Nasal continuous positive airway pressure with supplemental oxygen in coexistent sleep apnoea-hypopnoea syndrome and severe chronic obstructive pulmonary disease

G. Sampol*, M.T. Sagalés**, A. Roca*, M.D. de la Calzada**, J.M. Bofill*, F. Morell*

ABSTRACT: The objective of our study was to assess the application of nasal continuous positive airway pressure (nCPAP) with supplemental oxygen for correction of upper airway obstructive episodes and hypoxaemia during sleep in stable patients with sleep apnoea-hypopnoea syndrome (SAHS) and severe chronic obstructive pulmonary disease (COPD).

Ten male patients with symptomatic SAHS and severe COPD (forced expiratory volume in one second <50% of predicted) were studied for three consecutive nights. Diagnostic polysomnography was performed the first night and repeated with increasing nCPAP levels, with and without supplemental oxygen on the second and third nights, respectively.

Diagnostic polysomnography showed: mean (SD) apnoea-hypopnoea index 41 (22) events·h⁻¹; mean arterial oxygen saturation ($S_aO_2$) was 86 (2)% and mean desaturation nadir was 81 (4)% during non-rapid eye movement (nREM) sleep and 80 (7)% and 73 (9)%, respectively during REM sleep. The application of nCPAP during the second night corrected apnoeas and hypopnoeas, but $S_aO_2$ remained <90% in all patients. With the addition of oxygen at a flow of 1.5 L·min⁻¹ at suboptimal nCPAP levels, we observed an increase in apnoea frequency, persistence of apnoeas at nCPAP levels which eliminated them when no supplemental oxygen was administered, and longer duration of apnoeas and hypopnoeas. However, when the effective nCPAP level of the second night was reached with supplemental oxygen during the third night, its efficacy in eliminating apnoeas and hypopnoeas was maintained and, furthermore, all patients presented $S_aO_2 >90\%$, with no greater hypercapnia or cardiac arrhythmias.

We conclude that nasal continuous positive airway pressure with supplemental oxygen constitutes a practical therapeutic alternative for hypoxic patients with sleep apnoea-hypopnoea syndrome and chronic obstructive pulmonary disease.

Keywords: Chronic obstructive pulmonary disease, sleep apnoea-hypopnoea syndrome, sleep hypoxaemia

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occurs when the negative pressures produced by diaphragm and chest wall muscle contraction are inadequately opposed by contraction of upper airway muscles [9–11]. Hypoxaemia has been shown to influence this balance of forces and lead to a greater increase in upper airway activity compared with that of the diaphragm [12–14]. We wanted to determine whether the elimination of hypoxaemia by means of nCPAP with supplemental oxygen may, thus, constitute a mechanism favouring upper airway closure and increase the level of nCPAP needed to maintain upper airway patency.

Based on these considerations, we evaluated the effects of the application of nCPAP and nCPAP with supplemental oxygen on apnoeas and hypopnoeas and nocturnal oxygenation in hypoxaemic SAHS-COPD patients.

Methods

Ten male patients with symptomatic SAHS were recruited from those referred to our hospital for excessive daytime somnolence and severe snoring. All met the criteria for COPD [15], with mean (SD) forced expiratory volume in one second (FEV1) 36 (10)% of predicted value, mean FEV1/forced vital capacity (FVC) 47 (10)% and no appreciable improvement after nebulized bronchodilator (table 1). All subjects were on medical regimens for COPD and none had evidence of acute exacerbation of their lung disease within 8 weeks of the study. None were current smokers.

Patients were studied for three consecutive nights: diagnostic polysomnography (PSG) was performed during the first night; PSG with the application of increasing nCPAP levels during the second night; and PSG with nCPAP was repeated with oxygen applied to the nasal mask during the third night. All subjects gave informed consent to the study, which was approved by the Hospital Research and Ethics Committee.

Table 1. – Individual anthropometric, lung function values, awake and supine blood gases and apnoea-hypopnoea indices for the 10 subjects

<table>
<thead>
<tr>
<th>Subj No.</th>
<th>Age yrs</th>
<th>BMI kg·m⁻²</th>
<th>FVC % pred</th>
<th>FEV₁ % pred</th>
<th>FEV₁* % FVC</th>
<th>TLC % pred</th>
<th>RV % pred</th>
<th>Pₐ,O₂ kPa</th>
<th>Pₐ,CO₂ kPa</th>
<th>Sₐ,O₂ %</th>
<th>AHI</th>
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<td>48</td>
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<td>136</td>
<td>7.9</td>
<td>5.7</td>
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</table>

Mean (sd) 58 (7) 30.5 (4.9) 56 (8) 36 (10) 47 (10) 103 (15) 197 (54) 8.1 (0.4) 5.6 (0.6) 91 (1) 41 (22)

*: FEV₁%: FEV₁/FVC ×100. Subj: subject; BMI: body mass index; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; TLC: total lung capacity; RV: residual volume; % pred: percentage of predicted value [16, 17]; Pₐ,O₂: arterial oxygen tension; Pₐ,CO₂: arterial carbon dioxide tension; Sₐ,O₂: arterial oxygen saturation; AHI: apnoea-hypopnoea index.
nCPAP and was thereafter increased progressively in a similar way to that of the previous night.

**Arterial blood gas measurements.** Arterial blood gas measurements were performed during the second and third nights prior to the start of polysomnography, with the patient breathing room air whilst awake and supine. Multiple blood gases were later obtained during sleep at the end of apnoeas or hypopnoeas with 3 cmH₂O nCPAP and at random intervals with the maximum nCPAP level reached. All arterial blood samples and pH values were immediately analysed with a model IL-1312 blood gas analyser (Instrumentation Laboratories, Lexington, MA, USA).

Lung function was assessed using a Pulmonary Calculator System HP 47804A (Hewlett-Packard, Palo Alto, CA, USA) and a constant volume Jaeger plethysmograph (Würzburg, Germany).

**Data analysis**

Sleep stage was scored by standard criteria [19]. An obstructive apnoea was defined as absence of airflow at the nose and mouth for ≥10 s with continued respiratory effort. Hypopnoea was defined as a decrease in the Respitrace sum signal of ≥50% for ≥10 s when compared to the peak amplitude lasting for ≥10 s that occurred within the previous 2 min in the presence of continued airflow [20]. The apnoea plus hypopnoea index (AHI) was defined as the number of apnoeas and hypopnoeas per hour of sleep. Mean \( S_{a,O_2} \) during sleep was determined by averaging the saturation tracings every 10 s and a desaturation event was defined as a reduction in \( S_{a,O_2} \) by at least 4% for a duration of ≥10 s.

Given the variability of upper airway closing pressure in the different sleep phases [21], comparisons of AHI at each nCPAP level were made during periods of the same phase of nREM sleep (I-II or III-IV) with a minimum duration of 15 min. Comparisons were usually made in phases I-II, in which patients remained for the major part of the sleep, until effective nCPAP was reached and the appearance of phases III-IV was observed. With the aim of not underestimating possible deterioration in the acid base balance induced by oxygen administration, only maximum arterial carbon dioxide tension (\( P_{a,CO_2} \)) and minimum pH values were considered for analysis.

Data are expressed in the text and tables as mean (standard deviation). All statistical comparisons between data collected during the three nights were made by Friedman and Wilcoxon nonparametric tests, with significance adjusted by the Bonferroni method when simultaneous multiple comparisons between the three nights were performed. Significance was assigned at a p-value less than 0.05 or, when Bonferroni-corrected, at a p-value less than 0.0166 (0.05/3=0.0166).

**Results**

No significant quantitative or qualitative differences in sleep were found between the three nights except for a greater duration of slow wave and REM sleep in the second and third nights, usually when effective nCPAP was reached (table 2). Three patients (Nos. 2, 4 and 7) presented no apnoeas during sleep; however, all of them presented frequent hypopnoeas during recording. The number of desaturations·h⁻¹ was 50 (24) with a mean nadir of 81 (4)% in nREM sleep and 73 (9)% in REM sleep, and a mean minimum value of 69 (9)% and 61 (15)% in NREM and REM sleep, respectively. Mean \( S_{a,O_2} \) determined by pulse oximetry fell from a basal awake supine value of 90 (2)% to 86 (2)% during nREM sleep and 80 (7)% during REM sleep (p<0.03).

The maximum level of nCPAP applied during the second night was 9.5 (2.0) cmH₂O; at this level, AHI was 2.9 (3.7), and mean \( S_{a,O_2} \) during nREM sleep 88 (2)% with a mean minimum value of 83 (4)%.

<table>
<thead>
<tr>
<th>Table 2. – Sleep quality data</th>
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<tbody>
<tr>
<td><strong>Night 1</strong></td>
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<tr>
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<tr>
<td>Total sleep time min</td>
</tr>
<tr>
<td>Sleep efficiency %</td>
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<tr>
<td>Slow-wave sleep min</td>
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<td>REM sleep min</td>
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Values are presented as mean±sd in parentheses. REM: rapid eye movement. *: significant differences are in comparison with night 1 (p<0.01).
achieved REM sleep with the maximum nCPAP applied, and presented a mean $S_{a}O_{2}$ of 85 (4)%%%%%%%%%%%%%%%%%%% and a mean minimum value of 79 (6)%%%%%%%%%%%%%%%%%%% . Characteristically, the decrease in the number of obstructive apnoeas was achieved with lower pressures than those required in hypopnoeas (fig. 1) and, when low levels of nCPAP were applied, apnoea frequency decreased accompanied by an increase in hypopnoeas.

The application of oxygen associated with nCPAP during the third night improved oxygenation during sleep without producing a clinically significant increase in $P_{a}CO_{2}$ or induction of cardiac arrhythmias. This improvement was observed at low nCPAP levels despite the persistence of apnoeas and hypopnoeas (table 3). All patients presented a mean $S_{a}O_{2}$ above 91% in nREM phase during the third night with the maximum nCPAP applied. This value was not reached by any patient during the second night. In the seven patients who achieved REM sleep with maximum nCPAP, mean $S_{a}O_{2}$ was 91 (2)% , less than that corresponding to nREM sleep, 92 (2)% (p<0.05). The minimum $S_{a}O_{2}$ detected at any time in the REM phase was similarly lower, 87 (4)% vs 88 (3)% in REM and NREM sleep, respectively (p<0.05).

The application of nCPAP with supplemental oxygen produced a progressive decrease in apnoeas and hypopnoeas; however, this decrease differed from that observed with the application of nCPAP without associated oxygen. At low nCPAP levels an increase in apnoea index and apnoea-hypopnoea duration (table 4) were detected. Furthermore, the apnoeas persisted with nCPAP levels that eliminated them when applied without supplemental oxygen (fig. 1). With the exception of one patient (No. 5), who did not tolerate the level achieved during the second night, the progressive increase in nCPAP eliminated first apnoeas and then hypopnoeas as occurred during the second night, with the effectiveness of the maximum level reached during the second night being maintained. Seven patients (Nos. 2, 3, 4, 7, 8, 9 and 10) achieved REM sleep without obstructive apnoeas at the maximum level of nCPAP as occurred in nREM sleep at the same pressure, and a mean hypopnoea frequency, 4.3 (2.7) events·h$^{-1}$ and duration, 17.6 (10.3) s similar to those of the nREM phase, 2.6 (3.6) and 13.3 (2.8), respectively (ns).

### Discussion

In our patients, the coexistence of COPD and SAHS determined poor nocturnal oxygenation that was only partially corrected by the application of nCPAP. The mean value of $S_{a}O_{2}$ remained below 90% in all patients, despite correction of apnoeas and hypopnoeas. Improved $S_{a}O_{2}$ values during sleep were obtained by the addition of low flow supplemental oxygen to the nCPAP circuit.

Correction of nocturnal hypoxaemia in these patients by the application of oxygen alone is not an ideal therapeutic alternative. Goldstein et al. [22] administered oxygen by nasal prongs at a flow rate of 1–2 L·min$^{-1}$ to a group of 12 patients with severe COPD and observed marked hypercapnia during sleep and morning cephalalgia in three patients who presented associated SAHS. These authors did not describe the effect of oxygen therapy on episodes of upper airway obstruction or on heart rate. Alford et al. [23] administered oxygen at 4 L·min$^{-1}$ to 20 subjects with COPD and SAHS, detecting frank improvements in mean $S_{a}O_{2}$ during sleep and apnoea-associated bradycardia. However, they did observe the persistence of frequent upper airway obstructive episodes, which have been shown to lead to persistent cardiopulmonary haemodynamic alterations and, frequently, SAHS symptoms [5]. In addition, they detected decreased pH and increased $P_{a}CO_{2}$ during oxygen administration, which they attributed to the greater duration of apnoea episodes.
levels were applied supplemental oxygen induced the transition of some hypopnoeas to apnoeas. This transition may have been caused by the decrease in upper airway muscle activity normally present at the start of obstructive episodes [29]. Studies in animals [12, 13, 30, 31], normal humans [14], and SAHS patients [32] have shown that hypoxia and marked hypercapnia determine a preferential increase in upper airway muscle activity compared with that of the diaphragm, and an inverse effect of hyperoxia, hypocapnia and mild hypercapnia. Furthermore, in the range of $S_o_2$ values considered in our study, a strong linear relationship has been observed between $S_o_2$ and upper airway muscle activity [33] and upper airway resistance [34] (inverse and positive relationships, respectively). In accordance with the above observations, our results showed an increase in apnoeic episodes in a clinical context when hypoxia was corrected with no significant increase in $P_aCO_2$. The efficacy of higher levels of nCPAP would not be affected by upper airway muscle activity, since they would act only through passive pneumatic distension [33].

In summary, our results show the addition of oxygen to nCPAP to be a practical, effective therapy for hypoxic patients with coexistent SAHS and COPD, since it permits correction of both upper airway obstructive episodes and nocturnal hypoxaemia. In addition, we observed a higher frequency of apnoeic episodes at low nCPAP levels when oxygen was added. We speculate that this increase is observed only at levels below that of effective nCPAP without supplemental oxygen, which remains unaffected when oxygen is added. Further studies are required to elucidate this last point and establish whether control polysomnography with nCPAP and oxygen is necessary to determine the effective pressure in these patients.

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References


