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Original Article

Long-term Impact of Continuous Positive Airway Pressure Therapy on Arrhythmia and Heart Rate Variability in Patients With Sleep Apnea☆

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ABSTRACT

Introduction: Autonomic dysfunction can alter heart rate variability and increase the incidence of arrhythmia. We analyzed the impact of continuous positive airway pressure (CPAP) on this pathophysiological phenomenon in patients with severe sleep apnea–hypopnea syndrome.
Methods: Consecutive patients with recently diagnosed severe sleep apnea–hypopnea syndrome were prospectively considered for inclusion. Incidence of arrhythmia and heart rate variability (recorded on a 24-h Holter monitoring device) were analyzed before starting CPAP therapy and 1 year thereafter.
Results: A total of 26 patients were included in the study. CPAP was administered for 6.6±1.8 h during Holter monitoring. After starting CPAP, we observed a marginally significant reduction in mean HR (80±9 to 77±11 bpm, *P*=.05). CPAP was associated with partial modulation (only during waking hours) of *r-MSSD* (*P*=.047) and *HF* (*P*=.025) parasympathetic parameters and *LF* (*P*=.049) sympathetic modulation parameters. None of these parameters returned completely to normal levels (*P*<.001). The number of unsustained episodes of atrial tachycardia diminished (*P*=.024), but no clear effect on other arrhythmias was observed.
Conclusions: CPAP therapy only partially improves heart rate variability, and exclusively during waking hours, and reduces incidence of atrial tachycardia, both of which can influence cardiovascular morbidity and mortality in sleep apnea–hypopnea syndrome patients.

Impacto a largo plazo del tratamiento con presión positiva continua en la vía aérea superior sobre la incidencia de arritmias y la variabilidad de frecuencia cardiaca en pacientes con apnea del sueño

Palabras clave:
Apnea del sueño
Variabilidad de frecuencia cardiaca
Arritmias

RESUMEN

Introducción: La disfunción del sistema nervioso autonómico produce alteraciones en la variabilidad de la frecuencia cardiaca y aumenta la incidencia de arritmias. Analizamos este fenómeno fisiopatológico en pacientes con síndrome de apnea/hipoapnea del sueño severo y el impacto sobre el mismo del tratamiento con presión positiva continua en la vía aérea (CPAP).
Métodos: Pacientes consecutivos con síndrome de apnea/hipoapnea del sueño severo de reciente diagnóstico fueron prospectivamente considerados para inclusión. Se analizó la incidencia de arritmias y la variabilidad de la frecuencia cardiaca (obtenidos mediante registro Holter de 24 horas) antes de iniciarse tratamiento con CPAP y tras un año del mismo.

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Resultados: Se incluyeron 26 pacientes. El tiempo de uso de CPAP durante el registro Holter fue de 6,6±1,8 horas. Tras inicio de CPAP, se apreció una reducción marginalmente significativa en la FC media (80±9 a 77±11 lpm, p=0,05). El uso de CPAP se asoció a una modulación parcial y exclusivamente en horas de vigilia de los parámetros de modulación parasimpática *r-MSSD* (p=0,047) y *HF* (p=0,025) y de modulación simpática *LF* (p=0,049). Ninguno de estos revirtió completamente a la normalidad (p<0,001). Se observó una reducción de los episodios no sostenidos de taquicardia auricular (p=0,024), sin efecto demostrativo sobre otras arritmias.

Conclusiones: El tratamiento con CPAP se asocia a una mejora solo parcial y diurna de la variabilidad de la frecuencia cardiaca y disminuye la incidencia de taquicardia auricular. Ambos efectos podrían influir en la morbimortalidad cardiovascular de los pacientes con síndrome de apnea/hipoapnea del sueño.

Introduction

Changes in the autonomic nervous system are associated with diminished tachycardia and bradycardia responses to sympathetic and parasympathetic stimuli, reducing heart rate variability (HRV). This pathophysiological phenomenon is also associated with increased atrial and ventricular arrhythmias. HRV changes and the incidence of arrhythmias are associated with increased cardiovascular morbidity and mortality, particularly in patients with underlying heart disease.[1–4]

Imbalances between the parasympathetic or vagal nervous system and the sympathetic nervous system in sleep apnea–hypopnea syndrome (SAHS) are due to 2 mechanisms. One involves a disruption of the physiological increase in vagal tone during the transition from waking to sleep. In the other, hypoxia and recurrent arousals induce sympathetic hyperactivation and parasympathetic inhibition.[5] As a result of this pathophysiological process, heart rate (HR) modulation – particularly its vagal component – is compromised during sleep in patients with SAHS, and this alteration can continue during waking hours.[6]

Continuous positive airway pressure (CPAP) in the upper airways improves blood pressure control, and has a positive impact on the cardiovascular prognosis of patients with structural heart disease.[5–7] CPAP may correct the influence of the vagal response on HRV and reduce sympathetic hyperactivity.[8–10] However, there is scant evidence that CPAP has a continuous, positive effect on HRV and the incidence of arrhythmias, and what little is available is sometimes controversial.[8–20]

In this study, we analyzed the hypothesis that autonomic dysfunction attributed to SAHS can be characterized by 24-h Holter monitoring (primary objective) and that CPAP treatment has a modulatory effect on this phenomenon (secondary objective). We analyzed the behavior of 2 cardiovascular phenomena that are a direct consequence of an altered autonomic tone: HRV and the incidence of arrhythmias.

Methods

Study Population

Patients were recruited between January and March 2013 in the outpatient clinic of the Respiratory Sleep Disorders Unit of our hospital. In the initial visit, information relating to sleep disorders was collected (chronic snoring, apneas, excessive daytime sleepiness evaluated using the Epworth test, and cardiovascular history). Anthropometric parameters, such as body mass index (BMI) and neck circumference were also recorded. Patients then underwent polysomnography and lung function test. Patients who met any of the following criteria were excluded: daytime respiratory failure, severe heart failure, CPAP, home oxygen therapy, non-invasive mechanical ventilation, known history of arrhythmias, and underlying chronic obstructive lung disease (for which an independent association with altered HRV has been reported, in order to avoid bias in measures derived from the presence of overlap syndrome). Consecutive patients with a diagnosis of severe SAHS who did not present any of the exclusion criteria were included prospectively in the study, after signing informed consent. The study was approved by the Ethics Committee of our hospital.

Polysomnography and CPAP

The sleep study was performed using a monitored respiratory polygraph (eXea series 5; Bitmed, Zaragoza, Spain). The recordings were read manually, based on the definitions of respiratory events proposed by the American Academy of Sleep Medicine. The average number of apneas and hypopneas per hour was taken as the apnea–hypopnea index. The percentage of time with oxygen saturation <90% was identified as $CT_{90\%}$. According to the latest SEPAR guidelines, CPAP was indicated in patients with an apnea–hypopnea index ≥30/h, even in those with mild symptoms.[21]

CPAP therapy was initiated at an empirical pressure of 8 cmH_2O for 1 month. Subsequently, when tolerance to treatment was considered appropriate, optimal pressure was applied with auto-CPAP titration (S9 AutoSet, ResMed).[22]

Cardiology Evaluation

The cardiology evaluation included a 12-lead electrocardiogram (ECG), a 2D echocardiogram, and a 24-h Holter recording (Cardioscan II®, DM Software, Nevada, US) before starting CPAP treatment, and after 1 year of treatment. These recordings were examined for incidence of atrial and ventricular arrhythmias that could potentially affect cardiovascular morbidity and mortality, including frequent ventricular extrasystoles (VE) (>1% of total beats), periods of sustained or unsustained atrial (AT)/ventricular tachycardia (VT) (>30 s) and episodes of atrial fibrillation (AF). Arrhythmias with no deleterious impact on cardiovascular prognosis were excluded from the analysis (e.g., atrial extrasystoles and atrioventricular re-entrant paroxysmal supraventricular tachycardia). The total number of AT/AF/VT episodes and beats before CPAP and 1 year after CPAP initiation was calculated. Patients in persistent AF or with excessively frequent VEs (>20% of total beats) were excluded to avoid bias in the analysis of HRV derived from the absence of normal sinus rhythm.

Mean HR and HRV over a 24-h period (and separately for periods of waking and sleep) were determined on Holter recordings. Mean HR is liable to high intra- and inter-individual variability, so HRV is a better indicator of how HR responds to the vagal autonomous system (that reduces HR) and/or the sympathetic system (that increases HR). Altered HRV parameters, therefore, indicate an altered autonomic response. The following HRV variables were determined: standard deviation of beat-to-beat (NN) intervals (SDNN); standard deviation of average NN intervals (SDANN);