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A Successful Treatment of Obesity Hypoventilation Syndrome, the Cause of Respiratory Failure in a Patient with Severe Obesity

Ciddi Obezitesi Olan Hastada Solunum Yetmezliğinin Nedeni Obezite Hipoventilasyon Sendromunun Başarılı Tedavisi

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ABSTRACT

Obesity hypoventilation syndrome (OHS), also known as Pickwickian syndrome, is characterized by chronic alveolar hypoventilation in individuals with obesity, in the absence of other respiratory pathologies. It is often associated with hypercapnia (pCO_2> 45 mmHg), hypoxemia, and concurrent obstructive sleep apnea syndrome in 90% of the cases. If left untreated, OHS can lead to serious complications, including pulmonary hypertension and cor pulmonale. A 70-year-old female patient with a body mass index of 62, hypertension, type 2 diabetes, and hypothyroidism presented with progressive leg edema and hypoxemia (SpO_2= 66%). She was semi-mobile and dependent on a wheelchair. Arterial blood gas analysis confirmed compensated respiratory acidosis (pCO_2= 66 mmHg, pO_2= 55 mmHg, HCO_3= 30 mmHg). Initial treatment included switching from continuous positive airway pressure to bilevel positive airway pressure (BiPAP) for hypercapnia and improved oxygenation. Nutritional support, physiotherapy, and the initiation of liraglutide resulted in a 23 kg weight loss over six months. The patient's oxygen saturation improved to 88%, and her symptoms of chronic respiratory failure decreased. Effective management of OHS requires a multidisciplinary strategy to prevent severe complications, including pulmonary hypertension, cor pulmonale, and early mortality. Non-invasive ventilation, such as BiPAP, is the first-line therapy to address hypercapnia and improve gas exchange. Early initiation of BiPAP can reduce the risk of long-term cardiovascular and pulmonary complications. Weight loss is a crucial component of OHS treatment. Liraglutide and other GLP-1 receptor agonists have shown promise in promoting weight loss while improving glycemic control. In severe cases, bariatric surgery remains an option, though careful preoperative assessment is required due to elevated perioperative risks.

Key Words: *Hypercapnia, obesity hypoventilation syndrome, respiratory failure*

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ÖZ

Pickwickian sendromu olarak da bilinen obezite hipoventilasyon sendromu (OHS), diğer solunum patolojilerinin yokluğunda obeziteli bireylerde kronik alveolar hipoventilasyon ile karakterizedir. Genellikle hiperkapni (pCO_2> 45 mmHg), hipoksemi ve vakaların %90'ında eş zamanlı obstrüktif uyku apne sendromuyla ilişkilidir. Tedavi edilmezse, OHS pulmoner hipertansiyon ve kor pulmonale dahil olmak üzere ciddi komplikasyonlara yol açabilir. Vücut kitle indeksi 62, hipertansiyon, tip 2 diyabet ve hipotiroidi olan 70 yaşındaki kadın hasta ilerleyici bacak ödemi ve hipoksemi (SpO_2= %66) ile başvurdu. Yarı hareketliydi ve tekerlekli sandalyeye bağımlıydı. Arteriyel kan gazı analizi kompanse respiratuvar asidozu doğruladı (pCO_2= 66 mmHg, pCO_2= 55 mmHg, HCO_3= 30 mmHg). Başlangıç tedavisi hiperkapni ve oksijenasyonun iyileştirilmesi için sürekli pozitif hava yolu basıncından bilevel pozitif hava yolu basıncına (BiPAP) geçişi içeriyordu. Beslenme desteği, fizyoterapi ve liraglutid başlanması altı ay içinde 23 kg kilo kaybıyla sonuçlanmıştır. Hastanın oksijen satürasyonu %88'e yükseldi ve kronik solunum yetmezliği semptomları azaldı. Obezite hipoventilasyon sendromunun etkili yönetimi, pulmoner hipertansiyon, kor pulmonale ve erken mortalite gibi ciddi komplikasyonları önlemek için multidisipliner bir strateji gerektirir. Bilevel pozitif hava yolu basıncı gibi non-invaziv ventilasyon, hiperkapniyi gidermek ve gaz değişimini iyileştirmek için ilk basamak tedavidir. Bilevel pozitif hava yolu basıncının erken başlanması uzun vadeli kardiyovasküler ve pulmoner komplikasyon riskini azaltabilir. Kilo kaybı, OHS tedavisinin önemli bir bileşenidir. Ancak metabolik ve kas-iskelet sistemi kısıtlamaları nedeniyle bunu başarmak zor olabilir. Liraglutid ve diğer GLP-1 reseptör agonistleri, glisemik kontrolü iyileştirirken kilo kaybını teşvik etme konusunda umut vadetmektedir. Ağır vakalarda, bariatrik cerrahi bir seçenek olmaya devam etmektedir ancak yüksek perioperatif riskler nedeniyle dikkatli bir preoperatif değerlendirme gereklidir.

Anahtar Kelimeler: *Hiperkapni, obezite hipoventilasyon sendromu, solunum yetmezliği*

INTRODUCTION

Obesity hypoventilation syndrome (OHS), also known as Pickwickian syndrome, is characterized by chronic alveolar hypoventilation in individuals with a body mass index (BMI) greater than 30, in the absence of other known causes of respiratory failure, such as chronic obstructive pulmonary disease (COPD), pulmonary vascular diseases, hypothyroidism, or neuromuscular disorders. The defining feature of OHS is persistent hypercapnia, indicated by an arterial partial pressure of carbon dioxide (pCO_2) exceeding 45 mmHg, in the absence of significant lung pathology. OHS is often associated with hypoxemia and typically presents as chronic respiratory failure; however, it may occasionally present acutely in the presence of exacerbating factors such as infections or heart failure. The prevalence of OHS is estimated to range between 0.15% and 0.3% in the general adult population, increasing to 10-20% in individuals with obesity, approximately 90% of whom also suffer from obstructive sleep apnea syndrome (OSAS) (1,2).

The pathophysiology of OHS is driven by a combination of mechanical and neurohormonal factors associated with obesity. Increased body mass, particularly abdominal fat, imposes greater mechanical loads on the respiratory system, leading to reduced lung compliance, diaphragmatic dysfunction, and a diminished functional residual capacity, all of which contribute to alveolar hypoventilation. Additionally, obesity impairs the body's response to hypercapnia and hypoxia by blunting the respiratory drive, exacerbating hypoventilation (3). Approximately 75% of the patients are often misdiagnosed with chronic obstructive pulmonary disease; however, in OHS patients, pulmonary function tests typically show either normal or mildly restrictive results, with no significant evidence of airway obstruction (4). Diagnostic exclusion of OHS is supported by a serum bicarbonate level below 27 mmol/L, particularly when the pre-test probability is low (below 20%).

OHS is often diagnosed at an advanced stage, typically during hospitalization for acute complications such as respiratory failure, pulmonary hypertension, or cor pulmonale. This late diagnosis frequently occurs in the fifth or sixth decade of life when the disease has progressed significantly. This highlights the critical need for increased multidisciplinary awareness in the management of OHS. Internal medicine specialists play a pivotal role in recognizing the early signs of OHS and should maintain a high index of suspicion during the diagnostic phase.

CASE REPORT

A 70-year-old female with a BMI of 62 kg/m^2 (height= 160 cm, weight= 159 kg) presented with progressive generalized edema, particularly affecting the lower extremities, over a 15-day period. Her medical history was significant for hypertension, type 2 diabetes mellitus, and hypothyroidism, all managed with medications including candesartan, lercanidipine, linagliptin, and levothyroxine. The patient was semi-mobile and reliant on a wheelchair, which heightened her susceptibility to obesity-related complications.

Upon admission, the vital signs included a blood pressure of 135/90 mmHg, a heart rate of 85 beats per minute, and a fingertip oxygen saturation (SpO_2) of 66%, indicating severe hypoxemia. Despite this critically low oxygen saturation, the patient was alert and conversant, exhibiting no overt signs of dyspnea, tachypnea, or respiratory distress, suggesting chronic, compensated respiratory failure. Physical examination revealed pronounced bilateral pitting edema (3+), predominantly in the pretibial region.

Laboratory investigations were largely unremarkable, except for mild hyponatremia (Na= 129 mmol/L), with normal serum albumin levels, effectively ruling out hypoalbuminemia as the cause of the patient's edema. Thyroid stimulating hormone level was mildly elevated. Pro-BNP was 1300 pg/mL. Arterial blood gas analysis revealed a pH of 7.28, pCO_2 of 66 mmHg, pO_2 of 55 mmHg, and HCO_3 of 30 mmol/L, indicating compensated respiratory acidosis, a key marker of chronic hypercapnic respiratory failure in the context of OHS.

Electrocardiography revealed atrial fibrillation with a controlled ventricular rate of 85 beats per minute. Chest radiography revealed cardiomegaly, bilateral costophrenic angle blunting, and lower zone opacities, consistent with pulmonary edema (Figure 1). Echocardiography demonstrated a preserved left ventricular ejection fraction of 55%, effectively excluding heart failure as the primary contributor to her respiratory symptoms.

The patient had previously been prescribed CPAP for OSAS but had been poorly compliant with the therapy. Considering her clinical presentation and elevated pCO_2 levels, she was transitioned to BiPAP. Inspiratory positive airway pressure was set at 15 cmH_2O and expiratory positive airway pressure (EPAP) was set at 7 cmH_2O, to more effectively address her alveolar hypoventilation.

The patient showed a favorable response to the initial management, which included intravenous diuretics for pulmonary edema and anticoagulation therapy for atrial fibrillation. BiPAP therapy contributed to a gradual improvement in oxygen saturation, which rose to 75% within a few days. She was subsequently transitioned to oral diuretics. Given the potential role of lercanidipine in exacerbating her lower extremity edema, the medication was discontinued. Once renal function stabilized, metformin 1000 mg twice daily was initiated. Anemia was also managed with appropriate therapy. The patient's treatment plan was further

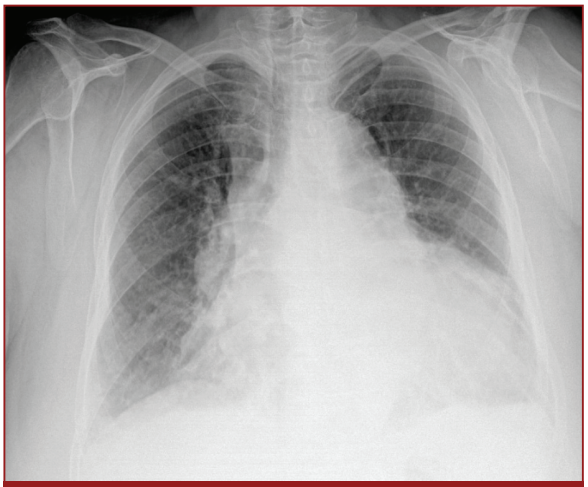

Figure 1. Patient's chest radiography.

modified by discontinuing linagliptin and initiating liraglutide, starting at 0.6 mg and titrated weekly to 1.8 mg daily. Nutritional and physiotherapy support were integral to her comprehensive care. Over a six-month period, this resulted in a significant weight loss of 23 kg and a marked improvement in her oxygen saturation levels (SpO_2 88-89%) (Table 1).

DISCUSSION

The management of OHS requires a multifaceted approach, as untreated cases can lead to serious complications, such as chronic pulmonary hypertension, cor pulmonale, and early mortality. The cornerstone of OHS management involves non-invasive ventilation (NIV) and weight reduction strategies. However, achieving significant short-term weight loss is often challenging due to coexisting metabolic and cardiovascular conditions. Although bariatric surgery may be an option, comorbidities frequently pose significant barriers to surgical intervention. Importantly, NIV should not be delayed in pursuit of weight loss, as it plays a critical role in alleviating respiratory failure and improving patient outcomes.

A comprehensive therapeutic approach, combining home NIV or CPAP with lifestyle modifications and structured rehabilitation programs, is essential to addressing the considerable cardiovascular and metabolic burden associated with OHS. Continuous positive airway pressure (CPAP) is typically the initial treatment of choice for OHS patients who also suffer from severe obstructive sleep apnea (OSA). However, NIV is generally more effective for individuals with sleep hypoventilation and milder OSA (5). Approximately 50% of the

Table 1. Clinical progression over time

Time Point	Weight (kg)	SpO_2 (%)	pCO_2 (mmHg)	pH	Treatment
Admission	159	66	66	7.28	Diuretics
Week 1	157	75	60	7.31	BiPAP initiated
Week 2	155	82	52	7.34	Liraglutide, dietary plan
Month 6	136	88-89	48	7.36	Multidisciplinary follow-up
Year 1	130	92	45	7.38	Liraglutide continued

patients with OHS develop pulmonary hypertension, a condition in which NIV may offer superior benefits compared to CPAP by reducing hypercapnia (6,7).

In our case, the patient presented with both OSAS and chronic respiratory failure, which prompted a switch from CPAP to BiPAP. This transition resulted in significant symptom relief and an improvement in her arterial blood gas parameters, highlighting the efficacy of BiPAP in managing her condition.

Weight loss is fundamental to managing OHS. Effective management requires a collaborative approach involving nutritionists, psychologists, internists, pulmonologists, and family members to provide comprehensive support. Nutritional therapy should be carefully tailored. There should be a focus on encouraging physical activity; however, musculoskeletal problems such as osteoarthritis and lumbar disc herniation may make mobility difficult. In such cases, physiotherapy becomes essential to increase physical capacity and facilitate weight loss.

Moreover, the increasing prevalence of prediabetes and diabetes among these patients necessitates careful regulation of oral antidiabetic medications and insulin therapy. Achieving a 25-30% weight loss leads to significant improvements in pulmonary function, resolution of hypoventilation, and a reduced need for mechanical ventilation (8). However, accomplishing this level of weight reduction can be particularly challenging in elderly or immobile patients, necessitating close dietary monitoring to mitigate the risk of sarcopenia. Additionally, a thorough assessment for comorbidities such as hypertension, hyperlipidemia, heart failure, atrial fibrillation, and chronic renal failure is essential, as these conditions may complicate both the management and prognosis of OHS.

Medications such as metformin and SGLT-2 inhibitors (dapagliflozin, empagliflozin, etc.) are often preferred for promoting weight loss in OHS patients. Additionally, glucagon-like peptide-1 (GLP-1) agonists, including exenatide, liraglutide, dulaglutide, and semaglutide, have demonstrated effectiveness in facilitating weight reduction among both diabetic and non-diabetic individuals with obesity. These agents not only assist in weight management but also exhibit favorable effects on cardiovascular health. However, literature specifically examining the use of GLP-1 agonists in patients with OHS is limited and further research is needed (9,10).

For individuals who struggle to achieve meaningful weight loss through medical interventions, bariatric surgery may be considered. It is essential to note that such procedures are associated with heightened risks in patients who present with significant cardiopulmonary comorbidities, necessitating a careful evaluation of the potential benefits versus risks before proceeding with surgical intervention.

Untreated OHS is frequently associated with serious complications, including pulmonary hypertension and cor pulmonale, affecting nearly 50% of patients. The pathophysiology underlying these complications often involves the cumulative effects of chronic hypoventilation and resultant hypercapnia, leading to increased pulmonary vascular resistance and subsequent right heart strain. In such cases, NIV may prove more effective than CPAP in mitigating pulmonary hypertension by directly addressing hypercapnia. Furthermore, it is crucial to exercise caution when administering supplemental oxygen, particularly high concentrations (e.g., 100% FiO_2), as this may exacerbate hypoventilation by diminishing the hypoxic respiratory drive (5). Alternative strategies for managing hypoxemia, such as low-flow oxygen therapy, should be carefully considered to avoid further respiratory compromise.

Early recognition of OHS is crucial, even in the absence of overt dyspnea or tachypnea. Subtle symptoms, such as fatigue, morning headaches, and leg edema, can be important clues. Non-invasive mechanical ventilation (NIV), especially BiPAP, is the cornerstone of treatment

for chronic hypercapnia in OHS. It can prevent progression to pulmonary hypertension and cor pulmonale. A comprehensive, multidisciplinary approach involving pulmonary rehabilitation, weight loss interventions, and close monitoring for metabolic comorbidities (e.g., diabetes, hypertension) is essential for improving long-term outcomes in OHS patients

CONFLICT of INTEREST

No conflict of interest declared.

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