. The sleep study is necessary to establish the presence of OSAS and the correct treatment indication.

Complications

Both the complications of obesity alone and the specific complications of OHS must be considered⁽²⁵⁾.

- Presence of PH - up to 2/3 of patients with OHS have mild or moderate pulmonary hypertension⁽²⁶⁾. Evaluation of AH by ECG and echocardiography should be indicated in all patients diagnosed with OHS.
- High blood pressure, congestive heart failure, insulin resistance are also common in patients with OHS.
- Cognitive disorder
- Chronic inflammation, endothelial dysfunction

Given the presence of these possible complications, OHS can be seen rather as a "systemic disease".

Treatment

For the correct therapeutic indication of OHS, considering the complexity of the diagnosis and the frequent presence of comorbidities, a multidisciplinary collaboration is necessary. Weight loss and positive pressure treatment are the main lines of treatment⁽¹⁴⁾.

Positive pressure treatment:

It should be started immediately after the diagnosis is confirmed and should not be delayed by the desire to lose weight. The

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choice of the initial mode of administration of positive pressure depends on the presence of OSAS and whether the diagnosis of OHS was established during emergency hospitalization for respiratory failure. For the stable patient, who associates OSAS, the initial mode is CPAP (continuous positive airway pressure). For the patient without OSAS, or who is hospitalized for respiratory failure, the initially chosen mode is BPAP (bi-level positive airway pressure).

BPAP is also indicated in those who do not tolerate CPAP due to the high pressures required for OSAS correction. In patients who have failed BPAP, a mixed mode of ventilation, volume and pressure support (VAPS) may be indicated.

CPAP has been shown to be effective in patients combining OSAS and OHS, leading to improved PaCO₂ and quality of life, most likely by remission of OSAS, improved respiratory muscle function, and “reset” of the respiratory drive⁽²⁷⁾. However, it does not lead to the normalization of PaCO₂ and SO₂ in all patients⁽²⁸⁾. When properly indicated, CPAP and BPAP are equally effective in terms of the number of hospitalizations, lung function, pCO₂ and pO₂ values, the need for additional O₂ and quality of life, including excessive daytime sleepiness⁽²⁹⁾. In patients who have failed CPAP or have an initial indication for BPAP, this mode should be indicated. Most often, BPAP is indicated in S mode. Expiratory

pressure (EPAP) is the pressure needed to correct obstructive respiratory events during sleep. The inspiratory pressure is gradually increased until the desired degree of ventilation is obtained. The greater the pressure difference between IPAP and EPAP, the greater the current volume administered to the patient, which will favor ventilation and amelioration of SpO₂ and pCO₂⁽³⁰⁾. Oxygen supplementation should only be considered in patients who experience hypoxemia despite appropriate pressure therapy. The use of additional O₂ in the absence of positive pressure therapy, improves nocturnal SpO₂, but cannot correct OSAS, does not improve ventilation and may aggravate CO₂ retention⁽³¹⁾.

There are no firm recommendations for evaluating the therapeutic response. In Marius Nasta Institute we consider useful to reevaluate the patient after one month of pressure therapy, by compliance with treatment, improvement of clinical signs and symptoms, correction of pCO₂, correction of day and night SpO₂, improvement of OHS complications, improvement of quality of life. We indicate the repetition of the sleep study if alveolar hypoventilation or daytime sleepiness persists.

Weight loss

Obesity is the major risk factor for OHS. In patients compliant with pressure therapy,

who do not lose weight, an increased cardiovascular and metabolic risk due to the presence of obesity persists^(32,33). Thus, weight loss will improve both OHS and OSAS, as well as cardiovascular and metabolic risk.

It is important to lose weight and maintain it, regardless of the method chosen. However, bariatric surgery is more effective in achieving sustainable weight loss⁽³⁴⁾. Some studies have shown superior efficacy to bariatric surgery in terms of “curing” OHS (defined by the absence of the need for positive pressure treatment) compared to lifestyle change interventions. Unfortunately, the studies that support the indication of bariatric surgery in the approach of the patient with OHS, are small.

Conclusions

Obesity-hypoventilation syndrome is an important health issue. It is burdened by multiple cardiovascular and metabolic complications, materialized by a decrease in quality of life and an increase in morbidity and mortality. Late recognition of this syndrome is common. Approaching the patient with suspicion or confirmed with OHS requires a multidisciplinary team. Positive pressure treatment remains the first line therapy, with the highest efficiency. The choice of how to administer pressure therapy depends on the presence of OSAS and the severity of respiratory failure. Weight loss should be recommended in all patients. Apparently, bariatric surgery is superior to lifestyle changes.

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