



Daytime Hypercapnia in Adult Patients With Obstructive Sleep Apnea Syndrome in France, Before Initiating Nocturnal Nasal Continuous Positive Airway Pressure Therapy*

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Context: Daytime hypercapnia in patients with obstructive sleep apnea syndrome (OSAS) has a highly variable prevalence in the published studies, and is usually thought to be the consequence of an associated disease, COPD, or severe obesity.

Study objectives: To assess the prevalence of daytime hypercapnia in a very large population of adult patients with OSAS, free of associated COPD, and with a wide range of body mass index (BMI), and to evaluate the relationship between daytime hypercapnia and the severity of obesity and obesity-related impairment in lung function.

Design: Retrospective analysis of prospectively collected data.

Methods: The database of the observatory of a national nonprofit network for home treatment of patients with chronic respiratory insufficiency (Association Nationale pour le Traitement à Domicile de l'Insuffisance Respiratoire Chronique) was used. Collected data at treatment initiation were age, apnea-hypopnea index, BMI, FEV₁, vital capacity (VC), and arterial blood gases. The study included 1,141 adult patients with OSAS treated in France with nocturnal nasal continuous positive airway pressure (CPAP), FEV₁ ≥ 80% predicted, FEV₁/VC ≥ 70%, and absence of restrictive respiratory disease other than related to obesity.

Results: The prevalence of daytime hypercapnia (PaCO₂ ≥ 45 mm Hg) before initiating CPAP therapy was 11% in the whole study population. The prevalence of daytime hypercapnia was 7.2% (27 of 377 patients) with BMI < 30, 9.8% (58 of 590 patients) with BMI from 30 to 40, and 23.6% (41 of 174 patients) with BMI > 40. Patients with daytime hypercapnia had significantly higher BMI values and significantly lower VC, FEV₁, and PaO₂ values than the normocapnic patients. Stepwise multiple regression showed that PaO₂, BMI, and either VC or FEV₁ were the best predictors of hypercapnia, but these variables explained only 9% of the variance in PaCO₂ levels. **Conclusion:** Daytime hypercapnia was observed in > 1 of 10 patients with OSAS needing CPAP therapy and free of COPD, and was related to the severity of obesity and obesity-related impairment in lung function. However, other mechanisms than obesity are probably involved in the pathogenesis of daytime hypercapnia in OSAS. (CHEST 2005; 127:710-715)

Key words: alveolar hypoventilation; carbon dioxide; hypercapnia; obesity; obesity-hypoventilation syndrome; Pickwickian syndrome; respiratory insufficiency; sleep apnea syndrome

Abbreviations: AHI = apnea-hypopnea index; ANTADIR = Association Nationale pour le Traitement à Domicile de l'Insuffisance Respiratoire Chronique; BMI = body mass index; CPAP = continuous positive airway pressure; NS = not significant; OSAS = obstructive sleep apnea syndrome; VC = vital capacity

Obstructive sleep apnea syndrome (OSAS) can be associated with daytime alveolar hypoventilation and hypercapnia. The prevalence of daytime hyper-

capnia in patients with OSAS is highly variable, from 12 to 43% in the published studies.¹⁻⁴ The prevalence of daytime hypercapnia is raised in particular

when OSAS is associated with COPD,^{3,4} or when OSAS is associated with severe obesity.⁵ Therefore, some authors⁶ have concluded that there is no direct link between sleep apneas and daytime hypercapnia, and that daytime hypercapnia observed in patients

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with OSAS is the complication of an associated abnormality: COPD or severe obesity. However, the results of these studies could be contested, in view of the relatively small number of patients included,^{1,2,5} or a biased recruitment with the inclusion of a high number of patients with COPD^{3,4} or severe obesity.⁵ Furthermore, it has been demonstrated that the disappearance of sleep apneas obtained by nasal continuous positive airway pressure therapy (CPAP) can induce a regression in daytime hypercapnia, and is thus a major argument in favor of a direct link between sleep apneas and daytime hypercapnia.⁷ The aim of this study was firstly to assess the prevalence of daytime hypercapnia before initiating CPAP therapy in a very large population of adult patients with OSAS, free of an associated COPD, and with a wide range of body mass index (BMI), and secondly to evaluate the relationship between daytime hypercapnia and the severity of obesity and obesity-related impairment in lung function.

MATERIALS AND METHODS

We used the database of the observatory of a national nonprofit network for home treatment of patients with chronic respiratory insufficiency (Association Nationale pour le Traitement A Domicile de l'Insuffisance Respiratoire chronique [ANTADIR]). ANTADIR was set up in France in the 1970s as a nonprofit network for the home treatment of patients with chronic respiratory insufficiency. Home treatment of patients with OSAS was started in 1985. ANTADIR has collected clinical data on treated patients in an observatory since 1984. At treatment initiation, data are collected from the social security form that is filled in by the prescriber concerning the patient's age, sex, height, weight, and etiology of chronic respiratory disease needing home treatment. In the patients with OSAS, the apnea-hypopnea index (AHI) is collected. FEV₁, vital capacity (VC), and arterial blood gases in room air are required in patients with chronic respiratory insufficiency, but not in patients with OSAS. However, a certain number of pulmonologists that prescribe home treatment for patients with OSAS in the ANTADIR network usually perform pulmonary function tests and arterial blood gas analysis in these

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patients. The anonymous registration of patients was approved by the "Commission Nationale de l'Informatique et des Libertés."

Patients

The inclusion criteria were as follows: (1) patients with OSAS needing home treatment with nasal CPAP, in whom FEV₁/VC, and arterial blood gas values were performed before starting CPAP therapy; (2) patient data collected in the ANTADIR observatory from January 1, 1985, until January 1, 2000; (3) AHI ≥ 10 /h⁸; (4) age ≥ 18 years; (5) absence of restrictive respiratory disease, other than that related to obesity, namely pulmonary fibrosis, sequels of pulmonary tuberculosis, chest wall diseases, and neuromuscular disorders; (6) FEV₁/VC ratio $\geq 70\%$; therefore, patients with an associated COPD defined by a FEV₁/VC ratio $< 70\%$ were excluded⁹; and (7) FEV₁ $\geq 80\%$ of normal European values predicted; therefore, we excluded patients with severe restriction which could account in itself for hypercapnia.

Statistical Analysis

Daytime hypercapnia was defined by PaCO₂ ≥ 45 mm Hg. This cut-off was chosen because daytime chronic alveolar hypoventilation is usually defined by a PaCO₂ ≥ 45 mm Hg.^{6,10} The anthropometric, polysomnographic, and functional characteristics of the patients with daytime hypercapnia (PaCO₂ ≥ 45 mm Hg) and of those with PaCO₂ < 45 mm Hg were compared using the χ^2 test and the Student *t* test. The correlations between PaCO₂ and anthropometric, polysomnographic, and functional data were studied by linear correlation and displayed graphically by dividing BMI, PaO₂, VC, and FEV₁ values into classes of 5 mm Hg, 10 mm Hg, 10% predicted, and 5% predicted, respectively. Multivariate analysis was performed using multiple linear regression and logistic regression, in order to find the best association of predictive factors for hypercapnia. Significance was recognized at *p* < 0.05 .

RESULTS

During the study period, 88,548 patients with chronic respiratory insufficiency and 30,131 patients with OSAS needing CPAP therapy were included in the ANTADIR observatory. The values of FEV₁, VC, and arterial blood gases were available in 2,217 adult patients with OSAS, defined by an AHI ≥ 10 events/h, and free of a restrictive respiratory disease other than that related to obesity. Age, sex ratio, BMI, and AHI did not significantly differ between the patients with OSAS in whom pulmonary function tests and arterial blood gas analyses were available, and those in whom they were not. After the exclusion of 614 patients with FEV₁/VC ratio $< 70\%$ and the exclusion of 462 patients with FEV₁ $< 80\%$ predicted, the study population included 1,141 patients (943 men and 198 women). The demographic, functional, polysomnographic, and anthropometric data for the study population according to sex are shown on Table 1.

The prevalence of daytime hypercapnia (PaCO₂ ≥ 45 mm Hg) was 11% (126 of 1,141 patients) in the study population. The prevalence of daytime hyper-

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