

Obesity Hypoventilation Syndrome

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Abstract

The obesity pandemic has caught up even in developing nations. With this arises complications affecting all the major organs of the body. As a pulmonologists skewed view of obesity; the lungs, chest wall bellows and the respiratory controllers are all affected. Though obstructive sleep apnoea (OSA) among obese people are now well recognised among pulmonologists, OSA with hypoventilation or the Hypercapnic OSA gets unrecognized. This has important implications, because compared with eucapnic obese patients, those with Obesity Hypoventilation Syndrome (OHS) present with severe upper airway obstruction, a restrictive physiology, blunted central respiratory drive, pulmonary hypertension, increased health care utilisation and increased mortality. Therefore it is important to identify Obesity Hypoventilation syndrome which is slowly becoming a common condition in the OPD and the ICU. This review will focus on the epidemiology, basic pathophysiology and principles in diagnosis and management of OHS.

Introduction

Obesity hypoventilation syndrome or OHS is characterized by obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$), daytime hypercapnia ($\text{PaCO}_2 \geq 45 \text{ mm Hg}$), and sleep-disordered breathing in the absence of other known causes of hypercapnia. The classical character in Charles Dickens "Posthumous papers of the Pickwick Club" in 1836, describes a plethoric, obese, sleepy boy Joe who used to sleep and snore always when idle. 120 years later, the term "Pickwickian syndrome" was thus adapted by Burwell and colleagues on seeing patients resembling Joe¹.

Epidemiology

By 2015, nearly 1 of 3 adults in the world are expected to be overweight ($\text{BMI} \geq 25 \text{ kg/m}^2$) and almost 1 in 10 adults will be obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). As per the WHO fact sheet, more than 1.4 billion adults, 20 and older were overweight. Of this around 200 million men and nearly

300 million women were obese. Ironically 65% of the world's population live in countries where overweight and obesity kills more people than underweight. The Overseas Development Institute (ODI), found that Indians form a massive chunk of the one in three adults now overweight or obese. Kerala, just second to Punjab leads this trend among states with a prevalence of 24.3% among males and 34% among females³. With this level of obesity, the prevalence of OHS is expectedly going to be high. Prevalence of OHS is also more among patients with a higher BMI^{4,5}. The aggregate prevalence of OHS among OSA patients referred to sleep disorder centers is 17% (range 4%–50%). The considerable range in prevalence reflects varying patient populations assessed across studies. The estimated prevalence of OHS among the general adult population is 0.15 - 0.3%. Unfortunately the data regarding OHS is not available from India primarily due to under recognition⁶. In ICU admissions, Marik and Desai found that 8% of all admissions met diagnostic criteria for OHS. Though all

OHS patients got admitted with acute on chronic hypercapnic respiratory failure, nearly 75% were misdiagnosed and treated for obstructive lung disease despite having no evidence of obstruction on pulmonary function testing⁷.

Morbidity and Quality of Life

Although obesity and severe OSA are associated with decreases in quality of life, OHS may contribute to further decrements in quality of life. Cardiovascular and metabolic comorbidities like Insulin resistance are more common in patients with OHS than in patients with eucapnic obesity. These may be present three or more years prior to a diagnosis of OHS^{8,9}. A study revealed that the prevalence of Pulmonary hypertension among a cohort of 34 OHS patients was 58% compared with just 9% among age, sex and weight matched OSA patients¹⁰. Another study showed that OHS patients were 9 times more likely to have a diagnosis of both cor pulmonale and congestive heart failure. Quality of life among this group is also worse compared to normal obese, OSA and other respiratory disorders, such as obstructive lung disease^{8,11}. As a consequence, the direct health costs like general healthcare visits, outpatient visits and medications per year of an OHS patient can reach twice that of an OSA or obese eucapnic patient, reach six times that of an age, gender and socioeconomic status matched control subject. In addition, labour income and employment rates are lower in OHS patients than in OSA or control subjects. There are increased hospital admissions including ICU admissions and thereby increased mortality as compared to age and weight matched controls^{12,13}.

Pathophysiology

The exact pathophysiology is unknown. OHS as compared to eucapnic obesity or simple OSA is mainly characterised by hypoventilation. The PCO_2 levels in blood are determined by the balance between CO_2 production and elimination. The hypercapnia in OHS is mainly due to hypoventilation. Obesity alone cannot be responsible for the development of hypercapnia because less than one third of morbid obese people develop hypercapnia. Mechanisms put forward for explaining hypoventilation include abnormal lung and chest wall mechanics due to obesity with an increased work of breathing, ventilation perfusion mismatch, disruption of the central respiratory control centres leading to an impaired response to hypoxia and hypercapnia and the presence of sleep disordered breathing with upper airway obstruction^{14,15}.

The increased adiposity load of obesity reduces chest wall compliance and lung volumes, including functional residual capacity. This low tidal volume breathing pattern reduces pulmonary compliance and also leads to expiratory flow limitation in the lower airways generating intrinsic positive end expiratory pressure and air trapping. These changes, together with upper airway resistance, further increase the load on the inspiratory muscles. As a result higher levels of ventilatory drive are required to maintain eucapnia and chemosensitivity is progressively impaired by rising carbon dioxide levels. The reduced ventilatory response in OHS to elevated CO_2 and low oxygen tensions compared to hypercapnic patients and obese control subjects has been demonstrated in studies^{16,17}.

During sleep, the partial pressure of carbon dioxide (PCO_2) rises during episodes of airflow obstruction and during episodes of impaired ventilation. In eucapnic individuals and those with OSA the acute hypercapnia which ensues from a brief apnoea or hypopnea episode is rapidly reversed by the increased tidal volumes in the successive few breaths (restorative breaths). Patients who develop OHS are unable to normalize the raised PCO_2 between such obstructive respiratory events. Studies have shown that if the obstructive event (apnoea) become 3 times longer than the intervening duration of restorative hyperpnoea, then such a patient will be unable to maintain eucapnea. So these intermittent cycles of hypercapnia continues. Daytime hypercapnia results from the inability to effectively eliminate carbon dioxide accumulated at night from sleep disordered breathing. Further the increased $PaCO_2$ causes a decrease in pH and leads to a compensatory increased renal bicarbonate retention. The bicarbonate levels often remain elevated, as the kidneys do not completely eliminate bicarbonate during the day. The kidneys retain bicarbonate to compensate for the elevated PCO_2 levels. Once CSF bicarbonate is elevated, ventilation is again depressed leading to elevated CO_2 levels. The elevated CO_2 levels cannot be then eliminated due to a blunted ventilatory response to hypercapnia while awake¹⁸.

Physiological alterations that are seen in obese patients tend to reduce ventilation to the lower lobes, with increased perfusion to the same areas because of increased pulmonary blood volume. This in turn produces a mismatch. Lastly there is also central leptin resistance. Leptin is normally produced from adipocytes as a satiety hormone acting on the hypothalamus to inhibit eating. It also acts as a ventilatory stimulant. Normally obese patients

have an increase in carbon dioxide production. This is countered by the presence of increased leptin levels which tend to stimulate ventilation and produce eucapnia. So the majority of severely obese patients are eucapnic. In OHS, there are elevated leptin levels but central leptin resistance. This appears to be responsible for the reduced ventilatory response and increased visceral fat. Fortunately the reduced ventilatory response is reversible with response to positive pressure ventilation^{19,20}.

Clinical features

As mentioned previously OHS is identified by the triad of obesity (BMI ≥ 30 kg/m²), chronic awake alveolar hypoventilation (PCO₂ ≥ 45 mm Hg and PaO₂ < 70 mm Hg), and sleep-disordered breathing. Severe obesity (BMI > 50 kg/m²) is one clue that OHS may be present, since nearly 50 percent of such individuals have OHS⁴. The symptoms and many of the physical findings are identical to obese OSA patients. Among OHS patients admitted to hospital, only 20% had previously received the diagnosis of OHS. A large proportion of patients are diagnosed with OHS only when presenting with acute respiratory failure. This highlights that OHS is underdiagnosed or that the diagnosis is dramatically delayed²¹.

OHS has a similar prevalence among both sexes, but slightly higher among males with an age at diagnosis usually in the fifth or sixth decade of life. Majority (90%) of OHS have OSA, with an Apnoea Hypopnea Index (AHI) of > 30 . A minority of patients around 10% may have an AHI of < 5 ie non obstructive sleep apnea which occurs during REM sleep²². Nonobstructive sleep hypoventilation is defined as an AHI < 5 events/hour (ie non obstructive) with a PaCO₂ increase by ≥ 10 mm Hg during sleep or an oxygen saturation $\leq 88\%$ for at least 5 min without obstructive respiratory events. As per the American Academy of Sleep Medicine scoring rules for respiratory events hypoventilation during sleep is defined as a

- 1) PCO₂ (transcutaneous or end-tidal carbon dioxide as surrogates) > 55 mm Hg for 10 min or
- 2) An increase in PCO₂ of > 10 mmHg from the awake supine value to a value exceeding 50 mm Hg for 10 min.

For those in the paediatric age range hypoventilation is scored when PCO₂ is > 50 mmHg for more than 25% of the total sleep time. All clinical features seen in OSA are commonly obtained like poor night time

sleep, unrefreshing sleep, excessive daytime somnolence, morning headaches and fatigue. OHS patients experience excessive daytime sleepiness that could be related to the severity of nocturnal rapid eye movement (REM) sleep hypoventilation (i.e. if the the percentage of REM sleep spent in hypoventilation is higher, higher is the excessive daytime sleepiness)^{23,24}.

A diagnosis is usually made when the obese patient presents with dyspnoea and has evidence of polycythemia, pulmonary hypertension and Sleep disordered breathing. They may also present with severe dyspnoea and obtundation indicating acute on chronic type 2 respiratory failure. The history in addition should focus on ruling out other causes of hypoventilation like severe COPD with FEV₁ $< 35\%$ or 1 Litre, excess sedatives, opioids, alcohol abuse, neuromuscular weakness like myasthenia gravis, muscular dystrophies, bilateral diaphragm palsy, severe kyphoscoliosis disorders of the central nervous system like stroke or spinal cord trauma, endocrine causes like severe hypothyroidism, peripheral causes like hypophosphatemia and severe hypokalemia and rarely congenital central hypoventilation syndrome.

Physical examination shows a drowsy, plethoric (due to polycythemia), obese patient with an enlarged neck circumference and a high mallampatti score. They are typically rapid shallow breathers but the rate increases during an exacerbation. Cyanosis may occur during exacerbations or in severe OHS. Paradoxical respiration may indicate diaphragm dysfunction or fatigue and impending failure. Cardiovascular examination may show systemic hypertension and evidence of Pulmonary hypertension with loud P2 and features of Right heart failure. Classically, mild to moderate Pulmonary hypertension is expected in OHS and this may persist even with therapy.

Several laboratory findings are supportive of OHS. One of the authority figures in this subject, Mokhlesi and colleagues first demonstrated that a threshold value of arterial bicarbonate of 27 mEq/L could be used as a screening tool to suggest chronic respiratory acidemia from hypoventilation. They showed that a value less than 27 mEq/L had a 97% negative predictive value for excluding a diagnosis of OHS^{15,25}. Another study by Macavei and colleagues showed that a calculated serum bicarbonate level of ≥ 27 mEq/L had a sensitivity of 85% and a specificity of 89% for the diagnosis of OHS among their patient sample. An elevated bicarbonate is an indirect evidence of "chronic" respiratory acidosis with compensation²⁶.

Hypoxemia during awakening is unusual of either OSA or obesity. So an abnormal pulse oximetry during wakefulness should prompt evaluation for OHS among obese OSA patients²⁷. Other tests include assessing for infection as a precipitant, checking for erythrocytosis, TSH, drugs and toxin levels like alcohol. Imaging may show evidence of right heart enlargement and prominent proximal pulmonary arteries. Once patient recovers from an exacerbation, a baseline spirometry can be done to exclude other causes for hypercapnia mentioned above. Common spirometry findings expected include a normal Forced expiratory ratio (FEV₁/FVC) with mild to moderate restriction. Additional pulmonary function testing may show reduction in maximum inspiratory and expiratory pressures due to abnormal respiratory mechanics and relative muscle weakness²⁸.

In a nutshell, clinically screen an obese patient by assessment of the SpO₂ and Serum HCO₃ levels. If there is hypoxemia with elevated bicarbonate, it may be a clue to further evaluation for OHS.

Management

In the Acute setting

As described earlier, OHS is frequently unrecognized until the individual presents with acute on chronic ventilatory decompensation. In the acute setting, hemodynamic stability and assessment of the arterial pH helps triaging the patient admission. In general, a conscious or adequately responsive patient who is hemodynamically stable with pH greater than 7.30 can be managed with NIV in a step down unit with vigilant monitoring and good nursing. Patients who have altered mentation, is hemodynamically unstable, has multiorgan failure and those who are intolerant to an initial trial of NIV or if pH is less than 7.30 are directly admitted to the ICU and may need intubation and mechanical ventilation. The treatment of choice is positive pressure ventilation either by non invasive (bilevel or BIPAP) or invasive mechanical ventilation. Though most patients require supplemental oxygen at baseline, it alone as a treatment modality is not useful²⁹.

Non invasive ventilation in OHS

The goal of ventilation is to improve alveolar ventilation and relieve upper airway obstruction. Typically Bilevel Positive airway pressure ventilation or BIPAP is used. BIPAP consists of 2 independent pressure settings-

Inspiratory positive airway pressure (IPAP) and an Expiratory positive airway pressure (EPAP) or PEEP. The EPAP is required to pneumatically splint up the airways, thereby relieving upper airway obstruction. The Pressure support or the difference between IPAP and EPAP provides degree of alveolar ventilation. In simple terms, higher the pressure support, greater are the tidal volumes achieved and greater the alveolar ventilation. Therefore in acute on chronic type 2 failure, the treatment of choice is bilevel positive airway pressure ventilation. The physiologic benefits of NIV include decreased work of breathing by unloading the respiratory muscles, improving central chemosensitivity after few days of use, opening the atelectatic lung regions, reduction of AHI with improvement in daytime sleepiness and improvement of right ventricular function.

Settings

NIV should be applied initially during sleep and wakefulness during the acute hospital setting. The interface(mask) selected should be of the proper size. An oronasal mask or a full face mask is recommended in the acute setting as higher pressures and thereby better tidal volumes can be generated and mouth breathing is tolerated. Nasal masks though more comfortable and tolerated may be ineffective due to mouth breathing. The interface can be later switched to a nasal mask once the patient is more stable. The straps should be just tight enough to allow two fingers to be passed beneath it. Early acclimatisation and better tolerance can be achieved by initiating with lower pressures and holding the mask without strapping. The pressures can be titrated up slowly and mask strapped on. Though each patient is different, and pressure settings have to be individualized, an initial starting pressure is usually 10 cm H₂O of IPAP and 5cm H₂O of EPAP. Strict and vigilant monitoring is required to observe for deterioration and complications. The first few hours of NIV are extremely important. Monitoring the level of consciousness, respiratory pattern and rate, presence of apneas and snoring, heart rate, blood pressure and SpO₂ will guide the physician in titrating pressure support. The EPAP can be gradually increased by 2 cm H₂O until apneas/snoring and accompanying cycles of desaturation are abolished. The IPAP can be stepped up by 2cm H₂O to obtain adequate tidal volumes of at least 8mL/kg to 10 mL/kg till the pulse oximeter reading shows a stable value with SpO₂>90%. This indicates adequate alveolar ventilation and oxygenation. It has been seen that OHS patients require a higher IPAP and EPAP as compared to COPD patients

because of the coexisting severe OSA²⁵. Infact studies conducted among OHS patients have shown that high IPAP (mean of 18 cm H₂O with a range 12–30 cm H₂O) and EPAP (mean of 9 cm H₂O with range 5–13 cm H₂O) with the IPAP at least 8 to 10 cm H₂O greater than EPAP to achieve adequate ventilation were required to produce a significant improvement in hypercapnia and hypoxia^{24,30,31}. Despite delivering high pressures many of these patients still remain hypoxic and may require the addition of supplemental oxygen.

Careful attention should be paid to air leak, nasal bridge/ facial skin breakdown, or discomfort from an improperly fitting mask. The patient should be given regular breaks every 2-4 hours and skin assessed for pressure effects. Breaks should be allowed for eating and communicating with bystanders. This will mitigate claustrophobia also. Improvement is seen by better mentation, reduction in respiratory rate to less than 25/minute, more synchronous respiratory efforts and sustained improvement in SpO₂ ≥ 90%. The ABG should be repeated at 1 hour and at least 20 % decline in PCO₂ is expected. Some patients may never reach eucapnia reflecting the chronic respiratory acidosis. So the pH may be the best marker of acute clinical improvement. A sustained pH more than 7.35 indicates acid base stability, and then daytime NIV can be discontinued. The nocturnal support should be continued for 2 more days. Most patients improve within 1-3 hours of adequate NIV and a stable pH is reached in 12-24 hours. It has been seen that acute on chronic type 2 failure in patients who have OHS resolves more rapidly compared with patients who have COPD and congestive heart failure^{30,32}. Other general care like head end elevation to 30 degrees, avoidance of sedative-hypnotics and narcotics, deep vein thromboprophylaxis and stress ulcer prophylaxis are also to be given.

NIV Failure

The need for vigilant monitoring by the physician and nursing staff is imperative for clinical success and for early detection of complications. Progressive deterioration of consciousness with cardiorespiratory arrest, vomiting with aspiration and even death can occur. Mouth breathing during acute respiratory failure results in gastric distension and the high IPAP applied may distend the gastroesophageal sphincter thereby producing vomiting. Early markers which should alert the clinician of impending respiratory failure (NIV failure) include a deteriorating mentation, persistent tachypnoea and accessory muscle

overactivity, poor patient synchrony, persistent hypoxemia and refractory hypercapnia even after 1-2 hours of NIV. The best predictor of early NIV failure (ie within the first 1 to 3 hours) is the lack of improvement in pH and PCO₂ after 1 hour of NIV³³. A prospective study done among 33 morbidly obese patients with acute respiratory failure from multiple causes reported a NIV failure rate of 36%. In this study, a higher BMI was predictive of failure (46.9 kg/m² in successful NIV versus 62.5 kg/m² in NIV failure)³⁴.

Carrilo et al carried out an interesting study comparing the use of NIV in acute exacerbations of COPD and OHS. Consecutive patients were treated with a similar NIV protocol based on the finding of respiratory acidosis, dyspnoea and respiratory rate of ≥ 25/minute. Initial settings were an inspiratory positive pressure of 12 cmH₂O, increasing by 2–3 cmH₂O as tolerated, and an expiratory positive pressure of 5 cmH₂O increased by 1–2 cmH₂O to improve hypoxaemia or comfort. OHS patients experienced less NIV failure (7% versus 13% in the COPD group), fewer ICU readmissions, and lower ICU and hospital mortality³⁵.

Invasive Ventilation

The clinical signs indicating early need for invasive mechanical ventilation have been described earlier. There are specific issues ubiquitous to the airway control of obese patients including bag and mask ventilation and intubation. Obesity itself is a risk factor for difficult bag and mask ventilation and intubation. Studies have shown that approximately 50% of morbidly obese patients with acute respiratory failure often have a difficult intubation defined as requiring more than two attempts with the same laryngoscope blade by an experienced laryngologist^{34,36}. Difficulty lies not only due to the short neck with reduced mobility and crowded oropharynx, but also to the difficulty in oxygenation. The physiological changes exclusive to obesity like low thoracic compliance, atelectasis and diminished functional residual capacity (FRC) may cause development of severe hypoxemia and even periintubation cardiorespiratory arrest. So the physician should anticipate these issues and have adequate knowledge of alternate airway control techniques or have assistance of an anaesthetist. Preoxygenation with 6cm CPAP to improve FRC and intubation with fiberoptic bronchoscope is a useful method in difficult situations³⁷. Mechanical ventilation is similar to conventional ventilation, except for accepting higher peak and plateau pressures needed to overcome poor chest wall compliance. High pla-

teau pressures may not indicate lung over distension because the pleural pressures are also elevated due to the stiff chest wall and hence transpulmonary pressures remain normal³⁸.

At discharge

Patients who are discharged from the ICU will require a formal Polysomnography, ABG and spirometry at follow up to assess severity of OSA and for CPAP titration. It is essential for these patients to be discharged from the ICU on adequate NIV therapy. Though OHS patients require BIPAP during the acute setting, most of them can be managed with CPAP at discharge. A prospective randomized study by Piper et al compared the long-term efficacy of BIPAP versus CPAP in OHS patients. This study showed that majority of OHS (80%) patients could be successfully titrated with CPAP. After 3 months of therapy, there was no significant difference between the groups in terms of adherence to PAP therapy or in improvement in daytime sleepiness, hypoxemia or hypercapnia. Therefore, BIPAP is not superior to CPAP and treatment should be individualized to each patient. But BIPAP should be used if the patient requires high CPAP pressures (>15 cm H₂O) and has difficulty in tolerating the high pressures, if hypoxemia persists despite resolution of obstructive respiratory events and lastly if the PCO₂ levels do not normalise after 3 months therapy with CPAP³⁹.

CPAP titration can be done to identify the pressure that will abolish apneas, hypopneas, Respiratory event related events and snoring both in supine and REM sleep. If oxygen saturation levels remain below 90% in spite of abolishment of obstructive events with CPAP, a BIPAP titration may be required. The IPAP is started at the identified CPAP level which abolished obstructive events and then titrated upwards till SpO₂ >90%. If the BIPAP is unable to maintain SpO₂ >90% in spite of a high IPAP (at least 8-10cm higher than EPAP), then it is advisable to add supplemental oxygen along with positive airway pressure ventilation⁵.

The role of newer modes - Volume Assured Pressure Support (VAPS)

VAPS is a hybrid mode of ventilation which combines the comfort of pressure support at the same time providing consistent Tidal volumes. Different manufacturers have given names for VAPS like Average VAPS (Respironics) and intelligent VAPS (Resmed), though the basic working mechanism remains the same. The under-

lying goal of these modes is to help in better adapting to the patient's own ventilatory pattern and requirements, which will clearly vary during different stages of sleep and with different activities during the day. In a randomised crossover trial of AVAPS versus standard pressure support in obesity hypoventilation patients a small improvement on nocturnal PCO₂ was seen, but no long-term quality of life improvement⁴⁰. In another trial by Murphy et al, they showed that there was no long-term advantage in AVAPS over optimally titrated bilevel pressure support, so these "intelligent" modes do not seem to have a role in the general population of OHS patients. They may be useful sometimes as an aid in OHS patients who are starting NIV for the first time. The devices are also costlier than conventional CPAP or BIPAP machines⁴¹.

Good outcomes are obtained only if the patient is adherent to Positive airway pressure therapy (PAP) whatever be the mode of non invasive ventilation. Adherence as in OSA may be defined as at least 4.5 hours/day of continuous CPAP usage. Early outpatient follow up is therefore mandatory with measurements of ABG and objective assessment of adherence to therapy. Improvement in blood gas values may be seen as early as one month after the institution of PAP therapy⁴².

Medical Management - Adjuvants in Treatment

Long Term Oxygen Therapy (LTOT).

Studies have shown that oxygen therapy may be needed in up to 50% of patients with OHS in addition to PAP therapy to keep oxygen saturation levels above 90% in the absence of hypopneas and apneas. LTOT alone is not recommended in patients with nocturnal hypoventilation as it may worsen hypercapnia and abolish hypoxic ventilatory drive⁴³. In a double-blind randomised crossover study involving OHS, participants breathed oxygen concentrations (FiO₂) 0.28 and 0.50, each for 20 min, separated by a 45 min washout period. Arterialised-venous PCO₂ (PavCO₂) and pH, Minute Ventilation (VE) and Dead space ventilation (Vd/Vt) were measured at baseline, then every 5 min. The authors showed that breathing at FiO₂ 0.5 and 0.28 produced a fall in minute ventilation with elevation in CO₂ levels and acidemia only among the OHS patients compared to age and sex matched healthy controls. The effect was higher when breathing at higher FiO₂ (.5) and suggested that ventilatory responses were the key determinant of PCO₂ rises highlighting the potential dangers of higher oxygen treat-

ment in OHS patients⁴⁴. Consistent usage of PAP therapy has shown to reduce the need for supplemental oxygen as seen in a retrospective cohort study by Mokhlesi et al. The need for daytime supplemental oxygen decreased from 30% to 6% in patients who were adherent to PAP therapy⁴². Therefore, patients should be reassessed for both diurnal and nocturnal oxygen requirements a few weeks to months after PAP therapy is instituted.

Phlebotomy

Secondary erythrocytosis is seen in hypoxemic patients as a compensatory physiological mechanism to increase oxygen carrying capacity and thereby oxygen delivery. But hyperviscosity impairs the beneficial effect of increased RBC numbers. Venesection is indicated in hypoxic lung disease when the hematocrit is >55% or features of hyperviscosity are present⁴⁵. Ultimately PAP therapy improves the secondary erythrocytosis by relieving hypoxemia.

Weight Reduction

Borel et al. examined the effects of NIV in OHS on cardiovascular, metabolic and inflammatory variables. As expected the NIV group showed significant improvement in sleep and ABG measures. But level of inflammatory markers, endothelial function and arterial stiffness did not improve. Weight loss was shown to improve both obstructive events and REM related hypoventilation in OHS. Reversal of cardiovascular damage is related to the duration and severity of obesity as well as genetic factors and so NIV should be combined with weight loss to produce a beneficial cardiovascular profile^{39,46}.

Medroxyprogesterone

It acts as a respiratory stimulant and increases respiratory drive thereby improving daytime hypercapnia. Data showing improvements in PCO₂ levels have been limited. In a series of 10 men with OHS treated with high doses of oral medroxyprogesterone (60 mg/day) for one month, the PaCO₂ decreased from 51 mm Hg to 38 mm Hg and the PaO₂ increased from 49 mm Hg to 62 mm Hg. All these patients were able to normalize their PaCO₂ with 1–2 min of voluntary hyperventilation, suggesting that there was no limitation to ventilation⁴⁷. Side effects include increased risk for deep vein thrombosis which is especially dangerous in an OHS patient who is mostly immobile with cor pulmonale and cardiac failure. It also produces break

through uterine bleed, decreased libido, erectile dysfunction in males.

Acetazolamide

It induces metabolic acidosis through carbonic anhydrase inhibition. This stimulates respiration which increases minute ventilation in normal subjects⁴⁸.

In addition optimal management of cor pulmonale and failure with diuretics and inotropes may be required.

Surgical Management

Bariatric Surgery

It has variable long-term efficacy in treating OSA. Most studies available were conducted on OSA patients with majority of them showing short term improvement only following surgery. Most of the patients had recurrence of OSA symptoms in spite of minimal or no weight gain indicating factors other than obesity to be responsible⁴⁹. There has been a single study which examined the impact of Bariatric surgery on OHS. In this study by Sugerman et al involving 31 OHS patients, an improvement in blood gases were noted initially. Preoperative PaO₂ increased from 53 mm Hg to 73 mm Hg one year after surgery, and PaCO₂ decreased from 53 mm Hg to 44 mm Hg. The patients were followed up and 5 years post surgery values had worsened, with the mean PaO₂ dropping to 68 mm Hg and PaCO₂ increasing to 47 mm Hg. The long term effects occurred despite a minimal increase in BMI postoperatively (38 kg/m² to 40 kg/m²). The deterioration after an initial improvement indicates that factors other than obesity are involved and may be due to the reappearance of sleep disordered breathing⁵⁰. Ideally, patients with OHS being planned for bariatric surgery should be treated with PAP therapy or tracheostomy, prior to surgery in order to decrease perioperative morbidity and mortality. PAP therapy should also be started immediately post extubation to avoid postoperative respiratory failure. There is no solid data to show that PAP therapy initiated postoperatively leads to anastomotic disruption or leakage of the surgical site.

Tracheostomy

This was the most primitive therapy that was described for management of OHS. With the advent of PAP it is rarely used now. Tracheostomy is now indicated only in patients who do not tolerate or are non compliant with

PAP therapy, in patients who have severe corpulmonale and persistent hypercapnia despite optimal adherence to PAP and in a OHS patient who cannot be extubated from invasive mechanical ventilation. Tracheostomy is effective in OSA by bypassing the area of upper airway obstruction reducing dead space. It results in resolution of hypercapnia in the majority of patients due to reduction in the severity of obstructive sleep events. But the hypoventilation is not addressed and so a polysomnography with open tracheostomy is needed to decide whether nocturnal ventilation is required⁵¹. But tracheostomy can be technically difficult even among experienced ENT surgeons because of the anatomical abnormalities expected in obesity. A low lying larynx may result in accidental perforation of great vessels by the tracheostomy tube. An increased risk of stoma site bleeding and infection occurs because of the excess granulation tissue production stimulated by the adipose tissue.

Summarising, weight reduction along with Non invasive ventilation applied through a good interface is the best option available at present for managing sleep disordered breathing and the alveolar hypoventilation associated with OHS.

Conclusion

Obesity hypoventilation is a specific entity which combines the issues of obesity, sleep disordered breathing and hypoventilation. With the rising trends of obesity universally, the prevalence of OHS is expected to rise with increased morbidity and mortality. A chronically compensated respiratory acidosis is a clue to suspecting the diagnosis in an obese patient, after ruling out other causes of hypoventilation. Positive airway pressure ventilation is the treatment of choice along with weight reduction. Future research on the pathophysiology of OHS and newer treatment modalities in addition to PAP will help to improve the outcome.

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