Journal of Anesthesiology & Clinical Research
https://hmpublisher.com/index.php/JACR/index
Vol 3 Issue 1 2022

Obesity Hypoventilation Syndrome

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ABSTRACT

Obesity Hypoventilation Syndrome or commonly abbreviated as OHS, is a respiratory disorder that often occurs in patients characterized by decreased oxygen levels and increased carbon dioxide in the blood. Based on the criteria of the World Health Organization (WHO), the definition of obesity is if the BMI is equal to or greater than 30 kg/m^2. The classification of obesity is BMI 30-34.9 kg/m^2, 35-39.9 kg/m^2 and > 40 kg/m^2. The pathophysiology of OHS is still not fully known with certainty. Severe obesity causes an increase in the burden on the respiratory system, weakness of the respiratory muscles, leptin resistance, and respiratory disturbances during sleep, causing a decrease in the sensitivity of the ventilation center response, which can lead to hypoventilation and hypercapnia. Basically, there are six points of OHS management, including a weight loss program, oxygen therapy, positive pressure ventilation, pharmacotherapy, tracheostomy, and management of OHS complications.

Keywords: obesity, obesity hypoventilation syndrome, respiration.

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Introduction

Obesity has become a global problem. According to the World Health Organization, there are more than 1.9 billion adults over 18 years who are overweight, and more than 600 million people are obese. Based on data from Riskesdas in 2010, the prevalence of obesity in Indonesia is divided by age, namely in children aged 6-12 years, around 9.2%, in children aged 13-15 years, around 2.45%, at the age of 16-18 years around 1, 4%, and over the age of 18 years around 21.6%.[1] Obesity is a public health problem in the world today because its prevalence tends to increase, becomes a risk factor for cardiovascular disease, and increases the cost of health services. Obesity also causes abnormalities in breathing patterns during sleep, such as obesity hypoventilation syndrome (OHS). Obesity hypoventilation syndrome (OHS) can increase the mortality and morbidity of patients and reduce their quality of life. Obesity hypoventilation syndrome is still rarely reported because it has symptoms that resemble other diseases, so the diagnosis of this disease is often unthinkable. OHS patients may also have obstructive sleep apnea (OSA) or isolated sleep hypoventilation.[2]

Obesity is a metabolic disease defined as an abnormally high level of fat tissue compared to muscle mass. Obesity can be a risk factor for other metabolic diseases such as coronary heart disease, ischemic stroke, and Mellitus. Obesity is classified using the Body Mass Index (BMI). Patients with a BMI of 30 kg/m^2 and above are called obese, 40 kg/m^2 are said to be morbidly obese, and 50 kg/m^2 are called super obese.[3] In obese patients, there can be changes in the distribution, binding, and clearance of anesthetic drugs. Serious side effects can easily occur if the dosage of the drug is based solely on actual body weight. In obese patients, there is also a change in the pharmacokinetic profile of anesthetic drugs due to an increase in total blood volume, cardiac output, and changes in plasma protein binding. The absorption and elimination of inhaled anesthetic gases are also influenced by changes in respiratory and cardiovascular function in obese patients.[1] An increased body mass index will increase the risk of obesity-related disease morbidity. Based on WHO estimates, in 2015, there were about 2.3 billion adults who were overweight and more than 700 million adults who were obese. Obesity hypoventilation syndrome is an obese patient who has hypercapnia ($PaCO_2$ > 45 mmHg) without other abnormalities that underlie the occurrence of hypoventilation.[4]

Pathophysiology

Hypercapnia in OHS is caused by a state of hypoventilation. Giving positive pressure ventilation (PAP) in a short time can improve hypercapnia even though body weight does not change. The pathophysiology of OHS is still not fully known with certainty. Severe obesity causes an increase in the burden on the respiratory system, weakness of the respiratory muscles, leptin resistance, and respiratory disturbances during sleep, causing a decrease in the sensitivity of the ventilation center response, which can lead to hypoventilation and hypercapnia.[4]

Obese patients generally have a large central fat distribution. Obese patients have a greater neck circumference and waist-to-hip ratio. The distribution of fat on the chest and abdominal walls, as well as a cephalic shift of the diaphragm in OHS patients, occurs when lying on the back, thereby reducing the expansion of the chest wall. Muscles must contract more forcefully to produce a higher negative pressure in the pleural space so that airflow is easier on inspiration.[4] Decreased expansion of the chest wall and lungs cause increased airway resistance and reduced functional residual capacity (KRF). Increased airway resistance in obese patients with eucapnics can reach 30%, while in OHS patients, it can reach 300%. The increase in airway resistance mainly occurs in small airways so that the ratio of forced expiratory volume in the first second and forced vital capacity (VEP1/KVP) will remain normal if there is no obstructive pulmonary disease. Airway resistance will increase, and KRF will decrease further when OHS patients lie supine because of the mass load generated by the large adipose tissue in the supralaryngeal area and the increased pulmonary blood flow.

The mechanism that causes the decreased strength of the respiratory muscles in obese patients is still not known with certainty but is thought to be due to excessive fat tissue infiltration in the muscles. Hypercapnia can also cause a decrease in the strength of the diaphragm muscles, so it is still difficult to confirm obesity or hypercapnia as the main cause of respiratory muscle weakness in OHS patients. Assessment of muscle strength can be done through the assessment of maximal inspiratory and expiratory pressures. Maximum inspiratory and expiratory pressures usually remain normal in obese patients with euphoria and decrease in patients with OHS.

Leptin is a hormone produced by white fat tissue with crystal structures similar to cytokines. This hormone can suppress hunger, so it plays a role in weight loss. Leptin circulates in the plasma in a free or protein-bound form. Leptin, in addition to having an anti-obesity effect and plays a role in increasing minute ventilation. Obesity causes an increase in the production of carbon dioxide (CO_2) which is caused by an increase in O_2 consumption for

respiration. Mass fat tissue in obese patients will stimulate white fat tissue to increase leptin production to stimulate an increase in minute ventilation as a compensatory mechanism to expel excess CO_2. This mechanism explains the pathophysiology of severely obese patients without hypercapnia.[8]

Respiratory disorders during sleep have an important role in the pathophysiology of OSH. Acute hypercapnia associated with OSA will cause the body's compensatory mechanism in the form of hyperventilation after a period of apnea which will release the remaining CO_2 accumulated during the period of apnea. Another mechanism is the increased levels of bicarbonate (HCO_3) in the serum by the kidneys to maintain the degree of acidity (pH). Disruption of these two compensatory mechanisms can lead to chronic hypercapnia.[3] In OHS patients, there is a shortened ventilation time between periods caused by the gradual adaptation of chemoreceptors caused by an increase in serum HCO_3 levels. In eucapnic arterial CO_2 pressure returns to normal upon awakening, and HCO_3 is excreted. During the transition from acute to chronic hypercapnia, there is a decrease and a slowdown in HCO_3 excretion caused by a decrease in the ventilation response to CO_2, resulting in an increase in serum HCO_3 levels.

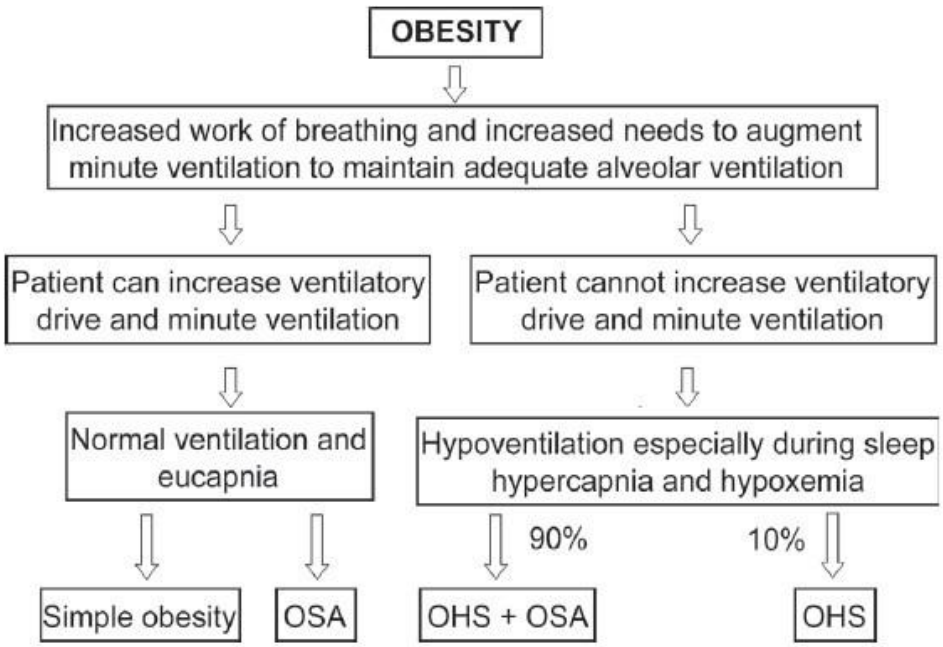

Figure 1. OHS Pathophysiology Algorithm[4]

Clinical manifestations

OHS patients may present with various clinical symptoms caused by breathing disturbances during sleep. Patients often complain of complaints such as fatigue, excessive drowsiness, frequent loud snoring during sleep, frequent awakenings at night due to choking or feeling suffocated, decreased enthusiasm for work, and headaches at night or in the morning. If the patient is not treated optimally, complications such as erythrocytosis, pulmonary hypertension, and right heart failure can occur.[4] Arterial blood gas analysis showed hypercapnia with acidosis and hypoxemia. An increase in serum HCO_3 levels as a compensatory mechanism for the body to buffer the fall in pH is one indicator of the presence of hypercapnia. The Nowbar study showed a group of OHS patients had higher serum HCO_3 levels than obese eucapnic (30±4 mEq/L versus 25±5 mEq/L, $p<0.01$).[2] Required pulmonary function tests performed such as spirometry, bronchodilator test, maximal inspiratory and expiratory pressures, and vital capacity in the supine position. The spirometry test can show normal results or mild or moderate restrictive abnormalities caused by body shape and no obstructive abnormalities (VEP1/FVC normal or close to normal). Expiratory reserve volume and KRF will decrease significantly in severely obese patients. The maximal inspiratory and expiratory pressures and the strength of the respiratory muscles also decrease.[4-8]

Management

The initial step in the management of OHS is a multidisciplinary approach from various medical and surgical subspecialties. Expected care from Internist to manage diabetes mellitus, hypertension, hyperlipidemia, heart failure, and hypothyroidism therapy. In addition, it is required on the part of a nutritionist for a weight loss program. No less important is the role of pulmonary specialists and intensivists in dealing with the emergency of respiratory failure. There are basically six points of OHS management, including a weight loss program, oxygen therapy, positive pressure ventilation, pharmacotherapy, tracheostomy, and management of OHS complications.[2]

Losing at least 10 kg of actual body weight can improve lung function and physiology by increasing vital capacity and forced expiratory volume. In addition, in OHS patients who also experience OSA, weight loss can reduce the risk of desaturation and apnea. In patients with very severe obesity, bariatric surgery has been shown to be a more effective modality than dietary management alone with medication. important to realize that weight loss is not the only way to treat OHS. Management of other comorbid diseases is required. In patients with a BMI

> 35 kg/m^2 without any comorbidities, bariatric surgery has been shown to be effective in preventing OHS.[2]

OHS is characterized by prolonged hypoxemia during sleep and during the day. Oxygen supplementation may be beneficial in patients with persistent hypoxemia, although upper respiratory tract obstruction can be managed with positive pressure ventilation to prevent long-term effects of hypoxemia on vital organs. It should be remembered, however, that treatment with oxygen alone is not adequate and is not recommended because it does not improve hypoventilation or airway obstruction on its own.[2]

Positive airway pressure (PAP) acutely and chronically improves gas exchange and functional status in patients with various forms of chronic respiratory failure, including those with OHS. The reason for progressive improvement after long-term use is still speculative and is thought to act through several mechanisms that ultimately lead to improvement in nocturnal and daytime symptoms. First of all, PAP reduces the obstructive component seen in the majority of patients with OHS. Second, it can effectively change the mechanics of the chest wall and lungs in severely obese patients and, finally, can increase the flow to central ventilation. The first successful trial to treat OHS involved the use of CPAP therapy in 2 patients with OSA and OHS. In patients with mild OHS, bi-level CPAP and PAP (a system that allows independent adjustment of inspiratory and expiratory PAP) have been shown to be equally effective in correcting daytime hypercapnia. Moreover, there was no difference in adherence between the two treatment modalities. However, in patients with persistent hypoventilation and desaturation, CPAP therapy and bi-level PAP should be attempted. It seems reasonable to start with CPAP, knowing that the majority of OHS patients have to accompany OSA. There are no clear guidelines on when to start or switch to bi-level PAP in patients with OHS. However, PAP two levels higher should be initiated if the patient cannot tolerate CPAP because of persistent massive air mask leakage or experiencing discomfort when exhaling against positive pressure or if the patient has frequent episodes of hypoventilation without airway obstruction. If hypercapnia persists despite the long-term use of CPAP, titration should be performed according to the American College of Chest Physicians (ACCP) protocol. Supplementation of oxygen should be added if the patient continues to be hypoxaemic even after the obstructive respiratory distress and hypoventilation have been completely eliminated.[2]

Several drugs known to have a stimulating effect on respiration, such as progesterone, acetazolamide, almitrine, and aminophylline, have been tried in patients with OSA. However,

the two drugs most widely used when dealing with people with OHS are medroxyprogesterone and acetazolamide. Medroxyprogesterone acetate, a synthetic progesterone derivative that is effective in stimulating respiration, has been used for a long time in managing patients with OHS. The resulting positive effect is mainly in increasing the ventilatory response to hypercapnia, which ultimately leads to increased ventilation with a decrease$_2$ and an increase in PaO_2.

Recent studies in a group of postmenopausal women who failed respiratory where, at the end of the study, $PaCO_2$ levels, leptin levels, and neuropeptide Y levels have shown that after 14 days of medroxyprogesterone acetate therapy, there was a significant difference in increased ventilation and reduced $PaCO_2$ without changing serum levels leptin or neuropeptide Y. Clearly, this approach to hormonal manipulation is not without its side effects, and the risk of inducing a hypercoagulable state should always be considered, especially in this group of patients who already have underlying predisposing factors such as obesity, reduced mobility, and heart failure.[2]

The carbonic anhydrase inhibitor acetazolamide is a weak diuretic that causes metabolic acidosis. When used in patients with OHS, it may cause a reduction in serum bicarbonate levels, which promotes metabolic acidosis leading to increased minute ventilation. In the end, it causes a decrease in $PaCO_2$ levels. There are currently recommendations strong can be made regarding the use of either as there is no data on the safety of long-term use.

Management of OHS complications

Obesity is a systemic process in which several organ systems are involved, among which the cardiovascular system, respiratory system, and metabolic system appear to be affected to a large extent. It is, therefore, important to approach obese patients with a multidisciplinary view and optimize pharmacological and non-pharmacological therapies for each affected system. For example, blood pressure, blood sugar, and lipid profiles should ideally be maintained within normal limits. Any systolic or diastolic disturbances concomitant with heart failure should be managed aggressively to avoid further complications of the cardiopulmonary system.[2] In addition, finding significant complications such as erythrocytosis and secondary pulmonary hypertension should be undertaken, and appropriate intervention implemented as a recommendation. Phlebotomy is a valid option in adult patients with symptoms of hyperviscosity. Several papers describe the role of the renin-angiotensin system and erythropoiesis, implying the potential benefit of blocking the system with angiotensin-

converting enzyme inhibitors or angiotensin II receptor blockers are leading to better management of polycythemia in these patients. In summary, obesity is a major public health problem worldwide and has a detrimental effect on the economy of health care systems at different levels.[2]

Conclusion

There are six points of OHS management, including a weight loss program, oxygen therapy, positive pressure ventilation, pharmacotherapy, tracheostomy, and management of OHS complications. In addition, cooperation from various sub-specialists such as internists, respirologists, intensivists, surgeons, and nutritionists.

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