Optimal continuous positive airway pressure in patients with obstructive sleep apnoea: role of craniofacial structure

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Although nasal continuous positive airway pressure (CPAP) is effective in improving nocturnal obstructive apnoea, daytime sleepiness and well-being in patients with obstructive sleep apnoea syndrome (OSAS), not all patients tolerate this treatment. Since optimal CPAP titration is essential to maintain compliance, it is important to elucidate the factors that help to determine the optimal pressure. However, the determinants of the optimal CPAP level are controversial.

The subjects comprised 27 Japanese male patients with OSAS who underwent standard polysomnography (PSG), pulmonary function tests, arterial blood gas analysis, cephalometry and CPAP titration. Twenty normal controls also underwent cephalometric analysis.

The apnoea–hypopnoea index (AHI), mean oxygen saturation (mean $S_{aO2}$) and the lowest $S_{aO2}$ during sleep were found to be $54 \pm 7\%$, $89 \pm 0\%$, and $69 \pm 9\%$, respectively by PSG. The mean optimal CPAP was $9 \pm 6\, \text{cmH}_2\text{O}$. The cephalometric angles (SNA, SNB and NSBa) were similar to those found in the control subjects, but MP-H, and PNS-P were significantly longer than those in the control subjects as shown by cephalometry. The optimal CPAP was correlated with the mean $S_{aO2}$ ($P<0.0001$), neck circumference ($P<0.05$) and three cephalometric variables (NSBa: $P<0.01$, MP-H: $P<0.05$, PNS-P: $P<0.05$). Multiple, step-wise, regression analysis showed that the mean $S_{aO2}$ and NSBa were independent variables that best predicted the optimal CPAP. These variables accounted for 57.5% of the total variance ($R^2=0.575$, $P<0.001$).

Optimal CPAP was closely correlated with oxygen desaturation during sleep. However, the craniofacial structure had additional effects such as an independent factor in determining the optimal CPAP level.

Key words: optimal CPAP; craniofacial structure; cephalometry; obstructive sleep apnoea syndrome; nasal CPAP.

Introduction

Over the past decade, nasal continuous positive airway pressure (CPAP) has become the first-line of treatment for obstructive sleep apnoea syndrome (OSAS) (1–3). Although nasal CPAP is effective in improving nocturnal obstructive apnoea, daytime sleepiness, cognitive function and well-being (4–7), not all patients tolerate this treatment (8–16). Approximately 10–50% of patients with OSAS cannot tolerate nasal CPAP and discontinue its use within a short period of time. Although a high level of CPAP abolishes upper airway obstruction during sleep, patients may feel uncomfortable and may discontinue its use. In addition, lower pressures may not be sufficient to eliminate apnoea or oxygen desaturation during sleep. Therefore, optimal titration of CPAP is essential to maintain compliance. It is important to elucidate the factors that help to determine the optimal pressure. Hoffstein et al. (17,18) demonstrated that the number of apnoea and hypopnoea events, body mass index (BMI) and neck circumference (NC) are closely correlated with an effective CPAP level. Sforza et al. (19) reported that the apnoea–hypopnoea index (AHI) is not correlated with the level of effective CPAP, but that the bulk of the soft palate and the degree of respiratory efforts are the primary determinants of the effective CPAP level. They found a relationship only between the effective CPAP level and the length of the soft palate.

A number of reports (20–25) demonstrated that patients with OSAS exhibit craniofacial abnormalities or upper airway soft tissue changes. However, only one study (19) examined the relationship between the effective CPAP level...
and craniofacial abnormalities in patients with OSAS. Therefore, the aim of this study was to assess the factors that determine the optimal CPAP level including cephalometric variables in patients with OSAS.

**Patients and methods**

The subjects comprised 27 Japanese men diagnosed as having OSAS. All subjects were hospitalized and gave informed consent to participate in this study. Standard full night polysomnography (PSG), cephalometry, pulmonary function tests and arterial blood gas analysis were performed. PSG was performed in a standard manner including electroencephalography, electrooculography, electromyography, electrocardiography, measurements of oronasal airflow and movement of the rib cage and abdomen, and oxygen saturation (SaO₂). Conventional spirometry and measurement of static lung volumes were performed by auto-spirometry (Chestak, Chest Co. Tokyo, Japan). Arterial blood samples were drawn with the patients in the supine position and were analysed by an auto-analysers (ABL 520, Radiometer Co, Tokyo, Japan). Lateral cephalometric radiography was obtained for all patients and all 20 control subjects (healthy male volunteers, technicians and doctors) while seated in the upright position using the technique of Riley et al. (20). The controls were age-matched healthy males without OSA symptoms such as heavy snoring, excessive daytime sleepiness, and respiratory abnormalities during sleep. PSG was not performed in the controls. All radiographs were taken at the end of expiration without swallowing. The following variables were measured by two pulmonary physicians: (1) SNA [angle measurement from sella (S) to nasion (N) to point A (subspinale)]; (2) SNB [angle measurement from sella (S) to nasion (N) to point B (supramentale)]; (3) NSBa [called cranial base flexure (angle formed by the intersection of lines drawn from nasium to sella and sella to basion)]; (4) MP-H [distance from mandibular plane (MP) to hyoid bone (H)]; (5) PNS-P [distance from posterior nasal spine (PNS) to the tip of the soft palate (P)]; and (6) posterior airway space (PAS).

Nasal CPAP titration was performed to determine the optimal CPAP level with a commercial CPAP device (7300H, France Bed Med, Tokyo) within 1 week of the first diagnostic PSG. The optimal level of CPAP was the minimum pressure that completely abolished apnoea and snoring and maintained a SaO₂ > 90% during sleep. We confirmed that apnoea and snoring were completely abolished and SaO₂ was maintained at over 90% during sleep with the optimal CPAP level during the next night.

Results were presented as the mean ± sd. Group differences were assessed with the unpaired t-test. Bivariate correlation analysis was performed using Pearson correlation coefficients. Multiple, step-wise regression analysis was performed to identify those variables that best explained the variance in the level of optimal CPAP. Statistical significance was set at a P-value less than 0.05. All statistical analyses were performed using a program (Statview) for the PC (Macintosh, version 8.0).

**Results**

Baseline characteristics of the patients are shown in Table 1. The mean age, body mass index (BMI) and neck

| Table 1. Anthropometric, pulmonary function and polysomnographic data |
|--------------------------|----------|----------------|
| Age (years)              | 51.5     | 9.6            | 34–66        |
| BMI (kg m⁻²)             | 28.1     | 2.7            | 17.2–39.4    |
| NC (cm)                  | 42.2     | 2.7            | 35–49        |
| VC (% predicted)         | 110.1    | 15.2           | 81.0–146.0   |
| FEV₁ (% predicted)       | 83.7     | 10.4           | 71.9–114.8   |
| ERV (ml)                 | 1075.2   | 425.3          | 470–1860     |
| FRC (ml)                 | 2461.7   | 710.7          | 1470–3870    |
| PaO₂ (mmHg)              | 80.2     | 10.1           | 62.8–100.2   |
| PaCO₂ (mmHg)             | 44.2     | 4.2            | 36.9–52.6    |
| AHI (n⁻¹)                | 54.7     | 22.6           | 13.0–91.0    |
| Arousal index (n⁻¹)      | 66.8     | 26.2           | 21.2–110.4   |
| Total sleep time (min)   | 384.2    | 44.1           | 280–450      |
| % REM sleep (%)          | 13.4     | 2.6            | 8.4–24.0     |
| % Non-REM sleep (%)      | 67.2     | 14.8           | 46.1–81.3    |
| Mean SaO₂ (%)            | 89.0     | 5.6            | 72.5–95.0    |
| Lowest SaO₂ (%)          | 69.7     | 9.0            | 50.0–86.0    |
| Optimal CPAP (cmH₂O)     | 9.6      | 1.8            | 7.0–14.0     |

BMI: body mass index; NC: neck circumference; VC: vital capacity; FEV₁: forced expiratory volume in 1 sec; ERV: expiratory reserve volume; FRC: functional residual volume; AHI: apnoea–hypopnoea index; SaO₂: oxygen saturation; CPAP: continuous positive airway pressure.
circumference (NC) were 51.5 years, 28.1 kg m\(^{-2}\) and 42.2 cm, respectively. Mean age and BMI of the control subjects were 46.4 ± 7.3 years and 24.1 ± 2.8 kg m\(^{-2}\). Although the mean age did not significantly differ between the patients and controls, the mean BMI in the controls was significantly lower than that of OSAS patients (Table 2). Pulmonary function tests were almost normal. Although the mean PaO\(_2\) and PaCO\(_2\) were within normal limits, four patients were hypoxaemic (PaO\(_2\) < 70 mm Hg) and 13 patients were hypercapnic (PaCO\(_2\) > 45 mm Hg). PSG revealed moderate to severe OSAS and oxygen desaturation during sleep, i.e. an SaO\(_2\) less than 75%, was found in 21 of 27 patients. The mean optimal CPAP was 9.6 ± 1.8 cm H\(_2\)O.

The results of cephalometry are shown in Table 2. The angles (SNA, SNB and NSBa) were similar to those found in control subjects, but MP-H and PNS-P were significantly longer than those in the control subjects. No significant relationships were observed between the cephalometric variables and AHI, the mean SaO\(_2\) and the lowest SaO\(_2\) during sleep.

Correlation coefficients of optimal CPAP were compared for 18 clinical variables which included anthropometric, pulmonary function, polysomnographic and cephalometric data. The results (Table 3) indicated that the optimal CPAP was significantly correlated with NC (P < 0.05), nocturnal oxygen saturation (mean SaO\(_2\); P < 0.0001) and the parameters of craniofacial structure (NSBa; P < 0.01, MP-H; P < 0.05 and PNS-P; P < 0.05). The mean SaO\(_2\) during sleep showed the greatest correlation with the optimal CPAP (r = 0.664; Fig. 1). The correlation of pulmonary function and arterial blood gas data was sufficiently low (r < 0.303) and was not considered a useful predictor of optimal CPAP. Multiple, step-wise regression analysis of these 18 variables with optimal CPAP as the dependent variable showed that the mean SaO\(_2\); (partial \(r^2 = 0.362\)) and NSBa (partial \(r^2 = 0.213\)) accounted for 57.5% of the total variance (\(r^2 = 0.575, P < 0.0001\)) by the following equation:

\[
\text{optimal CPAP} = 42.036 - 0.209 \times \text{mean SaO}_2 \\
- 0.009 \times \text{NSBa}.
\]

**Discussion**

The results in this study demonstrated that the optimal CPAP level was dependent on the oxygen desaturation...
During sleep and the craniofacial structure. Oxygen desaturation (mean $\text{SaO}_2$) during sleep was most highly correlated with optimal CPAP ($r = -0.664$). Although Miljeteig and Hofstein (17) investigated the relationship between effective CPAP levels and anthropometric and sleep data in patients with OSAS, and found that the AHI, BMI and neck circumference were correlated with CPAP levels, they observed no correlation between oxygen desaturation during sleep and CPAP levels. Sforza et al. (19) also reported the determinants of effective CPAP levels in patients with OSAS, and failed to find a correlation between effective CPAP levels and oxygen desaturation. This difference may be due to the fact that our subjects exhibited profound oxygen desaturation during sleep. The mean $\text{SaO}_2$ was lower than that of Miljeteig’s subjects (17) (88-9% vs. 91%), and the lowest $\text{SaO}_2$ in our group was also lower than that in Sforza’s study (19) (69-6% vs. 81-2%). In addition, we found that 13 of 27 patients with OSAS were hypercapnic. Ten of 13 patients were considered to have obesity–hypoventilation syndrome (OHS). It is reported that these patients had more profound oxygen desaturation during sleep as well as daytime hypoxaemia than patients without OHS (26). These differences may explain the inconsistency between our study and other studies.

Although oxygen desaturation (mean $\text{SaO}_2$) during sleep was strongly correlated with optimal CPAP, this variable, by itself, accounted for only 44% of the total variance. Multiple, step-wise, regression analysis showed that 57-5% of the total variance was accounted for by the incorporation of the NSBa into the regression. These data suggest that the craniofacial structure plays an important role in determining the optimal CPAP. A number of studies (20–25) emphasized that patients presenting OSAS exhibited cranio-mandibular and upper airway anatomic abnormalities. However, the extent of the contribution of craniofacial abnormalities to the development of OSAS is unclear. We found that there were significant differences on craniofacial structures between the patients and controls (MP-H and PNS-P). Changes in these parameters, in soft tissue components, may be induced by repeated snoring and upper airway obstruction during sleep.

Obesity seems to be a more important factor than craniofacial abnormalities in the development of OSAS in previous studies. Miljeteig and Hofstein (17) emphasized the strong association between body size (BMI and NC) and the effective CPAP level. We also found a significant correlation between the optimal CPAP level and the NC ($r = 0.380$, $P = 0.0499$) and a nearly significant correlation with BMI ($r = 0.377$, $P = 0.0524$). Therefore, body size likely plays a substantial role in determining the optimal CPAP. However, the role of body size may be less important than the craniofacial structure, since multiple, step-wise regression showed that oxygen desaturation during sleep and parameters of craniofacial abnormalities, but not obesity, were the important independent variables. We also observed differences in craniofacial structures between the patients with OSAS and normal subjects although our control subjects were not matched for BMI. Therefore, it is likely that craniofacial abnormalities are more important than obesity in the development of OSAS in our subjects.

Sforza et al. (19) also investigated the relationship between effective CPAP and cephalometric variables, and found that effective CPAP was closely correlated with the length of the soft palate (PNS-P) only. We found that the optimal CPAP was significantly correlated with PNS-P, NSBa, and MP-H. These results suggest that Japanese patients with OSAS have more abnormal craniofacial structures than Western patients, or it is possible that our findings could be replicated in any group of near-normal weight patients with severe OSAS.

We also showed that the mean $\text{SaO}_2$ during sleep was correlated most highly with the optimal CPAP. Since the mean $\text{SaO}_2$ was also correlated with BMI ($r = -0.680$, $P < 0.001$) and NC ($r = -0.509$, $P = 0.0059$), the effect of body size on optimal CPAP was predominantly exerted through these relationships. Since there was no significant correlation between the mean $\text{SaO}_2$ and cephalometric variables, the cranio-base angle (NSBa) showed effects independent of the mean $\text{SaO}_2$ in determining the optimal CPAP.

Sforza et al. (19) found that the length of the soft palate as well as respiratory effort during sleep was correlated with the effective CPAP level. Since we did not measure pleural pressure to evaluate respiratory effort, we cannot comment on the contribution of respiratory effort to optimal CPAP. The use of an oesophageal balloon to measure pleural pressure is invasive and not practical in predicting the optimal CPAP.

We did not show a direct relationship between craniofacial abnormalities and the development of OSAS because cephalometric parameters were not significantly associated with AHI, mean $\text{SaO}_2$ and lowest $\text{SaO}_2$. However, our findings that several markers of craniofacial abnormalities were associated with CPAP levels that protect against nocturnal upper airway obstruction suggest that craniofacial abnormalities are indirectly related to the development of OSAS.
References


