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Original Article

Continuous positive airway pressure and survival of very elderly persons with moderate to severe obstructive sleep apnea

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ABSTRACT

Objective: There is evidence of a beneficial effect of long-term continuous positive airway pressure (CPAP) on survival in elderly persons with obstructive sleep apnea (OSA), although the usual age cut off is between 60 and 70 years of age. Our objective was to determine this effect in very elderly patients (ie, those ≥80 years of age).
Methods: An observational study of a historic cohort of very elderly persons with moderate to severe OSA (apnea–hypopnea index ≥20) and the effect of long-term CPAP on their survival was performed. Two groups were formed: one prescribed CPAP treatment (≥4 hours per night), and one without CPAP treatment. Survival analyses, including Kaplan–Meier curves and Cox models, were carried out to determine the association of long-term CPAP with longer survival,
Results: A total of 155 very elderly persons (84 men and 71 women, mean age 81.5 ± 1.5 years) were followed up for 53 months (interquartile range, 41–77 months); 83 deaths occurred. CPAP was prescribed to 132 patients, and adherence was observed in 79 (60%). Kaplan–Meier curves showed longer survival in the treated OSA group (91 months, 95% confidence interval [CI] = 76–106) than in the untreated OSA group (52 months, 95% CI 41–64), which was statistically significant (log-rank 16.9, $p < 0.0001$). Although history of stroke was significantly associated with higher mortality (hazard ratio [HR] = 2.18, 95% CI = 1.14–4.17, $p = 0.02$), CPAP treatment was associated with higher survival rates (HR = 0.46, 95% CI = 0.27–0.78, $p = 0.004$) in an adjusted Cox analysis.
Conclusions: CPAP treatment might be associated with a longer survival in very elderly persons with moderate to severe OSA.

1. Introduction

Life expectancy has improved because of medical advances, resulting in the need for a thorough knowledge of disease in the elderly population. An increasing incidence of obstructive sleep apnea (OSA) with age has been described [1,2], although current guidelines do not address special considerations in relation to its diagnosis or treatment in elderly persons [3]. Continuous positive airway pressure (CPAP) is by far the recommended treatment for symptomatic or severe OSA; however, the existing evidence of the beneficial effect of CPAP has been obtained from middle-aged populations. Consequently, whether a CPAP device should be prescribed to very elderly persons often raises a reasonable doubt, as its role has not been adequately determined, and as lack of symptoms or an already impaired quality of life due to other comorbidities may bias the decision of a physician treating these patients.

Previous studies have concluded that long-term CPAP can reduce cardiovascular events and mortality rates in elderly persons [4–6], along with recent improvements in quality of life and neurocognitive features [7]; yet, consistent evidence of its benefit in very elderly persons is still to be determined, as the CPAP effect may differ from that in younger groups [8]. The main objective of this study was to analyze the effect of long-term CPAP on mortality of any cause in very elderly persons diagnosed with moderate to severe OSA, hypothesizing that longer survival might be a consequence of their adherence to treatment.

Part of this study was presented at the European Respiratory Society Congress in Amsterdam, Netherlands, on September 27, 2011.

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2. Methods

An observational study of a historic cohort of very elderly persons (≥80 years of age at OSA diagnosis) was performed. Between January 1996 and December 2010, patients attending the Sleep Unit (SU) of the 12 de Octubre University Hospital (Madrid, Spain) for suspected OSA were considered for inclusion. Exclusion criteria were an apnea–hypopnea index (AHI) of <20, previous treatment with CPAP or bi-level positive pressure, and diagnosis of central sleep apnea, obesity hypoventilation syndrome, or chronic respiratory failure. This study was conducted in accordance with the amended Declaration of Helsinki, and was approved by the local institutional review board (Comité Ético de Investigación Clínica, resolution 14/382); because of its retrospective nature, no informed consent was obtained from patients.

2.1. Data collection

Baseline variables were determined before the sleep study as follows: age, sex, body mass index (BMI), alcohol intake (>30 g per day), smoking habit (>20 pack-years), arterial hypertension (systolic/diastolic >140/90 mm Hg or use of antihypertensive medication), diabetes (fasting glucose levels >125 mg/dL in two or more measures or use of antihyperglycemic medication), and hyperlipidemia (fasting cholesterol or triglycerides >200 mg/dL or use of antihyperlipidemic medication), and previous cardiovascular events (CVE) such as stroke, ischemic heart disease, arrhythmias, and heart failure. Stroke was defined by the presence of confirmative image tests and compatible clinical context; heart failure was determined by echocardiographic data or other tests indicated for its conclusive diagnosis, or by the use of specific medication; arrhythmias were determined by electrocardiographic findings or the prescription of specific medication; and ischemic heart disease was determined based on conclusive data of coronarography or other myocardial ischemia tests, previous coronary revascularization, or prescription of specific antianginal medication. Specialists in the corresponding areas carried out all of these tests and treatments. The Spanish version of the Epworth Sleepiness Scale (ESS) was used to evaluate excessive daytime somnolence [9].

2.2. Sleep study and CPAP treatment

Patients were diagnosed by a full standard polysomnography (PSG) (Alice 5 Philips), or an in-laboratory or in-home respiratory polygraphy (RP) (ApnoeScreen Jaeger), following the American Academy of Sleep Medicine and the Spanish Society of Pneumology and Thoracic Surgery (SEPAR) guidelines stated at the time [10–13]. PSG included continuous recording of an electroencephalogram, electrooculogram, electrocardiogram, and electromyogram; and evaluations of nasal airflow, thoracic and abdominal band movements, and peripheral oxygen saturation (SpO_2), according to standard criteria. Respiratory polygraphy (RP) included continuous recording of oronasal flow and pressure, heart rate, thoracic and abdominal respiratory movements, and SpO_2. A full PSG was performed in all the patients undergoing RP who had recording artifacts or a discrepancy between the RP results and the pretest clinical probability/suspicion of OSA (especially in patients with a high pretest probability and RP results with no alterations), predominance of central events, or a subjective sleep time of <3 hours. All data were scored manually. Apnea was defined as an interruption of oronasal airflow of >10 seconds, and was classified as obstructive or central depending on whether respiratory effort was present or absent. Hypopnea was defined as a 30–90% reduction in oronasal airflow of >10 seconds and associated with a peripheral oxygen desaturation of ≥3% [13]. The AHI was defined as the number of apneas plus hypopneas per hour of sleep (PSG) or recording (RP). An AHI ≥20 was considered for inclusion in the study. Although long-term CPAP prescription was offered to all patients with an AHI ≥30, in patients with an AHI <30, the SU physician decided on an individual prescription in each case and followed the guidelines stated at the time. Before the year 2000, titration was carried out by a nocturnal pulse oximetry or RP if available. From 2000 to 2008, the initial CPAP settings were based on the formula proposed by Oliver and Hoffstein [14] as follows: $Ppred = (0.16 \times BMI) + (0.13 \times \text{Neck circumference[cm]}) + (0.04 \times AHI) - 5.12$. The settings were confirmed by a full standard PSG on a second night. After 2008, CPAP settings for all patients were based on automatic positive airway pressure devices. Settings were considered adequate when residual AHI was <5. Adherence was objectively assessed by reading the time counter of the device. Adequately treated OSA was determined when long-term CPAP adherence was ≥4 hours per day, and as untreated when CPAP was not prescribed, when the patient declined its use, or when the average cumulative adherence was <4 hours per day.

2.3. Follow-up and main endpoint

Follow-up ended on March 30, 2015. Visits to the SU outpatient clinic were usually scheduled three, six, and 12 months after CPAP prescription, and every 12 months after the first year. All data retrieved from the SU database were backed up by reviewing the clinical records of hospital, primary care databases, and the information provided by the supplier of the CPAP devices. Missing data were obtained by contacting the patient or relatives. A patient was considered lost to follow-up only if the endpoint data could not be established at the end of the study, although no exclusion from the survival analysis was carried out, taking into account the data from the last observation. The main endpoint was death from any cause. Information about the cause and date of death was obtained from the hospital medical records if the patient died in the hospital, or from primary care databases.

2.4. Statistical analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS Inc., Chicago, IL). Baseline characteristics are presented according to OSA severity groups, and two groups were proposed for the survival analysis, namely, patients with untreated and treated OSA. Qualitative variables are presented as absolute values and percentages, and quantitative variables as means and standard deviations (SD), median and interquartile range (IQR) or range, if needed. Normal distribution was assessed with the Kolmogorov–Smirnov test. Baseline differences of quantitative variables were analyzed by the Student *t*-test in case of normal distribution, or by the Kruskal–Wallis test when normality was not achieved. Qualitative variables were compared using the χ^2 test with the Fisher exact correction. Cumulative survival regarding death from any cause was analyzed with the Kaplan–Meier method comparing death in very elderly persons with treated versus untreated OSA, and mortality curves were compared by the log-rank test. Clinically relevant variables, in the opinion of the researchers as well as those independently associated with mortality in a nonadjusted Cox proportional analysis, were included in the final and adjusted multivariate Cox proportional model. The following variables were finally selected for evaluation in the Cox model: age, sex, body mass index (BMI), alcohol intake, diabetes, stroke, cardiac ischemic disease, and CPAP treatment. The results are expressed as hazard ratio (HR) and 95% confidence interval (CI), and a p value of ≤0.05 was considered statistically significant. Diagnostic and residual plots were examined to test the proportional hazard assumptions, where none of them were statistically significant. Sensitivity analysis was performed for the subgroups of patients with AHI ≥30 and CPAP prescription.