Obesity Hypoventilation Syndrome

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Pickwickian Syndrome


- Obese patient with hypercapnia, hypersomnolence and cor pulmonale noted the similarity to a character described by Charles Dickens in the Posthumous Papers of the Pickwick Club.
Definition

Criteria for the diagnosis include

- persistently elevated daytime PaCO2 > 45 mmHg
- a body mass index > 30 kg/m²
- and no other cause for hypoventilation
Table 2: Causes of Chronic Hypoventilation Other Than Obesity Hypoventilation Syndrome

1) Primary pulmonary disease  
   a. COPD/Overlap Syndrome  
   b. Advanced pulmonary parenchymal disease (eg interstitial lung disease)  
   c. Severe upper airway obstruction (eg tracheal stenosis)  
2) Chest wall disorders  
   a. Kyphoscoliosis  
   b. Thoracoplasty  
3) Neuromuscular disorders  
   a. Myopathies  
   b. Muscular dystrophies  
   c. Bilateral diaphragmatic paralysis  
   d. Guillain-Barret Syndrome  
   e. Amyotrophic lateral sclerosis  
   f. Myasthenia Gravis  
   g. Cervical spine injury  
4) Primary CNS disorders  
   a. Primary central hypoventilation syndromes  
   b. Brain stem infarction or tumor  
5) Myxedema  
6) Drugs (narcotics, sedatives)  
7) Metabolic abnormalities (hypokalemia, hypophosphatemia, hypomagnesemia, metabolic alkalosis)
Overlap syndrome

- OSA in patients with chronic obstructive pulmonary disease, is another hypercapnic sleep disorder.
- Hypercapnia may develop at a lower BMI in patients with Overlap Syndrome.
- OSA and Emphysema are distinct clinical conditions.
Obesity Hypoventilation Syndrome

Pathophysiology involves a combination of:

- abnormal respiratory mechanics
- increased work of breathing
- depressed central ventilatory control
- neurohormonal effects
Effects of Obesity on Respiratory Function

- The majority of obese patients do not retain CO2.
- This suggests that most obese patients are able to compensate for the negative respiratory effects of obesity.
- However in OHS patients these compensatory mechanisms fail resulting in daytime hypercapnia.
Effects of Simple Obesity on Respiratory Function

- Decreased lung volume (esp ERV)
- Decreased chest wall compliance
- Increased airway resistance
- Increased WOB
- Decreased FEV1 and FVC with normal ratio
Comparison of lung volumes and awake blood gases in individuals with eucapnic morbid obesity (solid bars) and those with obesity hypoventilation syndrome (OHS; hatched bars).

When all of the preceding changes are taken into account the WOB is three times worse for OHS patients versus simple Obesity patients.
OHS – Neurohormonal Mechanisms

- Leptin is a protein produced by adipocytes.
  - Respiratory stimulant
  - Suppress appetite
  - Increases energy expenditure

- The leptin-deficient (ob/ob) mouse shares many similarities to humans with OHS including obesity, daytime hypercapnia, and a blunted ventilatory response to CO2 during wakefulness and sleep.
Speculated that elevated leptin levels in obese humans may act as a compensatory mechanism to maintain an adequate level of ventilation.

However, fasting serum leptin levels are higher in obese hypercapnic individuals than in those who are able to maintain eucapnia.

Implying that eventually in some patients there is a resistance to the ventilatory stimulatory effects of leptin.
Schema outlining some of the potential interactions involved in the development of hypoventilation in a subgroup of individuals with morbid obesity.


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Increased work of breathing and increased needs to augment minute ventilation to maintain adequate alveolar ventilation

Patient can increase ventilatory drive and minute ventilation

Patient cannot increase ventilatory drive and minute ventilation

Normal ventilation and eucapnia

Hypoventilation especially during sleep hypercapnia and hypoxemia

90%

10%

Simple obesity

OSA

OHS + OSA

OHS
Obesity Hypoventilation Syndrome.

Hypercapnic Sleep Breathing Disorders

- Obesity
- OSA
- OHS
- OHS w/o OSA
- Obstructive or central hypoventilation
- Hypercapnic OSA w/o Obesity +/- Overlap syndrome
- OHS w/ OSA
- OIHS w/o OSA
Relationship between OSA and OHS

- 90% of patients with OHS have OSA
- 10 to 20% of OSA patients have OHS
- OSA and OHS are similar to emphysema and chronic bronchitis in that CB +OHS are associated with daytime hypercapnia and emphysema and OSA are not.
Generally speaking, patients with OHS tend to have more comorbidities than patients with eucapnic obesity, including systemic hypertension, heart failure, angina, and insulin resistance.
OHS – Clinical Manifestations

- Obese
- S+S of OSA, excessive daytime sleepiness, loud snoring, choking during sleep, resuscitative snorting, fatigue, hypersomnolence, impaired concentration and memory, small oropharynx, thick neck
- signs of pulmonary hypertension with right-sided heart failure (eg, elevated jugular venous pressure, hepatomegaly, and pedal edema) and, occasionally, a plethoric complexion from polycythemia
Symptoms

**OSA**
- Snore
- Nocturnal awakenings
- EDS
- AM Headache
- Depression
- Cognitive impairment
- Decreased vigilance

**OHS**
- Daytime hypoxemia
- Daytime hypercapnia
- EDS
- AM Headache
- Polycythemia
- Cor pulmonale
- RHF symptoms
OHS – Clinical Manifestations

- **Clues to diagnosis**

- OHS more dyspnea with exertion than OSA
- Severe obesity (BMI >50 kg/m²)
- Polycythemia suggest chronic hypoxemia
OHS - Presentation

- Acute
  - Hypoxemia, resp acidosis, RHF
  - Often require hospitalization (ICU)
  - Frequently change in mental status due to hypercapnia

- Chronic
  - Frequently referred after abnormal sleep study
OHS – Diagnostic Tests

- arterial blood gases
- pulmonary function tests
- chest radiographs
- electrocardiography
- echocardiography
- polysomnography

“Now just relax and go to sleep!”
OHS – Arterial Blood Gases

- Necessary for the evaluation of suspected OHS
- Hypercapnia (PaCO2 > 45 mmHg) is always present during wakefulness
- Hypoxemia (PaO2 < 70 mmHg) is usually present.
- High Bicarbonate suggests hypercapnia
OHS – Pulmonary Functions

- PFT characteristic of obesity
  - Low forced vital capacity (FVC)
  - Low forced expiratory volume in one second (FEV1)
  - Normal FEV1/FVC ratio
  - Low expiratory reserve volume (ERV)
  - Low TLC
Morley’s Sign
- X-ray plate is turned sideways and patient still completely fills it
- Wad of flesh around neck

X-ray may reveal other reasons for hypercapnia
X-Ray may show other reasons for hypercapnia.
OHS - Cardiac Studies

- EKG - p pulmonale, RAD, RBBB
- Echocardiogram – elevated PAP, dilated RV
- Catheterization – pulmonary hypertension
Sleep Study
Nocturnal Polysomnogram

EEG
Eye movement (EOG)
EKG
Chin leads (EMG)
Leg Movement (EMG)
Airflow
Respiratory Motion
Pulse oximeter
OHS - Polysomnogram

- 90% of OHS patients will demonstrate an elevated AHI

- OHS patients tend to have more severe oxygen desaturation than OSA alone
OSA Severity: Apnea Hypopnea Index

- **Normal**: AHI < 5
- **Mild OSA**: AHI 5 < 15
- **Moderate OSA**: AHI 15 < 30
- **Severe OSA**: AHI > 30
Goals of Therapy for OHS (1)

- Normalization of the PaCO2 during wakefulness and sleep
  - improving ventilatory drive, relieving respiratory muscle fatigue, and/or decreasing the work of breathing
Goals of Therapy for OHS (2)

- Prevention of oxyhemoglobin desaturation, erythrocytosis, and cor pulmonale
  - by eliminating sleep disordered-breathing, normalizing alveolar ventilation, and improving ventilation-perfusion mismatch.
Goals of Therapy for OHS (3)

- Relief of hypersomnia and altered mentation
  - relief of sleep fragmentation and restoration of eucapnia
Weight Loss for OHS

- Weight loss is an important therapeutic goal in patients with OHS.
- Both medical (voluntary) and surgically-induced weight loss have been associated with improvement in and sometimes normalization of awake PaCO2 and PaO2.
- Other potential benefits include improvement in nocturnal oxyhemoglobin saturation, decreased AHI, resolution of pulmonary arterial hypertension, improvement in left ventricular dysfunction, and improvement in pulmonary function.
Weight loss lowers PCO2 in OHS

Weight loss in patients with the obesity hypoventilation syndrome (OHS) lowers the arterial PCO2. Each line represents a different patient.

Original figure modified for this publication. Rochester, DF, Enson, Y. Current concepts in the pathogenesis of the obesity-hypoventilation syndrome. Am J Med 1974; 57:402. Illustration used with the permission of Elsevier Inc. All rights reserved.
Problems with Weight Loss

- It is not easy.
- It is not clear exactly how much weight loss is required for OHS improvement.
- Supervised, sustained weight loss is required.

"What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?"
Lifestyle Modifications
Diet, Exercise, Behavioral Modification

- Individuals with OHS, who are generally morbidly obese (more than 50 percent above ideal body weight), may have more difficulty with successful long-term weight loss than persons with uncomplicated obesity because of exercise limitations related to their cardiorespiratory failure.
PHARMACOLOGIC THERAPY

Works (limited role)
- Progestins
- mechanism of action is predominantly ventilatory stimulation
- Does not address nocturnal airway occlusion and increased work of breathing due to obesity

Doesn’t Work
- acetazolamide
- theophylline
- nortriptyline
- fluoxetine
- Avoid benzodiazepines
- Opiates
- Barbiturates
Medications for Weight Loss

Noradrenergic drugs
- amphetamines
- mazindol
- phentermine
- phenylpropanolamine
- sibutramine

Serotonergic drugs
- fluoxetine
- fenfluramine
- sibutramine
Bariatric Surgery

- Gastric "Sleeve"
- Pylorus
- Excised Stomach
- Pouch
- Old or Excluded Stomach
- Roux limb
- Bypassed Small Intestine
Consensus Indications for Bariatric Surgery

- Adults with OHS or OSA are considered candidates for bariatric surgery;
  - If they have a body mass index greater than 35 kg/m²
  - No other comorbidities that would preclude surgery
  - Can cooperate with postoperative treatment
  - Can avoid pregnancy during the period of rapid weight loss

- Because of the risk of airway compromise in the perioperative period and the extended period of time over which weight loss will occur, patients with OHS should undergo preoperative polysomnography to define the nature and extent of breathing abnormalities during sleep.
**Objective** To determine the impact of bariatric surgery on weight loss, operative mortality outcome, and 4 obesity comorbidities (diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea/OHS).

**Data Sources and Study Selection** Electronic literature search of MEDLINE, Current Contents, and the Cochrane Library databases plus manual reference checks of all articles on bariatric surgery published in the English language between 1990 and 2003. Two levels of screening were used on 2738 citations.
Data Extraction A total of 136 fully extracted studies, which included 91 overlapping patient populations (kin studies), were included for a total of 22094 patients. Nineteen percent of the patients were men and 72.6% were women, with a mean age of 39 years (range, 16-64 years). Sex was not reported for 1537 patients (8%). The baseline mean body mass index for 16 944 patients was 46.9 (range, 32.3-68.8).
**Data Synthesis** A random effects model was used in the meta-analysis. The mean (95% confidence interval) percentage of excess weight loss was 61.2% (58.1%-64.4%) for all patients; 47.5% (40.7%-54.2%) for patients who underwent gastric banding; 61.6% (56.7%-66.5%), gastric bypass; 68.2% (61.5%-74.8%), gastroplasty; and 70.1% (66.3%-73.9%), biliopancreatic diversion or duodenal switch. Operative mortality (30 days) in the extracted studies was 0.1% for the purely restrictive procedures, 0.5% for gastric bypass, and 1.1% for biliopancreatic diversion or duodenal switch. Diabetes was completely resolved in 76.8% of patients and resolved or improved in 86.0%. Hyperlipidemia improved in 70% or more of patients. Hypertension was resolved in 61.7% of patients and resolved or improved in 78.5%. Obstructive sleep apnea was resolved in 85.7% of patients and was resolved or improved in 83.6% of patients.
Table 3. Patient Characteristics*.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>No./Total (%) of Patients</th>
</tr>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3769/19388 (19.4)</td>
</tr>
<tr>
<td>Female</td>
<td>14,082/10,388 (72.6)</td>
</tr>
<tr>
<td><strong>Current or former smoker</strong></td>
<td></td>
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<tr>
<td>Nonsmoker</td>
<td>397/571 (69.5)</td>
</tr>
<tr>
<td>Prior bariatric surgery</td>
<td>265/3799 (4.4)</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>2507/16,342 (15.3)</td>
</tr>
<tr>
<td>Glucose tolerance impairment</td>
<td>1118/4331 (25.8)</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>2900/16,342 (17.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5808/16,421 (35.4)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1021/2668 (35.6)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>2588/6391 (40.2)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>1092/4488 (24.3)</td>
</tr>
<tr>
<td>Asthma</td>
<td>279/2601 (10.7)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>132/1887 (7.0)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8/348 (2.3)</td>
</tr>
<tr>
<td>Degenerative joint disease</td>
<td>4160/6277 (50.3)</td>
</tr>
<tr>
<td>Depression</td>
<td>402/2306 (17.4)</td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
<td>1983/4583 (43.3)</td>
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</table>

*The range of patient ages is 16 to 64 years and is based on ages reported in 87% of the trials. The body mass index range is 32.3 to 68.8 and is based on body mass indices reported in 77% of the trials. Body mass index is calculated as weight in kilograms divided by the square of height in meters.
†Not reported for 1537 patients (8%).
‡Includes hyperglycemia, hyperinsulinemia, metabolic syndrome, and impaired glucose tolerance.

Buchwald, H. et al. JAMA 2004;292:1724-1737
Conclusions  Effective weight loss was achieved in morbidly obese patients after undergoing bariatric surgery. A substantial majority of patients with diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea experienced complete resolution or improvement.
Outcome of Bariatric Surgery

- Perioperative mortality related is dependent on comorbidities and the procedure performed, but is reported to be less than 2 percent.
- The impact of surgically-induced weight loss should be assessed by polysomnography prior to discontinuation of positive pressure therapy or removal of a tracheostomy tube.
Outcome of Bariatric Surgery

- The early (less than one year) rapid loss of weight (typically 45 to 70 percent of excess body weight) is often associated with clinically significant improvement of the apnea-hypopnea frequency and amelioration of both OHS and OSA.

- Most patients remain obese (more than 20 percent above ideal body weight) and some have persistence of their sleep-disordered breathing (OHS and OSA).
Nocturnal Oxygen Therapy for OHS

- Not routinely recommended as solo therapy.
- May be used in patients with Overlap syndrome.
Tracheostomy and OHS

- Not useful for patients without OSA
- Rarely used with OSA/OHS
- Helpful in rare patients
Positive Airway Pressure for OHS

- Positive airway pressure ventilation (PAP) acutely and chronically improves gas exchange and functional status in patients with various forms of chronic respiratory failure, including those with OHS.
MODES OF NONINVASIVE POSITIVE PRESSURE THERAPY

- Continuous positive airway pressure (CPAP)
- Noninvasive positive pressure ventilation (NPPV)
  - bilevel positive airway pressure (BPAP)
  - volume cycled positive pressure ventilation (VCPPV).
- Average volume-assured pressure support (AVAPS) is a hybrid mode of NPPV
## Comparative features of different methods for administering positive pressure

<table>
<thead>
<tr>
<th>Mode of positive pressure ventilation</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>CPAP</td>
<td>Inexpensive</td>
<td>Lack of inspiratory pressure support</td>
</tr>
<tr>
<td></td>
<td>Widely available</td>
<td></td>
</tr>
<tr>
<td>Bi-level</td>
<td>Widely available</td>
<td>Tidal volume may be limited by patient-related factors</td>
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<tr>
<td></td>
<td>Can provide inspiratory pressure support to augment tidal volume</td>
<td></td>
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<tr>
<td></td>
<td>Leak tolerant</td>
<td></td>
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<tr>
<td>Volume-cycled</td>
<td>Can set specific respiratory parameters</td>
<td>More expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less widely available</td>
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<tr>
<td></td>
<td></td>
<td>Less well-tolerated than pressure support devices</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leaks lead to loss of tidal volume</td>
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</table>
CPAP for OHS

- Reduction of awake arterial carbon dioxide tension (PaCO2) has been demonstrated after the initiation of chronic nocturnal CPAP therapy.

- Since nocturnal CPAP does not directly augment ventilation other than by maintaining upper airway patency, improvement of hypercapnia during both wakefulness and sleep may be due to relief of ventilatory muscle fatigue and/or augmentation of central ventilatory drive.
Failure of CPAP to improve Nocturnal O2 Sats

- Patients who benefit from nocturnal CPAP therapy tend to have a higher baseline apnea hypopnea index (AHI), less restrictive physiology on spirometry, and less severe oxyhemoglobin desaturation during baseline polysomnography than patients who do not improve with CPAP.
How do you know the OHS patient on CPAP has persistent Nocturnal hypercapnia?

- nocturnal dyspnea
- a sensation of smothering at night
- chronic morning headaches
- failure of awake arterial blood gases to improve
Long-Term Outcome of Noninvasive Positive Pressure Ventilation (i.e. BiPAP) for Obesity Hypoventilation Syndrome

Methods: One hundred thirty consecutive patients with OHS (56 women) who started NPPV between January 1995 and December 2006 either under stable conditions (stable group, n = 92) or during ICU management of acute hypercapnic exacerbation (acute group, n = 38) were retrospectively analyzed.

Conclusions: The results of this study support long-term NPPV as an effective and well-tolerated treatment of OHS whether initiated in the acute or chronic setting.
Flow diagram of subjects during the study.

130 OHS patients

38 Acute
8 (21.1%)
24 (63.2%)
6 (15.8%)

92 Stable
16 (17.4%)
58 (63.0%)
18 (19.6%)

24 dead
Mean follow-up of 3.46 yrs

84 still treated
Mean follow-up of 4.7 yrs

24 discontinued
Mean follow-up of 1.6 yrs

Arterial blood gases at baseline (n = 130) and after 6 months of noninvasive positive airway pressure (n = 121) for the overall study population, the stable group, and the acute group.

Survival curve by Kaplan-Meier analysis for the overall population (N = 130) and for patients with (n = 20) and without (n = 110) supplemental oxygen.

Percentage of patients using NPPV over time for the overall population (N = 130), male patients (n = 74), and female patients (n = 56).


With a mean follow-up of 4.1 ± 2.9 years, 24 (18.5%) patients died and 24 (18.5%) discontinued NPPV.

Much better survival than historical controls.

<table>
<thead>
<tr>
<th>Five Year Survival</th>
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<tbody>
<tr>
<td>1-Year</td>
<td>97.5%</td>
</tr>
<tr>
<td>2-Year</td>
<td>93.0%</td>
</tr>
<tr>
<td>3-Year</td>
<td>88.3%</td>
</tr>
<tr>
<td>5-Year</td>
<td>77.3%</td>
</tr>
</tbody>
</table>
Conclusions: The results of this study support long-term NPPV as an effective and well-tolerated treatment of OHS whether initiated in the acute or chronic setting.
Start with CPAP and build up pressure to eliminate obstructive events

Switch to Bi-level PAP if:
- Patients cannot tolerate CPAP due to persistent air leak or discomfort exhaling against high pressure
- Frequent episodes of hypoventilation and desaturation without obstructive events

↑ IPAP over the last CPAP until SaO₂ > 90%

Add O₂, if the patient continues to desaturate <90% despite elimination of obstructive apneas/hypopneas and hypoventilation
Conclusions

- OHS is common and is associated with worse abg findings both at night and during the day the OHS.

- Weight loss, elimination of adverse factors (sedatives, hypothyroid, smoking), Nocturnal PAP and sometimes nocturnal oxygen and all important in improving function and prognosis.