Control of breathing in obstructive sleep apnoea and in patients with the overlap syndrome


ABSTRACT: In some patients obstructive sleep apnoea (OSA) may co-exist with chronic obstructive pulmonary disease (COPD) and respiratory failure; the so-called "overlap syndrome". Obstructive, hypercapnic patients have both blunted ventilatory and mouth occlusion pressure responses during CO2 stimulation. The purpose of this study was to compare the pattern of breathing and CO2 response between OSA patients and those with the overlap syndrome.

Twenty obese men with OSA and normal lung function (Group A), 11 obese men with overlap syndrome (Group B) and 13 healthy nonobese subjects (Group C) were examined. Lung function tests, breathing pattern, mouth occlusion pressure (P0.2) at rest, and respiratory responses during CO2 rebreathing were investigated. Diagnosis of OSA was established by standard polysomnography.

There were no statistical differences between Groups A and B in apnoea+ hypopnoea index (62 vs 54), mean arterial oxygen saturation (SaO2) during sleep (85 vs 84%) and in body mass index (BMI) 34.3 vs 36.3 kg·m². Minute ventilation, mean inspiratory flow and P0.2 at rest were increased in both groups of patients in comparison to controls. During CO2 rebreathing, group A had normal ventilatory and P0.2 responses, similar to controls, (2.7±1.1 vs 2.1±0.4 l·min⁻¹·mmHg⁻¹ and 0.7±0.3 vs 0.7±0.25 cmH2O·mmHg⁻¹, respectively). However, Group B had significantly decreased ventilatory and P0.2 responses to CO2 (0.71±0.23 l·min⁻¹·mmHg⁻¹ and 0.34±0.17 cmH2O·mmHg⁻¹, respectively).

This comparison showed that patients with OSA had normal CO2 response when awake, whereas those with overlap syndrome had diminished CO2 response when awake. It seems that co-existence of COPD with hypercapnic respiratory failure is the main cause of decreased CO2 response in the overlap syndrome.

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Material and methods

Two groups of patients and a control group were investigated. Group A consisted of 20 obese men with OSA, without respiratory symptoms and with almost normal lung function results. Their mean age was 45±6 yrs, and body mass index (BMI) 34.4±6.3 kg·m⁻². Group B consisted of 11 obese men with OSA and hypercapnic respiratory failure due to COPD (overlap syndrome). Their mean age was 53±8 yrs, and BMI 36.3±5.8 kg·m⁻².

Group C consisted of 13 healthy, nonobese subjects with no sleep complaints and no sleep symptoms typical of OSA. Their mean age was 34±7 yrs, and BMI 22.3±3.0 kg·m⁻².

In all Group A and B patients, lung function tests, including volumes, maximal expiratory flows and airway resistance were performed with the use of body plethysmograph (Masterlab, Jaeger). Predicted values were those of the European Coal and Steel Community (ECSC) [13]. Blood gases were measured in arterialized capillary blood using a Corning 168 analyser.
The pattern of breathing, minute ventilation ($V_E$) and mouth occlusion pressure ($P_{O.2}$) were measured with the use of a pneumotachograph, electromanometer and occlusion pressure valve, with the subject in the sitting position, awake and at rest. Ventilatory and mouth occlusion pressure responses during $CO_2$ rebreathing test, according to Read, were measured with the same set of equipment. $CO_2$ concentration before and during rebreathing was measured with the use of a mass spectrometer (Centronix). Inspired volume, and end-tidal $CO_2$ were recorded continuously on a six-channel recorder (Watanabe). The respiratory response was evaluated from minute ventilation and mouth occlusion pressure slopes ($\Delta V_E/\Delta P_{O.2}$) and $\Delta P_{O.2}/\Delta P_{CO_2}$ and from absolute values of ventilation and $P_{O.2}$ at an end-tidal carbon dioxide tension ($P_{ET,CO_2}$) 60 mmHg. The strength of respiratory muscles, maximal inspiratory (MIP) and expiratory (MEP) pressures, were measured at the mouth with the use of a manometer.

The diagnosis of OSA was established by standard polysomnography, and was performed using a computerized system (Somnostar 4100; Sensormedics). Sleep staging was carried out according to standard criteria [14]. Sleep efficiency was defined as percentage ratio of total sleep time to sleep period. Breathing disorders were classified as obstructive, central or mixed. Apnoea was defined as cessation of nasal or oral airflow for at least 10 s [15]. Hypopnoea was defined as a 50% decrease of thoracic and abdominal respiratory signal for 10 s or more [16]. Significant desaturation was defined as a fall in $SaO_2$ of 4% or more from the preceding stable $SaO_2$ when asleep [17]. Sleep and respiration were scored visually on a high resolution screen. The apnoea +hypopnoea index (AHI) was calculated from hand-scoring of polygraphic data as a mean number of disordered breathing episodes for one hour of sleep. AHI was considered diagnostic for OSA when ≥10.

Statistical significance of differences between data were tested with the unpaired t-test.

**Results**

Polysomnography confirmed the diagnosis of OSA in both groups of patients. There were no statistical differences between Groups A and B in BMI, AHI and mean $SaO_2$ during sleep (table 1). Lung function values were within normal limits in Group A, with the exception of a decreased mean value of maximal expiratory volume at 25% forced vital capacity (MEF25). Mean arterial oxygen tension ($Pa_o2$) was 8.9 kPa (66.7 mmHg). All patients were normocapnic (table 2), with the exception of one having an arterial carbon dioxide tension ($Pa_{CO_2}$) 6.4 kPa (48 mmHg).

All patients in Group B had symptoms of bronchial obstruction, lung hyperinflation, moderate hypoxaemia, slight hypercapnia and increased serum bicarbonate concentration. They also had lower values of maximal inspiratory and expiratory pressures, probably due to lung hyperinflation (table 2).

In both groups, we found increased resting ventila-

| Table 1. – Results of polysomnography in patients with OSA (Group A) and overlap syndrome (Group B) |
|-----------------|-----------------|-----------------|
|                  | Group A (n=20)  | Group B (n=11)  | p-value |
| Age yrs          | 45±6            | 53±8            | <0.01   |
| BMI kg·m⁻²       | 34.3±6.3        | 36.3±5.8        | NS      |
| Sleep efficiency %| 67±10           | 83±14           | <0.01   |
| AHI              | 62±19           | 54±22           | NS      |
| Mean $SaO_2$ during sleep % | 85±5 | 84±3 | NS |

| Table 2. – Mean results of lung function tests in patients with OSA (Group A) and overlap syndrome (Group B) |
|-----------------|-----------------|-----------------|
|                  | Group A (n=20)  | Group B (n=11)  | p-value |
| FVC % pred      | 107±16          | 64±19.1         | <0.001  |
| FEV % pred      | 98±15           | 43±15           | <0.001  |
| FEV/FVC %       | 76±5            | 53±11.8         | NS      |
| Raw kPa·l⁻¹·s   | 0.22±0.06       | 0.73±0.38       | <0.001  |
| TGV % pred      | 104±20          | 140±24          | <0.01   |
| TLC % pred      | 105±10          | 102±16          | NS      |
| $Pa_o2$ mmHg    | 6.8±0.8         | 6.8±0.6         | <0.001  |
| $Pa_{CO_2}$ mmHg| 5.3±0.5         | 6.8±1.0         | <0.001  |
| $HCO_3$ mmol·l⁻¹| 23.3±3.6        | 29.7±26.2       | <0.001  |
| MIP cmH₂O       | 120±37          | 77±33           | <0.05   |
| MEP cmH₂O       | 198±47          | 131±32          | <0.001  |

Data are presented as mean±SD. FVC: forced vital capacity; % pred: percentage of predicted value; FEV: forced expiratory volume in one second; Raw: airways resistance; TGV: thoracic gas volume; TLC: total lung capacity; $Pa_o2$: arterial oxygen tension; $Pa_{CO_2}$: arterial carbon dioxide tension; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; OSA: obstructive sleep apnoea; NS: nonsignificant.

In Group A it was due mainly to increased tidal volume ($V_t$), and in Group B it was predominantly due to higher frequency of breathing. Patients in Group B had lower $V_t$, higher frequency of breathing and higher mouth occlusion pressure compared with Group A. Mean inspiratory flow ($V_{t/Ti}$) and mouth occlusion pressure ($P_{O.2}$) were increased in both groups in comparison to controls (table 3).

During $CO_2$ rebreathing, Group A patients had ventilatory and $P_{O.2}$ responses similar to those of the control group. However, Group B patients had significantly decreased ventilatory and $P_{O.2}$ responses during rebreathing (table 4) in comparison to controls. Also, absolute values of ventilation and $P_{O.2}$ at $P_{ET,CO_2}$ of 60 mmHg were decreased in Group B patients. The differences in respiratory response between Group A and B patients were also statistically significant (p<0.001).

**Discussion**

The pattern of breathing was abnormal in both groups of patients with OSA in comparison to control, nonobese
There are few studies of CO₂ sensitivity in patients with OSA and co-existing hypercapnia. Garay et al. [6] demonstrated an inverse relationship between waking PCO₂ and hypercapnic ventilatory response. Berthon-Jones and Sullivan [22] and, more recently, Verbraecken et al. [10] also found decreased ventilatory response in OSA patients with hypercapnia. In addition, hypercapnic patients with COPD and without sleep disorders had decreased CO₂ sensitivity [23–25].

In obstructive patients with the overlap syndrome, a low ventilatory response to CO₂ is caused mainly by disturbed lung mechanics and gas exchange. Mouth occlusion pressure response to CO₂ in patients with the overlap syndrome may have been affected in several ways. In these patients with chronic hypercapnia, we found increased blood bicarbonate concentration. This factor inhibits CO₂ sensitivity and decreases mouth occlusion pressure response [23–25]. Some authors [26] have postulated that hyperinflation of the lung may also decrease mouth occlusion pressure response. As hyperinflation was also found in patients with overlap syndrome, this factor has to be taken into account. In addition, lower respiratory muscle strength and constitutional or genetic factors may be responsible for lowered ventilatory and mouth occlusion pressure responses in patients with overlap syndrome (Group B), as has been suggested in hypercapnic COPD patients [27].

Comparison of the two groups of patients showed that those with OSA had normal CO₂ response, whereas those with the overlap syndrome had diminished CO₂ response like hypercapnic patients with COPD alone. It seems that co-existence of COPD with hypercapnic respiratory failure is the main cause of decreased CO₂ response in overlap syndrome. However, breathing pattern was abnormal in both groups of patients with OSA, probably as a consequence of obesity and changed thoracic mechanics.

### References

6. Garay SM, Rapoport D, Sorkin B, Epstein H, Feinberg...
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