“OBESITY HYPOVENTILATION SYNDROME: CPAP vs NIV”
Hypoventilation mechanisms

- OHS
  - ↑ Mechanical load
    - Work breathing
      - Muscle deficiency
  - Leptin resistance
  - Breathing sleep disorders
  - REM hypoventilation
  - ↑ Threshold arousal
    - Sleep hypercapnia
      - ↑ Serum bicarbonate
  - Daytime hypercapnia

NIV action
CPAP action

Clinical and functional improvement results
Daytime gas exchange with NIV

OHS

N = 22

\[ \text{PaO}_2 \]

\[ \text{PaO}_2 \]

KIPHOSCOLIOSIS

N = 14

\[ \text{PaO}_2 \]

\[ \text{PaCO}_2 \]

Masa. Chest 2001;119
Daytime gas exchange with CPAP

29 stable OHS patients

Salor N, Respirology (2013) 18, 1135–1142
Daytime gas exchange with both PCO2tc during the night

A Randomized Crossover Trial including 10 OHS patients

Storre JH, CHEST / 130 / 3 / SEPTEMBER, 2006
Patients were included if they had a favorable response to an initial night with CPAP treatment.

### Table 4 Change in daytime gas exchange, weight and subjective sleep quality following 3 months of positive pressure in the three treatment groups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Change in CPAP group Mean (SD)</th>
<th>Change in BVS group Mean (SD)</th>
<th>Mean difference between treatments (95% CI)</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paco₂ (mm Hg)</td>
<td>-5.8 (8.4)*</td>
<td>-6.9 (6.7)*</td>
<td>1.04 (-4.5 to 6.6)</td>
<td>0.7</td>
</tr>
<tr>
<td>Awake SpO₂ (%)</td>
<td>6 (3)*</td>
<td>8 (5)*</td>
<td>1.9 (-5.2 to 1.3)</td>
<td>0.24</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>-2.3 (8.5)*</td>
<td>-2.5 (2.5)*</td>
<td>0.2 (-4.2 to 4.6)</td>
<td>0.93</td>
</tr>
<tr>
<td>Weight loss (kg)</td>
<td>-4.9 (7.8)*</td>
<td>-5.6 (9.4)*</td>
<td>0.7 (-5.2 to 6.5)</td>
<td>0.82</td>
</tr>
<tr>
<td>Mean nightly therapy use (h)</td>
<td>5.8 (2.4)</td>
<td>6.1 (2.1)</td>
<td>0.33 (-1.8 to 1.2)</td>
<td>0.66</td>
</tr>
<tr>
<td>ESS</td>
<td>-6 (8)*</td>
<td>-9 (5)**</td>
<td>2.89 (-1.78 to 7.56)</td>
<td>0.21</td>
</tr>
<tr>
<td>PSQI</td>
<td>-1.93 (3.5)</td>
<td>-5.6 (3.9)**</td>
<td>3.67 (0.82 to 6.5)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

BVS, bilevel ventilatory support; CPAP, continuous positive airway pressure; Paco₂, arterial carbon dioxide tension; SpO₂, oxygen saturation; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index.  
*p<0.05, **p<0.001, within group changes from baseline.  
†p Value denotes mean difference between CPAP and BVS treatment groups using unpaired t tests.

### Weaknesses
- Selected patients
- Low sample for a negative result
NIV vs lifestyle counseling


Baselined assessment

Screened obese patients (n=143)

5 patients had PaCO2 ≥ 45 mmHg but met one exclusion criteria or declined to participate

101 patients had PaCO2<45mmHg

Randomized (n=37)

Received lifestyle counseling treatment (n=18)

Withdrawals: (n=1) acute respiratory failure

Follow-Up of 1 month

Completed the study (n=17)

Received nocturnal NIV (n=19)

Withdrawals: (n=1) Cardiac pacing during follow-up

Completed the study (n=18) 4 patients had less than 4h of NIV nightly use

Mild hypercapnia

Weakness

• Selected patients with mild hypercapnia
Hemodynamic effect

24 OHS patients followed up for 6 months

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Echocardiographic and 6-min walk test results at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (1)</td>
</tr>
<tr>
<td>PASP (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>44 ± 15</td>
</tr>
<tr>
<td>RVO at diagnosis</td>
<td>58 ± 11</td>
</tr>
<tr>
<td>No RVO at diagnosis</td>
<td>32 ± 5</td>
</tr>
<tr>
<td>Patients with RVO</td>
<td>13 (43.3%)</td>
</tr>
<tr>
<td>Distance on 6MWT, m</td>
<td>350 ± 110</td>
</tr>
<tr>
<td>mSaO₂ during 6MWT, %</td>
<td>83.8 ± 5.6</td>
</tr>
</tbody>
</table>

Data represent mean ± standard deviation or numbers (%) of patients.

6MWT, 6-min walk test; mSaO₂, mean arterial oxygen saturation; PASP, pulmonary artery systolic pressure; RVO, right ventricular overload.

*Castro-Añon O, Respirology (2012) 17, 1269–1274*
Hemodynamic and functional capacity

- 18 patients with daytime pulmonary hypertension and hypoventilation
- After 3 months of NIV.

Held M, Eur Respir J 2014; 43: 156–165
Hemodynamic and functional capacity

- 18 patients with daytime pulmonary hypertension and hypoventilation
- After 3 months of NIV.

Held M, Eur Respir J 2014; 43: 156–165
HOSPITAL DAYS AND SURVIVAL WITH CPAP OR NIV
32 patients with OHS treated with CPAP or NIV: 70% of reduction in hospitalization days after treatment.

Berg Chest 2001; 120:377
69 patients

41 AHRF
- 7 Rejected NIPPV
  - 4 died (57%)
  - 3 survived

34 NIPPV

28 CRF
- 8 Rejected NIPPV
  - 3 died (37%)
  - 5 survived

- 20 NIPPV
  - 2 died (1%)
  - 18 survived

Follow-up: 50±25 months (12-105)
Composition of the observed survivals from different studies with and without treatment with NIV

But there are not studies comparing the mortality between NIV and control

NIV: survival

Mortality with treatment

From two retrospective cohorts, 110 patients with OHS and 220 patients with OSAS were studied.

Castro-Añon, PLOS ONE DOI: 10.1371/journal.pone.0117808
February 11, 2015
Different treatment alternatives for OHS

Large multicentric Spanish study

PICKWICK STUDY
17 participant centers

- San Pedro de Alcántara Hospital. Caceres (Coordinator Center)
- San Pablo Hospital. Barcelona.
- General Yague Hospital. Burgos.
- Arnau de Vilanova Hospital. Lérida.
- 12 de Octubre Hospital. Madrid.
- La Paz Hospital. Madrid.
- La Macarena Hospital. Sevilla
- San Juan Hospital. Alicante
- Gregorio Marañón Hospital. Madrid.
- Valdecilla Hospital. Santander.
- Virgen del Rocío Hospital. Sevilla.
- Txagorritxu Hospital. Vitoria.
- Miguel Servet Hospital. Zaragoza.
- Complejo Universitario Insular. Las Palmas
- Departamento de fisiología. Universidad de Valladolid
Flow chart and phases

- OHS
  - OSA≥30
    - CPAP
    - NIV
    - Lifestyle modification
  - OSA<30
    - Lifestyle modification
    - NIV
    - NIV

- Re-randomization

- 2 months
- 36 months
Phase 1: short term efficacy

Outcomes for short term (2 months):

- **Treatment efficacy (main objective):**
  - Clinic-functional daytime: symptoms, PO2, PCO2 and QL.
  - Sleep period: PSG.
  - Biochemical and endothelial markers.
  - PAP (echocardiography).

- **Genesis of daytime alveolar hypoventilation (secondary objective):**
  - Comparison of daytime PCO2/AHI and duration event/AHI ratios between responders and non responders to CPAP treatment.
  - Comparison of leptin levels between responders and non responders to CPAP treatment and with IAH ≥ 30 group treated with VNI.

- **Role of intermittent-persistent hypoxia model in the genesis of metabolic alterations and endothelial dysfunction (secondary objective):**
  - Change of related substances levels between groups related to AHI.
Long term efficacy of treatments for OHS

Outcomes for long term (3 years):

- **Clinical-functional daytime:**
  - Symptoms, PO2, PCO2 and QL.
  - Biochemical and endothelial markers.

- **Repercussions:**
  - PAP (echocardiography).
  - BP (standardized registry).
  - Hospitalization days.
  - Cardiovascular events incidence (hypertension included).
  - Abandons.
  - Mortality.

Flowchart:

- OHS 440 patients
  - SAHS>30
    - VNI 110 patients
    - CPAP 110 patients
  - SAHS<30
    - VNI 110 patients
    - Lifestyle modification 110 patients
Selected 351

Excluded = 49
- Psycho-physical incapacity to complete questionnaires = 9
- Severe chronic illness = 11
- Severe nasal obstruction = 1
- Absence of informed consent = 28

No severe OSA = 81
(Referred to other parallel study protocol)

Randomized 221

NIV 71
- Oxygen therapy 17
  (All no medic causes)
  Finished protocol 64

CPAP 80
- Oxygen therapy 16
  (All no medic causes)
  Finished protocol 69

Control 70
- Oxygen therapy 20
  (One medic cause)
  Finished protocol 67

Dropout = 7
(All no medic causes)

Dropout = 11
(All no medic causes)

Dropout = 3
(One medic cause)
Clinical symptoms evolution

**NIV**
- Dysnea
- Unrefreshing sleep
- Tiredness
- Nocturia
- Headache
- Morning confusion

**CPAP**
- Dysnea
- Unrefreshing sleep
- Tiredness
- Nocturia
- Headache
- Morning confusion

**Control**
- Dysnea
- Unrefreshing sleep
- Tiredness
- Nocturia
- Headache
- Morning confusion

Graphs show the percentage of symptoms over time for NIV, CPAP, and Control groups.
PaCO\textsubscript{2} evolution
PaCO2 changes comparison for unadjusted and adjusted
PaCO₂ changes related to weight change and compliance

Baseline values of the variable analyzed, age, gender, BMI, and AHI.
Changes in Functional parameters

PO2  FVC  FEV1  6MWD

- NIV
- CPAP
- Control

NS  NS  
P<0.05  P<0.01

p<0.05

p<0.01
PSG parameters

- Arousal index: P<0.001
- AHI: P<0.001
- Desaturation index: P<0.001
- SatO2: P<0.001
- %TTS<90: P<0.001

Legend:
- NIV
- CPAP
- Control
CONCLUSIONS

- In comparison with the control arm:
  - Both, NIV and CPAP, improved clinical symptoms and PSG parameters.
- NIV produced higher functional improvement than CPAP.
- Long-term studies are necessary to determine if NIV or CPAP reduce hospitalization days, CVD incidence or mortality.