ACOI
Clinical Challenges in Inpatient Care
April 26-29, 2018
Chicago Marriott Downtown Magnificent Mile, Chicago, IL
Registration now open

Timothy J. Barreiro, DO, MPH, FCCP, FACOI, FACPM
Section Chair, Associate Professor of Medicine
NIH Health Minority & Harvard Macy Scholar
Ohio University Heritage College of Osteopathic Medicine
Northeast Ohio Medical University
Director Pulmonary Health & Research Center
tbarreir@neomed.edu
Disclaimers: Remember when evaluating this lectures quality

• Dr. Barreiro has no financial or industry disclosures.

FULL DISCLOSURES:
• I have no relationship with Russia.

• Dr. Barreiro is responsible for the contents of this lecture, although he will adamantly blame Dr. Greco for any failures.
Objectives

• Review the pulmonary pathophysiology associated with obesity.

• Discuss what is the diagnostic criteria for obesity hypoventilation (OHS) and how to identify patients with OSH better.

• Discuss the acute care treatment errors in patients with OHS.

• Overview the best treatment decision and modalities for obesity hypoventilation syndrome.
Fig 1. Joe the “Fat Boy” Illustration by S. Etyinge, Jr.
(from Dickens C. The posthumous papers of the Pickwick Club. Boston: Ticknor and Fields: Boston; 1867.)

Prevalence of Obesity Among Adults: 1989

[CDC map showing prevalence of obesity across states with color coding for < 10%, 10-15%, > 15%]
Prevalence of Obesity Among Adults: 1998

Body Mass Index
Prevalence of OHS

- BMI 25.0-29.9 kg/m²: Overweight
- BMI 30.0-34.9 kg/m²: Grade I
- BMI 35.0-39.9 kg/m²: Grade II (morbid)
- BMI >40 kg/m²: Grade III (extreme)

Obesity

↓ Lung Volumes
↑ Work of Breathing
↑ CO₂ production
Leptin Resistance

Impaired respiratory muscle performance

↓ tidal volume

↑ PaCO₂
↑ Bicarb

Airway Obstruction

Sleep hypoventilation

Hypoxia

Altered Neurotransmitters Chemoreceptors

Reduced ventilator arousals

Source: Sleep-Related Hypoventilation Syndromes, Fishman's Pulmonary Diseases and Disorders, 5e
Citation: Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, Siegel MD. Fishman's Pulmonary Diseases and Disorders, 5e; 2015
The QOL with OHS

• Matched patients to OHS to patient with OSA (eucapnic) by age, BMI, and lung function showed:

  • No significant difference in Short Form-36 scores
  • Exception with social functioning (OHS $p < 0.01$)
  • Sleeper by Epworth Sleepiness Scale (14.6 verses 12.5; $p < 0.05$)
  • After CPAP for 6 months = no changes noted.

Morbidity of OHS

- Groups with obesity hypoventilation syndrome carry combined diagnoses including:
  - congestive heart failure (odds ratio 9; 95% confidence interval 2.3 - 35),
  - angina (odds ratio 9; 95% confidence interval 1.4 - 57),
  - cor pulmonale (odds ratio 9; 95% confidence interval 1.4 - 57)

- No difference was found in the likelihood of having osteoarthritis, diabetes, hypertension, hypothyroidism.

- Same group found obesity hypoventilation syndrome more likely to be:
  - Hospitalized,
  - Greater admitted to the intensive care unit (40% versus 6%),
  - The rate of hospitalizations decreased 2 years after treatment was instituted.

## Respiratory System Mechanics in Health Subjects, Obese and OHS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Units</th>
<th>Healthy</th>
<th>Obese</th>
<th>OHS</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crs (Compliance)</td>
<td>L/cmH$_2$O</td>
<td>0.11</td>
<td>0.05</td>
<td>0.06</td>
<td>37% Δ</td>
</tr>
<tr>
<td>Rrs (Resistance)</td>
<td>cmH$_2$O/L/sec</td>
<td>1.2</td>
<td>4.0</td>
<td>7.8</td>
<td>44% Δ</td>
</tr>
<tr>
<td>Pi$_{max}$</td>
<td>cmH$_2$O</td>
<td>100</td>
<td>95</td>
<td>60</td>
<td>30% Δ</td>
</tr>
<tr>
<td>Pe$_{max}$</td>
<td>cmH$_2$O</td>
<td>150</td>
<td>125</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>MVV</td>
<td>L/min</td>
<td>159</td>
<td>129</td>
<td>89</td>
<td>55% Δ</td>
</tr>
</tbody>
</table>

Crs, respiratory system compliance; Rrs, respiratory system resistance.

Pi$_{max}$, maximal inspiratory pressure; Pe$_{max}$, maximal expiratory pressure; MVV, maximal voluntary ventilation.

Schema depicting a proposed inadequate compensatory ventilatory response to CO₂ loading during obstructive respiratory events in the obesity hypoventilation syndrome. The dark-shaded areas depict CO₂ loading due to reduced CO₂ excretion during respiratory events while the light-shaded areas depict CO₂ unloading due to compensatory hyperventilation between respiratory events. (Reproduced with permission from Berger KI, Goldring RM, Rapoport DM. Obesity hypoventilation syndrome. Semin Respir Crit Care Med. 2009;30(3):253–261.)
A. Nocturnal oximetry in a patient with severe obstructive sleep apnea demonstrating recurrent desaturations in nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. Each apneic event results in an oxyhemoglobin desaturation that improves as the apnea is terminated. The degree of desaturation is greater in REM sleep and resolves when continuous positive airway pressure (CPAP) of 5 cm H₂O is applied. In contrast to A, this nocturnal oximetry demonstrates prolonged desaturation in a patient with obesity hypoventilation syndrome (OHS). The desaturation corresponds to periods of prolonged hypoventilation. Although not diagnostic, this pattern is highly suggestive of OHS.

Source: Sleep-Related Hypoventilation Syndromes, *Fishman’s Pulmonary Diseases and Disorders, 5e*
Citation: Grippi MA, Elias JA, Fishman JA, Kopoloff RM, Pack AI, Senior RM, Siegel MD. *Fishman’s Pulmonary Diseases and Disorders, 5e*; 2015
Available at: http://accessmedicine.mhmedical.com/content.aspx?bookid=1344&sectionid=81196238 Accessed: January 20, 2018

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### The Role of Leptin in OHS

#### Reference (year)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Main message</th>
<th>Main limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ip et al (^{68}) (2000)</td>
<td>Leptin significantly correlated with AHI</td>
<td>Only males/Limited number of patients/Potential influence by comorbidities/No adjustment for FM</td>
</tr>
<tr>
<td>Campo et al (^{78}) (2007)</td>
<td>Higher leptin is associated with reduced respiratory drive and reduced hypercapnic response</td>
<td>Conditions of blood sampling unknown/Potential influence by comorbities</td>
</tr>
<tr>
<td>Philips et al (^{82}) (2000)</td>
<td>Increased leptin in OSAHS</td>
<td>Only males/Limited number of patients/Low statistical power</td>
</tr>
<tr>
<td>Barcelo et al (^{86}) (2005)</td>
<td>Decrease in leptin after nCPAP treatment in non-obese OSAHS</td>
<td>Only males/Limited number of patients/No adjustment for FM</td>
</tr>
<tr>
<td>Shimizu et al (^{90}) (2002)</td>
<td>Significant decrease in leptin after 1 day of nCPAP The decrease of leptin correlated with cardiac sympathetic function</td>
<td>Only males/Limited number of patients/Potential influence by comorbidities Low statistical power</td>
</tr>
<tr>
<td>Phipps et al (^{96}) (2002)</td>
<td>Leptin is a predictor for the presence of hypercapnia</td>
<td>Limited number of patients/Sex unknown</td>
</tr>
</tbody>
</table>

**Abbreviations:** FM: Fat Mass
Why should we care about OHS

• Clinical Presentation
  • OSH is established >80% in hospital
  • In the 5th or 6th decade of life (mean 52 years (42 - 61))

• 3 most common presentations
  - Acute on chronic respiratory acidosis admitted to the ICU
  - Misdiagnosed acute on chronic decompensated heart failure that declines (↑CO₂) with diuresis
  - Misdiagnosed of acute on chronic exacerbation of Chronic obstructive pulmonary disease

Diagnosis of Obesity Hypoventilation

- Body mass index (BMI) > 30 kg/m²
- Sleep disorder breathing
- Chronic daytime alveolar hypoventilation (PaCO₂ > 45 mmHg & PaO₂ < 70 mmHg)
- Serum HCO₃⁻ > 27 mEq/l
- Rule out other causes of hypoventilation
  - Severe obstructive disease,
  - Chest wall deformities, severe hypothyroidism, neuromuscular diseases, central hypoventilation syndrome such as congenital hypoventilation syndrome or Arnold-Chiari type II malformations.

The average number of patient visits to the doctor for each group is plotted against each year of the study. The average number of physician visits for OHS patients was significantly higher each year compared to OBCs and GPCs.

The large arrow indicates the time of diagnosis and the institution of treatment.
# Adverse Events during Hospitalization, Length of Stay, and Discharge Status among Patients with Simple Obesity or Obesity-Associated Hypoventilation (n=150)

Consecutive admissions to internal medicine services were screened over a 6-months hospital course and mortality at 18 months.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Simple Obesity (n = 103)</th>
<th>Obesity-Associated Hypoventilation (n = 47)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%) or Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care</td>
<td>27 (26%)</td>
<td>19 (40%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0</td>
<td>3 (6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>3 (3%)</td>
<td>2 (4%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>6 ± 9</td>
<td>8 ± 11</td>
<td>0.16</td>
</tr>
<tr>
<td>Discharge to long-term care facility</td>
<td>2 (2%)</td>
<td>9 (19%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Survival curves for patients with obesity-associated hypoventilation or simple obesity after discharge from hospital, with adjustment for age, sex, body mass index, electrolyte abnormalities, renal insufficiency, history of thromboembolism, and history of hypothyroidism. (n=150)

At 18 months, mortality was 9%

At 18 months, mortality was 23%

Hazard ratio for mortality of 4.0 (95% confidence interval [CI]: 1.5 to 10.4).

Most of the deaths associated with obesity-associated hypoventilation occurred in the first 3 months following hospital discharge.

Only 13% (6/47) were discharged with a recommendation for long-term treatment for hypoventilation (n=47)
The Clinical Characteristics and Hospital and Post-hospital survival of patients with OHS

- **Methods:**
  - EMR of patient with unequivocal OHS admitted (index)
  - 5 years retrospective chart review
  - 600 enrolled
    - Mean Age $58 \pm 15$
    - Mean BMI $48.2 \pm 8.3$ kg/m$^2$
    - $\frac{\text{♀}}{\text{♂}} = 64\%, 46\%$
    - DM Type II 37%
    - 43% misdiagnosed - COPD

- Died 90 (15%) during index hosp.
- Survivors follow for $3.2 \pm 1.3$ yrs

The clinical characteristics and hospital and post hospital survival of patient with OHS

Survivors follow for 3.2 ± 1.3 years

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n=600)</th>
<th>Survivors (n=510)</th>
<th>Died (n=90)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58.4 ± 15.2</td>
<td>57.2 ± 14.9</td>
<td>65.6 ± 14.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatine (mg/dL)</td>
<td>1.59 ± 1.73</td>
<td>1.3 ± 1.5</td>
<td>2.8 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>376 (63%)</td>
<td>300 (59%)</td>
<td>76 (84%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>12.4 (3.5%)</td>
<td>91 (18%)</td>
<td>33 (37%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU admission (n, %)</td>
<td>370 (61%)</td>
<td>296 (58%)</td>
<td>74 (82%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

In follow-up 98 of 510 (19%) died
Cumulative mortality of 31.3%

SECOND OPINION

AIRLINE PERKS WE'D LIKE TO SEE...

IN THE EVENT OF SEVERE SNORING, A CPAP MASK WILL DROP FROM THE COMPARTMENT ABOVE...

Z
↑CO₂ noted as AHI > 30

# Predictors of hypercapnia in patients with OHS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt; 40</td>
<td>1.8 (0.9 – 3.5)</td>
<td>0.1</td>
</tr>
<tr>
<td>AHI &gt; 50</td>
<td>2.2 (1.1 – 4.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Oxygen desaturation nadir &lt; 60% during polysomnography</td>
<td>4 (2 - 8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate to severe restriction on pulmonary function testing</td>
<td>10 (5 - 24)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Predictors of hypercapnia in patients with OHS syndrome using a logistic regression model*

Serum bicarbonate level

Sleep Apnea
BMI ≥ 30 kg/m²
n = 522

Serum HCO₃ ≤ 27 mEq/L
n = 257
3% with OHS

Serum HCO₃ ≥ 27 mEq/L
n = 265
50% with OHS

Lowest SpO₂ (<60%) during sleep
or AHI >100
n = 79
76% with OHS

Sleep apnea referral
Obese > 30 kg/m^2
n = 329

Serum bicarbonate level
Serum HCO₃⁻ ≥ 27 mEq/L

No
159 (0%) with OHS

Yes
170 (38%) with OHS

Respiratory restriction
forced vital capacity of less than 60% of predicted

or
Severe OSA
AHI > 30/hour

Both
84 (56%)

Either
65 (25%)

Neither
21 (10%)

Sleep Apnea Testing/Diagnosis

• Dissatisfied with sleep then…

• Screening Tests
  ( All have low quality of evidence )

  • Epworth Sleepiness Scale
  • Berlin Questionnaire (PCP)
  • STOP-BANG (Pre-Op)
  • Sleep Quality Index

Suggested algorithm for preoperative evaluation

Suspected OHS Pre Op Assessment

Screening STOP-Bang questionnaire
SpO2 & Serum HCO3 level

STOP-Bang ≥ 3
SpO2 < 90%
Serum HCO3 level ≥ 27 mEq

STOP-Bang < 3
SpO2 > 90%
Serum HCO3 level ≤ 27 mEq

Routine management

Perioperative OHS Precautions
Potential difficult airway
Opioid – induced ventilator impairment
Post-extubation PAP therapy

Sleep medicine consult
Polysomnography for PAP therapy
Assessment of PaCO2, RV function & PAH.

Common pitfalls of management in obesity hypoventilation syndrome.

- Excessive administration of oxygen
  - $\uparrow CO_2$ production, reduced minute ventilation

- Excessive diuresis contraction alkalosis
  - $\uparrow$ serum bicarbonate & alkalemia

- Excessive psychotropic/sedatives/opiates
  - $\uparrow$ upper airway collapsibility

Pitfalls in management:
- Blunted ventilator response
- Worsening hypercapnia

The Effect of Supplemental Oxygen on Hypercapnia in Subjects With Obesity-Associated Hypoventilation

Double blinding, randomized, controlled, crossover trial
n = 24 outpatients with OHS
100% oxygen for 20 mins on 2 separate days

PtCO\textsubscript{2} increased by 5.0 mm Hg (95% CI, 3.1–6.8; P < .001)
Minute ventilation decreased by 1.4 L/min (95% CI, 0.11–2.6 L/min; P = .03)
Dead space to tidal volume ratio increased by 0.067 (95% CI, 0.035–0.10; P < .001) with oxygen compared with room air

Treatment options for OHS

- Treatment has traditionally followed **three** modalities:
  - Reversal of sleep disorder breathing.
    - CPAP / NIV
  - Weigh reduction.
    - lifestyle modification,
    - bariatric surgery
  - Pharmacotherapy.
    - Weight loss medications,
    - Respiratory stimulants

Treatment options for OHS

- Reversal of sleep disorder breathing.
- PAP therapy was first described in 1982
- CPAP verses NIV
  - Prospective study of outpatients with severe OHS, based on the severity of obesity and OSA and the degree of hypercapnia,
  - 57% of patients were titrated successfully with 13.9 cmH$_2$0.

Efficacy of Different Treatment Alternatives for Obesity Hypoventilation Syndrome. Pickwick Study

OHS
n = 221

Spanish study
4 years, 15 – 80 years of age, 16 centers,
Strict OHS enrollment criteria

Control
n = 70

Lifestyle modification;
• 1,000 calorie diet;
• maintenance of sleep hygiene, (avoid supine sleep, maintain a regular sleep time and exercise);
• no use of sedative, stimulants, or alcohol;
• no smoking;
• avoiding heavy meals within 4 hours of sleep.

CPAP
n = 80

Lifestyle modification; +
• Fixed PAP during sleep period > 4 hours

Data collected Start, 1 month, 2 month follow up

Parameters collected: +
Primary Outcome: = PaCO₂
Secondary Outcomes:
• Anthropometric data;
• Clinical symptoms;
• Medical Research Counsel dyspnea scale,
• Epworth sleepiness score,
• Health related quality of life testing,
• Short form 36 (SF-36),
• Visual analogical well being score,
• PSG,
• Spirometry for lung function;
• 6 minute walk test

NIV
n = 71

Lifestyle modification; +
• Ventilator mode = Bi-level pressure with assured volume.
• EPAP was between 4 to 8 cmH₂O;
• Inspiratory PAP between 18 – 22 cmH₂O ( delta > 7 at all times);
• Pressures adjusted to normalize oxygenation,
• Respiratory rate = 12 – 15 breaths/min.
• Target volume was set 6 ml/kg of actual weight,
• Trigger, pressure and volumes adjusted for asynchronies;
• After 30 minutes ABG was done – to adjust.

Efficacy of Different Treatment Alternatives for Obesity Hypoventilation Syndrome. Pickwick Study

Intergroup PaCO₂ changes (means and 95% confidential intervals), adjusted according to basic adjustments (PaCO₂, age, sex, body mass index, and apnea–hypopnea baseline values), weight change, and continuous positive airway pressure (CPAP)/noninvasive ventilation (NIV) use (more or less than 4 h/night). NS = not significant.

### Efficacy of Different Treatment Alternatives for Obesity Hypoventilation Syndrome. Pickwick Study

Baseline Values and Changes in the Epworth Sleepiness Scale Score, Health-related Quality-of-Life Test Results, and Weight

<table>
<thead>
<tr>
<th></th>
<th>Baseline [Mean (SD)]</th>
<th>Intragroup Differences [Mean (SD)]</th>
<th>P Value of Intergroup Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NIV</td>
<td>CPAP</td>
<td>Control</td>
</tr>
<tr>
<td><strong>ESS</strong></td>
<td>11 (5.1)</td>
<td>11 (4.8)</td>
<td>11 (5.3)</td>
</tr>
<tr>
<td><strong>FOSQ</strong></td>
<td>73 (22)</td>
<td>71 (21)</td>
<td>77 (23)</td>
</tr>
<tr>
<td><strong>SF-36, physical</strong></td>
<td>36 (10)</td>
<td>36 (10)</td>
<td>37 (11)</td>
</tr>
<tr>
<td><strong>SF-36, mental</strong></td>
<td>44 (13)</td>
<td>42 (14)</td>
<td>44 (12)</td>
</tr>
<tr>
<td><strong>VAWS</strong></td>
<td>50 (22)</td>
<td>45 (24)</td>
<td>47 (19)</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>110 (19)</td>
<td>117 (25)</td>
<td>115 (24)</td>
</tr>
</tbody>
</table>

Definition of abbreviations: AHI = apnea–hypopnea index; BMI = body mass index; CPAP = continuous positive airway pressure; ESS = Epworth sleepiness scale; FOSQ = Functional Outcomes of Sleep Questionnaire; NIV = noninvasive ventilation; NS = not significant; SF-36 = Medical Outcome Survey Short Form 36; VAWS = visual analogical well-being scale.

*P < 0.001 intragroup difference (2 mo − baseline).
†P values of intergroup differences unadjusted or adjusted by basic adjustment (baseline values of the variable analyzed and age, sex, BMI, and AHI): NIV and control.
‡P values of intergroup differences unadjusted or adjusted by basic adjustment (baseline values of the variable analyzed and age, sex, BMI, and AHI): CPAP and control.
§P < 0.05 intragroup difference (2 mo − baseline).
∥P < 0.01 intragroup difference (2 mo − baseline).

Effectiveness of NIV in OHS compared with control therapy.

PaCO₂ (Δ = −3.5 mm Hg; 95% CI, −6.2 to −0.8)

HCO₃⁻ (Δ = −2.0 mmol/L; 95% CI, −0.44 to −3.65)

*P < .05

**P < .001.

**PART I**

- OSH not tolerate to CPAP
- CPAP = 8.9 ± 1.0

**PART II**

- 10 patients (mean age, 53.5 ± 11.7 years;
- mean BMI, 41.6 ± 12.1 kg/m²;
- mean FEV1/FVC ratio, 79.4 ± 6.5%;
- mean transcutaneous [PtcCO2], 58 ± 12 mm Hg)

**AVAPS**

Ventilator mode = Bi-level pressure with assured volume.
EPAP was between 4 to 8 cmH₂O;
Inspiratory PAP between 18 – 22 cmH₂O (delta > 7 at all times);
Pressures adjusted to normalize oxygenation;
Respiratory rate = 12 – 18 breaths/min.
Target volume was set 7 - 10 ml/kg of ideal weight,

In OHS patients who did not respond to therapy with continuous positive airway pressure, the effects of BPV with the spontaneous/timed (S/T) ventilation mode with and without AVAPS over 6 weeks

Effect of liraglutide 3.0mg in individuals with obesity and severe OSA: The SCALE Sleep Apnea randomized clinical trial

Change in AHI and body weight over 32 weeks of treatment and the relationship between weight loss and change in AHI.

Data are mean ±s.e. Weight category represents the change in body weight (%) from baseline after 32 weeks of treatment. PSG assessments were performed at weeks (baseline), 12 and 32.

Screening

Age = 20 – 60 years
BMI > 30 kg/m²
AHI > 40/hr

n = 23

Placebo = lower 500kcal /day
light exercise
lifestyle changes (LEARN)

Treatment = Drugs +
lower 500kcal /day
light exercise
lifestyle changes (LEARN)

From: A Randomized, Double-Blind, Placebo-Controlled Study of an Oral, Extended-Release Formulation of Phentermine/Topiramate for the Treatment of Obstructive Sleep Apnea in Obese Adults

Pharmacotherapy for OHS

• Few drugs known for their respiratory stimulant effects:
  • progesterone,
  • acetazolamide,
  • Almitrine,
  • Aminophylline (never studies in OHS)

• All have been tried in patients with sleep apnea syndromes; however, the two most widely quoted drugs when dealing with OHS patients are medroxyprogesterone and acetazolamide.

## Progesterone therapy

<table>
<thead>
<tr>
<th>N = 15</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>67.5</td>
<td>6.0</td>
<td>56 – 76 years</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>26.9</td>
<td>4.9</td>
<td>15.4 – 35.2</td>
</tr>
<tr>
<td>Smoking (pack-year)</td>
<td>8.8</td>
<td>13.9</td>
<td>0 – 50</td>
</tr>
<tr>
<td>FEV(_1) (L)</td>
<td>0.76</td>
<td>0.3</td>
<td>0.44 – 1.80</td>
</tr>
<tr>
<td>FEV(_1) (%)</td>
<td>34%</td>
<td>12.4</td>
<td>15 – 63</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.38</td>
<td>0.05</td>
<td>7.25 – 7.45</td>
</tr>
<tr>
<td>PaCO(_2) (Torr)</td>
<td>45</td>
<td>8.2</td>
<td>41.2 – 74.2</td>
</tr>
<tr>
<td>PaO(_2) (Torr)</td>
<td>67</td>
<td>9.0</td>
<td>42 – 94.5</td>
</tr>
</tbody>
</table>

Randomized, placebo controlled; Respiratory failure = COPD ABG & blood levels chemoreceptors

Changes in fasting serum leptin concentration versus changes in the carbon dioxide pressure in arterial blood (Pa,CO2) in postmenopausal females with moderate-to-severe chronic respiratory impairment showing a positive correlation (r=0.60, p=0.031).

MPA 60 mg day
Over 2 weeks

positive correlation (r = 0.60, p = 0.031).
mean CO₂ Δ = 8 mmHg

Ten patients with the Pickwickian syndrome, MPA 20 mg Q8 sublingual

Figure 1. Improvement in arterial blood gases in 10 patients after institution of medroxyprogesterone acetate therapy. PaO₂ reached 62 ± 2.3 mm Hg (Denver normal = 69 ± 1.2 mm Hg). PaCO₂ showed a complementary decrease to 38 ± 1.2 Hg (Denver normal = 36 ± 0.6 mm Hg). These improvements were sustained throughout treatment. Bars represent standard error of the mean.

Figure 3. During 1 month withdrawal of medroxyprogesterone acetate therapy, significant decreases in PaO₂ and increases in PaCO₂ were observed. These values reverted to previous treatment levels 1 month after reinstitution of therapy. Bars represent standard error of the mean.
Acetazolamide therapy

Examples of individual DEF runs in one subject after placebo and acetazolamide intake, respectively. Upper traces are end-tidal Pco2. Breath-by-breath ventilatory data are represented by small open circles. The solid line through these actual ventilatory data is the model output. V'c and V'p are the calculated contributions of the central and peripheral chemoreflex loops, respectively. CO2 sensitivities of both chemoreflex loops are similar after placebo and acetazolamide. In both the placebo and acetazolamide condition, 2 to 3 DEF runs were performed in all subjects.

Hypercapnic respiratory failure in obesity-hypoventilation syndrome: $CO_2$ response and acetazolamide treatment effects.

- 25 obesity-hypoventilation-syndrome patients mechanically ventilated for hypercapnic respiratory failure ready for weaning.

- Weaning = SBT $F_{IO_2}$ $\leq$ 0.5; PEEP $\leq$ 8 cmH$_2$O; and $Pa/F_{IO_2}$ $>$ 150 mmHg.

- ABG prior to Mechanical Ventilation:
  - pH $7.18 \pm 0.08$
  - $CO_2$ $102 \pm 25$ mmHg
  - SAPS II score $35 \pm 10$ (mortality = 2.9% - 8.9%)
  - Ventilator days $6.7 \pm 5.3$ d (mean 5 d)

- Acetazolamide was NG for 4 days dose 500 - 2,750 mg.

Hypercapnic respiratory failure in obesity-hypoventilation syndrome: CO₂ response and acetazolamide treatment effects.

Airway-occlusion pressure 0.1 s after the start of inspiratory flow ($P_{0.1}$) versus $P_{aCO_2}$, and minute volume ($V_E$) versus $P_{aCO_2}$, increase in 8 patients, before (solid lines) and after (dashed lines) acetazolamide treatment.

- Plasma HCO₃ reduced by 8.4 ± 3.0 mmol/l (p = 0.01)
- Hypercapnic drive response increase by 0.14 ± 0.16 cmH₂O/mmHg (p = 0.02)
- CO₂ response was 5.9 ± 6.9
- Ventilator days 6.7 ± 5.3 d (mean 5 d) versus 3.3 ± 2.1 d (mean d 2)
- 3 patients died (no explanation)

Conclusions

• In summary, obesity is a major health problem and has detrimental effects on the health-care systems at many levels.

• OHS is a far more serious problem, frequently missed and improperly treated.

• Better recognition of OHS may lead to better outcomes.

• Currently, the best available options for treating OHS patients are weight reduction and non invasive ventilation > positive airway pressure ventilation.