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Original article

Long-term adherence to nasal continuous positive airway pressure therapy by hypertensive patients with preexisting sleep apnea

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ABSTRACT

Background and objective: Although positive screening for and treatment of obstructive sleep apnea (OSA) have been recommended for patients with cardiovascular problems, patient adherence to nasal continuous positive airway pressure (CPAP) therapy primarily for a cardiovascular concern is unknown. Therefore, this study aimed to determine the adherence to CPAP therapy by hypertensive patients with OSA after a screening test performed regardless of OSA-related symptoms.
Subjects and methods: CPAP therapy was administered to 194 of the 1365 hypertensive patients who underwent the screening. The monthly dropout from CPAP therapy and the adequate use level (4 h every night, 70% days in a month) were assessed using the Kaplan–Meier analysis over a 3-year follow-up period.
Results: Of the patients, 106 (55%) refused or abandoned the therapy by the end of the follow-up period (adherence, 45%). An adequate use level was maintained by 76 patients (39%). Most of the patients' background characteristics, including age, sex, Epworth sleepiness scale scores, and parameters obtained on polysomnography, were not related to adherence or adequate use level. The good-compliance level on the first visit after CPAP therapy introduction was most strongly related to adherence (95% CI, 0.05–0.32; $p < 0.001$) and adequate use level (95% CI, 0.06–0.33; $p < 0.05$). Fourth quartile of apnea hypopnea index value (greater than 67/h) was also related to adherence (95% CI, 0.21–0.98; $p < 0.02$) and adequate use level (95% CI, 0.19–0.88; $p < 0.05$).
Conclusions: The adherence and use level in this population may not be satisfactory but are comparable with those in previous sleep center reports treating symptomatic OSA patients. Thus, the present results would encourage hypertensive patients to undergo positive screening for OSA, regardless of OSA-related symptoms. However, an outcomes study with the same cohort is needed.

Introduction

Obstructive sleep apnea (OSA) is characterized by recurrent collapse of the pharyngeal airway during sleep, resulting in episodes of oxygen desaturation and arousal. Experimental data suggest that OSA predisposes patients to increased rates of cardiovascular disease through mechanisms such as increased sympathetic activation, endothelial dysfunction, insulin resistance, inflammation, and oxidative stress [1]. An association between OSA and cardiovascular problems [1–3] has most convincingly been demonstrated in hypertensive patients with OSA [1], and several observational studies showed a beneficial effect of continuous positive airway pressure (CPAP) therapy on cardiovascular outcomes [4–6]. On the basis of these reports, intervention by CPAP therapy for hypertensive patients with moderate-to-severe OSA is recommended in the guidelines of the Japanese Society of Hypertension [7] and Japanese Circulation Society [8].

In our previous study [9], we developed a screening method using portable apnea-detecting devices to effectively detect severe sleep apnea cases among outpatients with hypertension or other cardiovascular problems. We performed the screening procedure in conjunction with pulse wave velocity measurements, regardless of the presence of OSA symptoms. Therefore, we were able to detect many severe OSA patients who did not exhibit excessive daytime sleepiness or other OSA-related subjective symptoms. On the basis of existing guidelines and the Japanese health insurance policy, we

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recommended CPAP therapy to patients with an apnea hypopnea index (AHI) ≥ 20. However, we encountered CPAP therapy nonadherence by many patients after treatment introduction. Therefore, we considered it helpful to obtain long-term data on CPAP therapy adherence of our patients to provide a sample measure for hypertensive OSA patients without specific symptoms. Should patient adherence be too low, an alternative screening workflow would be necessary to detect patients who could maintain better CPAP therapy adherence.

Previous reports [10–22] have indicated various adherence levels, ranging from 28% to 89%, without showing any consistent association between CPAP therapy adherence and patient background factors, including age, sex, OSA severity, and measurements during sleep studies. In previous reports, the observation periods for CPAP therapy adherence varied from a few weeks to several months. Although the beneficial effect of CPAP therapy on cardiovascular outcome is known [23], the relationship between therapy duration and outcome has not yet been established. The relationship between daily mask-on time and outcome is also unclear. Some studies [4,11,24] suggest that even low levels of application provide some benefit to clinical outcome. In this context, knowledge regarding the time course before CPAP therapy dropout and changes in mask-on time could be important information when considering CPAP therapy for cardiovascular event prevention.

Thus, in the present study, we evaluated the long-term adherence of OSA patients to CPAP therapy after our screening method and further assessed the data on treatment dropout and adequate treatment use in a survival curve analysis. We also evaluated the relationships between these measures and the patients' backgrounds.

Methods

We conducted a retrospective cohort study in a single institute. The study design was approved by the ethics committee of the Teikyo University School of Medicine (approval No. 09-059; May 27, 2010).

Screening session and polysomnography

The precise method for sleep apnea screening using pulse wave velocity (PWV) measurement sessions followed by overnight polysomnography (PSG) has been described previously [9]. In accordance with the original method, we used only 1 portable recording device (FM-500; Fukuda Denshi, Tokyo, Japan) throughout the session. Later, we used 3 portable devices to improve apnea detection. The features of these devices and the apnea-related measurements obtained during the screening sessions have been reported previously [25]. The sleep apnea screening test was usually prescribed to ordinal hypertensive patients and performed during regular hospital visits. No patients with non-cardiovascular problems such as respiratory or gastrointestinal diseases were included in this study. Patients who underwent screening between January 2005 and December 2010 were included in the present study. We recommended PSG to the patients having a respiratory disturbance index 22/h or more in the screening session according to the previous report [9].

CPAP treatment

After the first overnight PSG, CPAP titration was recommended to all the patients and performed with attendant manual titration under PSG monitoring. CPAP therapy with fixed pressure was prescribed to the patients. Meanwhile, auto CPAP therapy was prescribed to patients who refused to undergo CPAP titration.

Before treatment initiation, all of the subjects attended an educational session on the use of CPAP therapy, including face-to-face information provided by the treating physicians. Mask interface was selected according to the patients' preference. All the patients received a CPAP unit (REMstar Pro or REMstar Auto M; Phillips, Murrayville, PA, USA) that recorded daily mask-on time (i.e. the time the CPAP circuit was pressurized at the prescribed level) on a data card. The data cards were collected approximately once per month. The first day of CPAP therapy use was defined as the first day during which any pressurized mask-on time was recorded by the CPAP electronic card monitor after delivery of the CPAP device to the patient.

Outcome and statistical analysis

Monthly CPAP therapy use and sufficient mask-on time during the follow-up period were the primary outcomes of our analyses. We defined *dropout event* as a patient's first month without CPAP therapy use (i.e. total mask-on time in a month was 0). The event included the refusal to undergo CPAP therapy during the educational session. CPAP therapy adherence was calculated as the fraction in the cohort of patients who did not experience a dropout event at a given point. We also defined *poor-compliance event* as the point from which *adequate mask-on time* was no longer observed. *Adequate mask-on time* was defined as a minimum of 70% of days with at least 4 h of mask-on time in a month. Dropout events were counted in the poor-compliance events. Adequate use level was calculated as the fraction in the cohort of patients who had no poor-compliance events at a given point.

A statistical software package (JMP v. 9.04, SAS Institute, Cary, NC, USA) was used for data processing and statistical analysis. Continuous variables were expressed as mean ± SD values; and qualitative variables, as percentages. A t test or an analysis of variance was used for continuous variables; and a χ^2 test, for qualitative variables. Event rates were calculated according to the Kaplan–Meier method, and adherence and adequate use level were compared using the log-rank test. The log-rank test for trend was used to assess the probability of a trend in events across the groups. Assumption of proportional hazards was assessed graphically using a log-minus-log survival graph. In the first phase, a univariate analysis based on a proportional hazards model was performed to determine any relationship between the adherence-related events and the following independent pretreatment variables: age, sex, BMI, Epworth sleepiness scale (ESS) score, current or previous smoking habit, systolic and diastolic blood pressures before CPAP therapy, number of antihypertensive medications, resistant hypertension [26], comorbidity (dyslipidemia, diabetes mellitus, and ischemic heart disease), AHI, ODI (oxygen desaturation index), total sleep time, percentage sum of sleep stages III and IV, percentage of REM sleep, and final mode of CPAP therapy (auto or fixed). Good compliance (absence of a poor-compliance event) on the first visit after CPAP therapy introduction was analyzed as an independent factor. AHI was categorized into quartiles with cut points 24.5, 40.7, and 67.1 to allow for the demonstration of a possibly nonlinear association. Participants in the lowest quartile of AHI served as the reference group. Variables found to have possible relations (i.e. $p < 0.10$) were included in a multivariate analysis using a time-dependent Cox model; however, the assumption of proportional hazards was not verified. The interaction between OSA severity and categories of CPAP therapy compliance was included in the Cox analysis. The results of the Cox multivariate analysis were expressed as the risk ratio with a 95% confidence interval. A 2-tailed $p < 0.05$ was considered to be statistically significant.