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Clinical Research

Predictors of Blood Pressure Fall With Continuous Positive Airway Pressure Treatment in Hypertension With Coronary Artery Disease and Obstructive Sleep Apnea

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ABSTRACT

Background: The present study aimed to investigate the predictors of changes in blood pressure (BP) with continuous positive airway pressure (CPAP) treatment in hypertensive patients with coronary heart disease (CHD) and obstructive sleep apnea (OSA).

Methods: Seventy-one hypertensive patients with CHD and OSA were enrolled in this study. Daytime systolic BP (SBP), diastolic BP (DBP), Epworth Sleepiness Scale (ESS), and anthropometric characteristics were assessed at baseline and follow-up.

Results: Sixty-six patients completed the study. The median follow-up period was 36 months (interquartile range, 24-60 months). The mean duration of CPAP application was 4.3 ± 1.2 hours per night. From baseline to follow-up, SBP and DBP were reduced by 5.6 mm Hg (95% confidence interval [CI], 3.0-8.1) and 3.0 mm Hg (95% CI, 0.8-5.3), respectively. Daytime somnolence was significantly improved (ESS, from 9.5 ± 3.4 at baseline to 3.6 ± 2.0 at follow-up; $P < 0.001$); the mean improvement in ESS was 6.0 (95% CI, 5.1-6.9). Correlation analysis of the fall in mean BP (MBP) showed that baseline MBP, change in ESS, heart rate, and CPAP compliance

RÉSUMÉ

Introduction : La présente étude avait pour but d'examiner les prédicteurs de changements dans la pression artérielle (PA) par le traitement par ventilation spontanée en pression positive expiratoire continue (CPAP : *continuous positive airway pressure*) des patients hypertendus souffrant de coronaropathie et d'apnée obstructive du sommeil (AOS).

Méthodes : Soixante-et-onze (71) patients hypertendus souffrant de coronaropathie et d'AOS ont été recrutés pour cette étude. La PA systolique (PAS) et la PA diastolique (PAD) diurnes ainsi que l'échelle de somnolence d'Epworth (ESE) et les caractéristiques anthropométriques ont été évaluées au début et durant le suivi.

Résultats : Soixante-six (66) patients ont mené à terme l'étude. La durée médiane de suivi a été de 36 mois (intervalle interquartile, 24-60 mois). La durée moyenne de l'utilisation de la CPAP a été de 4,3 ± 1,2 heures par nuit. Entre le début et la période de suivi, la PAS et la PAD ont respectivement diminué de 5,6 mm Hg (intervalle de confiance [IC] à 95 %, 3,0-8,1) et de 3,0 mm Hg (IC à 95 %, 0.8-5,3). La somnolence diurne s'est significativement améliorée (ESE, de 9,5 ± 3,4

Obstructive sleep apnea (OSA), an important public health problem, is characterized by recurrent complete (apnea) or partial (hypopnea) upper airway obstruction during sleep.[1] Such repeated airway obstructions often expose patients with OSA to intermittent hypoxemia/hypercapnia and sleep fragmentation. There is considerable evidence that OSA carries substantial morbidity and mortality, particularly from cardiovascular complications.[2,3] The current prevalence estimates of moderate to severe sleep-disordered breathing (apnea-to-hypopnea index, measured as events per hour ≥ 15) are 10% among 30- to 49-year-old men, 17% among 50- to 70-year-old men, 3% among 30- to 49-year-old women, and 9% among 50- to 70-year-old women.[4] One study has shown that 56% of hypertensive patients exhibit OSA.[5] Meanwhile, the most common cause of resistant hypertension and poor response to antihypertensive medications is OSA.[6,7] This is likely to be a risk factor for hypertension; however, some studies have demonstrated the lack of a relationship between OSA and hypertension.[8-11] Most studies indicate that continuous positive airway pressure (CPAP) is effective in reducing blood pressure (BP), although the reported efficacy has been variable. Several randomized controlled trials (RCTs) have shown that CPAP decreases BP in patients with OSA,[12-15] although the findings of recent large RCTs suggest that the observed average decrease in BP is relatively small.[16-18] Further, a recent systematic review and meta-analysis, which included 16 RCTs with 1000 treated patients with OSA, showed similar results, ie, CPAP treatment promoted significant but small reductions in BP in individuals

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showed a positive correlation, whereas the baseline body mass index (BMI) and ESS had an inverse relationship. Stepwise multiple linear regression analysis, however, indicated that only baseline BMI, baseline MBP, and CPAP compliance were independently correlated with the fall in MBP.

Conclusions: Long-term CPAP treatment reduces BP in hypertensive patients with CHD and moderate/severe OSA; baseline BMI, baseline MBP, and CPAP compliance are independent predictors of the decrease in BP with CPAP treatment in these patients.

au début à 3,6 ± 2,0 durant le suivi; $P < 0,001$); l'amélioration moyenne selon l'ESE a été de 6,0 (IC à 95 %, 5,1-6,9). L'analyse de corrélation de la baisse de la PA moyenne (PAM) a montré que la PAM initiale, le changement à l'ESE, le rythme cardiaque et l'observance de la CPAP avaient une corrélation positive, tandis que l'indice de masse corporelle (IMC) et l'ESE au début avaient une relation inverse. Cependant, l'analyse séquentielle de régression linéaire multiple a indiqué que seuls l'IMC initial, la PAM initiale et l'observance de la CPAP avaient indépendamment corrélé avec la baisse de la PAM.

Conclusions : Le traitement à long terme par CPAP réduit la PA des patients hypertendus souffrant de coronaropathie et d'AOS modérée et grave; l'IMC initial, la PAM initiale et l'observance de la CPAP sont des prédicteurs indépendants de la diminution de la PA de ces patients traités par CPAP.

with OSA.[19] In clinical practice, however, a reduction in BP is not observed in all patients undergoing CPAP. Surprisingly, some patients even demonstrate an increase in BP after CPAP treatment. The exact mechanism underlying this difference in the effects of CPAP therapy remains unclear.

Uncontrolled hypertension may exacerbate the conditions of patients with coronary heart disease (CHD) and OSA. There are scarce data regarding the predictors of a decrease in BP with CPAP treatment in hypertensive patients with CHD and OSA. Examining these predictors may provide a deeper insight into the mechanism of hypertension associated with OSA. The aim of this study was thus to evaluate the predictors of changes in BP after CPAP therapy in hypertensive patients with CHD and OSA.

Methods

Design and setting

From January 2009-December 2013, we performed a prospective cohort study including 71 patients attending the Sleep and CHD Trials Unit, Fuwai Hospital, National Centre for Cardiovascular Medicine. This study was approved by the Ethics Committee of Fuwai Hospital. All participants provided written informed consent.

Selection of patients

Consecutive patients of both sexes from outpatient and inpatient departments of Fuwai Hospital were recruited into the long-term follow-up study. Patients were eligible for the trial if they were newly diagnosed with moderate to severe OSA, hypertension, and CHD. Further, the following criteria were also fulfilled: (1) both men and women were included and (2) patients who had received at least 3 months of previous standardized treatment for hypertension according to the current guideline were included.[20] The participants were excluded if they had secondary hypertension (including primary aldosteronism, renal artery stenosis, or chronic renal disease), central sleep apnea, New York Heart Association class III/IV, diagnosis of malignant cancer with a life expectancy of < 2 years, severe hepatic failure or pulmonary disease, long-term use of drugs known to have an impact on BP (including corticosteroids or sedative drugs), significant psychiatric disease, chronic alcohol use or addiction, history of pharyngeal surgery for OSA, or current use of CPAP treatment for OSA. They were also excluded if they declined to participate or were unable to provide informed consent.

Procedures

Initial visit

Hypertensive patients with CHD suspected of having OSA were screened after obtaining written informed consent. Hypertension was defined as (1) systolic BP (SBP) $\geq$ 140 mm Hg or diastolic BP (DBP) $\geq$ 90 mm Hg (or both) at rest or (2) as ongoing treatment with antihypertensive drugs. CHD was diagnosed based on the results of selective coronary angiography showing at least 1 major epicardial coronary artery luminal stenosis segment $\geq$ 70% or stenosis in the left main coronary artery $\geq$ 50% or based on a history of myocardial infarction or coronary artery bypass grafting documented in medical records. Moderate OSA was defined as an apnea-hypopnea index (AHI) of 15-29 episodes per hour and severe OSA as an AHI of at least 30 episodes per hour. When participants were diagnosed with moderate to severe OSA, demographic data including age, sex, medical history, current medicine, lifestyle habits, height (cm), weight (kg), waist circumference (cm), hip circumference (cm), and neck circumference (cm) were recorded, and body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). The Epworth Sleepiness Scale (ESS) was used to quantify daytime somnolence.[21] Patients underwent regular clinical examinations and laboratory testing to exclude secondary hypertension. Participants were assigned antihypertensive and CHD drug treatment according to current guidelines in a 3-month run-in period that allowed for modifications in the therapeutic regimen. Patients were asked to bring the empty blister packs of their pills to evaluate compliance for drug therapy at each visit.

Sleep studies

All patients underwent overnight polysomnography in the Sleep Center of Fuwai Hospital. The Embletta X100 (Medcare Flaga, Reykjavik, Iceland) was used, as described previously.[22] Apneic episodes were defined as airflow reduction to 10% or less of the baseline value for $\geq$ 10 seconds. Hypopnea was defined as a 30%-90% reduction in the oronasal airflow for $>$ 10 seconds, associated with an oxygen desaturation of $\geq$ 4%. Central sleep