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【 CASE REPORT 】

Continuous Positive Airway Pressure Therapy Improves Heterogeneity of R-R intervals in a Patient with Obstructive Sleep Apnea Syndrome

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Abstract:
Obstructive sleep apnea (OSA) is associated with the occurrence of various kinds of bradyarrhythmia and tachyarrhythmia. The activation of the autonomic nerve system is an important causative factor of the pathogenesis of the arrhythmia in OSA patients. Previous studies have shown that the R-R interval is an effective parameter for evaluating autonomic nerve activities. However, whether or not OSA can induce variations in the R-R interval and whether or not continuous positive airway pressure (CPAP) therapy can improve these variations in OSA patients are unclear. The present study explored whether or not CPAP therapy could improve the regularity of the R-R interval.

Key words: obstructive sleep apnea, continuous positive airway pressure therapy, R-R interval, bradyarrhythmia

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Introduction

Bradyarrhythmia, such as sick sinus syndrome or atrioventricular (AV) block, is a common arrhythmia that requires pacemaker therapy. Deciding whether or not to treat a patient with permanent pacemaker implantation should take into account underlying heart diseases or any symptoms related to the bradyarrhythmia. However, evaluating the indications for pacemaker therapy in patients with nocturnal symptoms or experiencing bradyarrhythmia events during sleep is difficult, as they do not show typical symptoms.

Obstructive sleep apnea (OSA) is a common disease characterized by repetitive upper airway obstruction during sleep due to decreasing upper airway muscle tone; it is highly associated with the occurrence of various kinds of arrhythmia (1). Patients with OSA intermittently experience hypoxia, hemodynamic changes, and intrathoracic pressure fluctuations during sleep, resulting in activation of the sympathetic and parasympathetic tone (2). The activation of the autonomic nervous system induces changes in the R wave interval (R-R interval) (3); thus, the R-R interval in the electrocardiogram (ECG) of polysomnography (PSG) is an effective finding for assessing the influence of OSA on the autonomic nervous system.

Whether or not sleep apnea syndrome can induce variations in the R-R interval and whether or not continuous positive airway pressure (CPAP) therapy can improve these variations in patients with OSA is unclear at present. In the present study, we extracted ECG data from PSG data and analyzed the R-R interval in a patient with severe OSA. In addition, we assessed the changes in the R-R interval before and after CPAP therapy. We report our findings in order to highlight the importance of respiratory management in patients with bradyarrhythmia accompanied by OSA.

Case Report

A 52-year-old man was admitted to our cardiovascular department for surgical repair of a dissecting thoracic aortic

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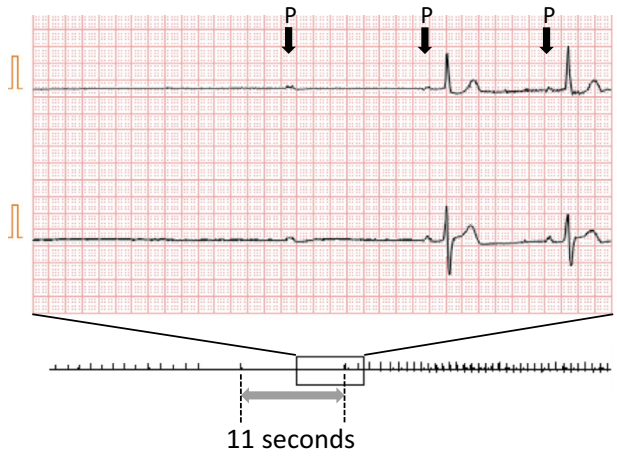

Figure 1. Representative data of sinus arrest and AV block during 24-h ECG monitoring in the present case before CPAP therapy. AV: atrio-ventricular, ECG: electrocardiogram, CPAP: continuous positive airway pressure

aneurysm. An endovascular stent graft was placed inside the thoracic aortic aneurysm to prevent aortic rupture. The postoperative course was uneventful.

ECG monitoring in the cardiovascular ward showed a 20-s sinus arrest with severe snoring on the first postoperative day (data unavailable). A 24-h ECG recording showed that the R-R interval was significantly distributed, and sinus arrest or temporary AV block was frequently observed (Fig. 1). The maximum sinus arrest time was 11 seconds (Fig. 1). A total of 101,064 heartbeats were recorded, and neither paroxysmal atrial fibrillation nor premature ventricular contractions was observed. His echocardiogram was unremarkable with a normal biventricular size and function. He was not receiving any drug therapy (beta blockers or calcium channel blockers) that could have precipitated the bradycardia. His physical examination findings were unremarkable except for a body mass index of 43.2 kg/m^2.

Because he reported excessive daytime sleepiness, severe snoring, and nocturnal awakening, which are well-recognized symptoms of OSA, he agreed to undergo a PSG examination (Profusion Sleep Software; Compumedics, Victoria, Australia). The PSG data are summarized in Table. The PSG analysis showed that the sleep cycle, defined as a period of non-rapid eye movement (REM) sleep followed by a period of REM sleep, was not fully established. Abnormal respiratory events, mostly consisting of obstructive apnea events, were significantly observed, and the apnea-hypopnea index was 114.6 counts per hour. The arousal index score was high (115.0 counts per hour), as was the snoring count (1,695 counts per night). Oxygen saturation was frequently decreased during the obstructive apnea events, and the lowest oxygen saturation level was 59% on room air. The oxygen saturation tended to decrease the most during REM sleep. Remarkable heart rate fluctuations were also recorded during the PSG examination. Because the patient did not awaken during the PSG examination, the bradyarrhythmic events occurred during sleep.

Table. Changes of ECG, Sleep and Laboratory Data before and after CPAP Treatment.

Parameter	Before CPAP	After CPAP
<ECG data>		
SDNN (ms)	112.5	102.5
SDANN (ms)	54.7	91.5
LF (ms^2)	1,539.1	268.9
HF (ms^2)	325.7	116.9
LF/HF	4.88	3.34
<Sleep data>		
AHI (n/h)	114.6	11.6
AI (n/h)	86.3	0.7
Obstructive (n/h)	41.9	0
Central (n/h)	0.2	0.7
Mixed (n/h)	44.2	0
HI (n/h)	28.3	10.9
Minimum SpO_2 (%)	59	85
Arousal Index (n/h)	115.0	8.8
<Laboratory Data>		
BNP (pg/mL)	115.4	23.4

CPAP: continuous positive airway pressure, SDNN: standard deviation of the NN interval, SDANN: standard deviation of the average of the NN interval, LF: low frequency power, HF: high frequency power, AHI: apnea hypopnea index, AI: apnea index, HI: hypopnea index, BNP: brain natriuretic peptide

Given these findings, CPAP therapy was initiated to prevent obstructive apnea events, and titration of the CPAP therapy was performed one month after its initiation. Auto-mode CPAP was set at a minimum pressure of 4 cmH_2O and a maximum of 20 cmH_2O. During CPAP titration, the pressure was changed from 4 to 15 cmH_2O, and the mean pressure of CPAP was 11.0 cmH_2O. The usage rate of the CPAP device was 92.9%, and the average CPAP usage time was 5.4 hours per a day.

Table shows the changes in the sleep parameters before and after CPAP therapy. The apnea-hypopnea index decreased by 89.9% (from 114.6 to 11.6 per hour) after CPAP therapy. Furthermore, CPAP therapy improved obstructive apnea events (from 41.9 to 0 per hour) and the arousal index. Fluctuations in the oxygen saturation and heart rate were also not observed after CPAP therapy. The snoring count and arousal index were 19 per night and 8.8 counts per hour, respectively. In addition, the plasma brain natriuretic peptide levels decreased after CPAP therapy.

As described above, both sympathetic and parasympathetic nerve activation in OSA can cause fluctuations in the R-R interval. To investigate this, we retrieved ECG data from the PSG recording and analyzed the distribution of the R-R interval and autonomic nerve functions before and after CPAP therapy (Fig. 2). A mathematical analysis of the biological signals was performed with the MATLAB software program, version R2016a (MathWorks, Natick, USA). The mean R-R interval before CPAP therapy was 773 ms, and

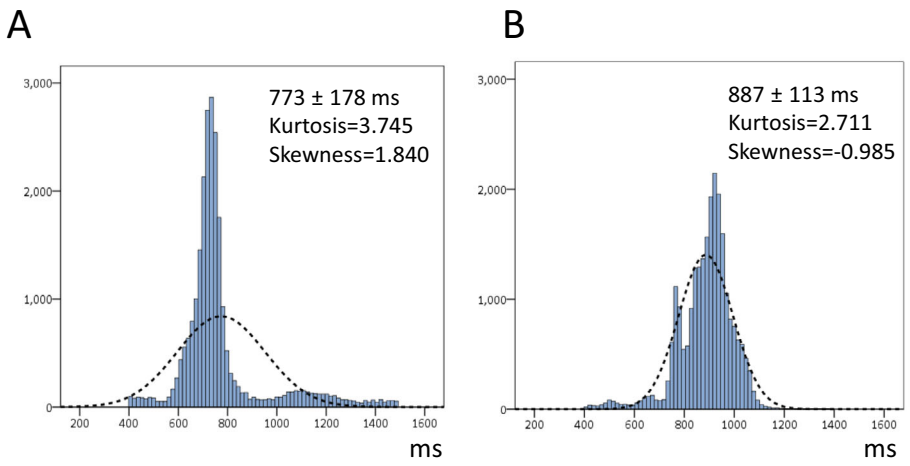

Figure 2. **The histogram of the R-R intervals during the PSG analysis before and after CPAP therapy. PSG: polysomnography, CPAP: continuous positive airway pressure**

the standard deviation was 178 ms. After one month of CPAP therapy, a decreased R-R interval distribution was observed (mean R-R interval: 887 ms, standard deviation: 113 ms). The kurtosis of the R-R interval data was 3.745 before CPAP therapy and 2.711 after CPAP. The skewness of the R-R interval was 1.840 before CPAP therapy and -0.985 after CPAP therapy. The standard deviation of the average NN interval (SDANN) was remarkably decreased after the initiation of CPAP therapy; however, the standard deviation of the NN interval (SDNN) did not markedly differ before and after CPAP therapy. The ratio of the low-frequency power to the high-frequency power (LF/HF) was decreased after CPAP therapy (Table). Furthermore, bradycardia events, such as sinus arrest or AV block, were not observed after CPAP therapy.

Discussion

Previous studies have shown that OSA can be associated with various cardiovascular diseases, such as ischemic heart diseases (4), heart failure (5), aortic diseases (6), and cardiac arrhythmia (1). We herein report a patient who experienced sinus arrest and AV block accompanied by OSA. Apneic and hypoxic episodes in OSA can cause a cardiac vagal activation reflex, which is responsible for bradyarrhythmia (7). At the same time, the persistent increase in the sympathetic tone due to intermittent oxygen desaturations and increases in the arterial carbon dioxide levels can lead to tachyarrhythmia (7), resulting in large distributions of the R-R interval. In this case, bradyarrhythmia related to OSA could not be treated with pacemaker therapy and was instead treated by CPAP therapy primarily.

In the present case, CPAP therapy was an effective and non-invasive therapeutic option for preventing bradyarrhythmia, as has been reported previously (8). The plasma BNP levels in our patient decreased after CPAP therapy, implying that CPAP therapy reduced the volume overload caused by bradyarrhythmia. OSA can progress to a dissecting thoracic aortic aneurysm (6). The thoracic aortic aneurysm in the present patient may have been caused by severe obstructive apnea. CPAP therapy can be effective for suppressing not only the occurrence of bradyarrhythmia but also the progression of the aortic aneurysm after its operation.

We also analyzed the R-R interval recorded during the PSG analysis. Very few studies have shown an improvement in the R-R interval distribution after CPAP therapy in patients with OSA (9). It has been well established that the R-R interval analysis provides information with respect to the autonomic nervous system. Our study shows that the R-R interval distribution after CPAP therapy approximates the normal distribution, indicating that the balance of the autonomic nervous system is maintained. In the present case, the LF/HF levels decreased, and the SDANN level increased, suggesting that sympathetic nerve activities decreased after CPAP therapy. Therefore, improvements in the distribution of the R-R intervals in this case reflected the stabilization of the autonomic nervous system through respiratory control using CPAP therapy. The fluctuation of the autonomic nervous system due to unstable respirations can induce bradyarrhythmia and tachyarrhythmia, suggesting that primary respiratory control is an effective approach for managing patients with OSA.

The authors state that they have no Conflict of Interest (COI).

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