Case Report

Efficacy of adaptive-servo ventilation (HEART PAP™) for an elderly patient with chronic heart failure who had Cheyne—Stokes respiration with central sleep apnea

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Summary
An 82-year-old male patient, who had been diagnosed with chronic heart failure due to dilated cardiomyopathy and combined valvular disease and who had atrial fibrillation with complete atrioventricular block, was admitted to our hospital owing to the exacerbation of chronic heart failure. During admission, the patient became aware of drowsiness during daytime hours and had periodic apnea during sleep. Polysomnography (PSG) revealed Cheyne—Stokes respiration with severe central sleep apnea as evidenced by an apnea—hypopnea index (AHI) of 93.5/h. Nocturnal oxygen therapy failed to sufficiently suppress apnea, and arousal reactions occurred frequently. Therefore, we conducted titration by adaptive-servo ventilation (ASV; HEART PAP™). Consequently, subjective symptoms and respiratory sleep parameters improved. The patient showed excellent adherence to loading the device at home. PSG at 3 months after implementation of HEART PAP™ indicated improvement in the AHI to 13.5/h, and the patient exhibited marked improvements in breathlessness and awareness of drowsiness during daytime hours. HEART PAP™ was found to be a useful device for Cheyne—Stokes respiration with central sleep apnea that is associated with chronic heart failure even for very elderly patients.

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Introduction

Recent epidemiologic studies have clarified that sleep-disordered breathing (SDB) is a complication in approximately half of patients with chronic heart failure (HF), is involved in the pathogenesis and exacerbation of HF, and
Efficacy of adaptive-servo ventilation is an important clinical entity that adversely affects life prognosis [1]. In addition, Cheyne–Stokes respiration with central sleep apnea (CSR-CSA) that includes central apnea and hyperventilation has been reported to be an important prognostic factor of chronic HF [2], and closely related to worsening quality of life (QOL) in HF patients [3]. Here we report the case of an elderly patient with severe CSR-CSA that was associated with chronic HF for whom one of the interventions, adaptive-servo ventilation (ASV; HEART PAP™, Respironics, Inc., Murrysville, PA, USA), was markedly effective.

**Case report**

An 82-year-old male patient, who suffered from New York Heart Association class III chronic HF due to dilated cardiomyopathy, mitral regurgitation, and tricuspid regurgitation and who had been implanted with a permanent pacemaker for chronic atrial fibrillation with complete atrioventricular block, was being treated as an outpatient. The patient received torasemide (8 mg), furosemide (20 mg), spironolactone (50 mg), candesartan cilexetil (4 mg), and warfarin (3 mg) and had a history of several admissions to the hospital due to the exacerbation of HF. These medications did not change in this hospitalization. During the present admission due to the repeated acute exacerbation of HF, the patient presented with periodic apnea during sleep. We suspected that the patient’s complications included SDB because he complained of drowsiness during daytime hours and nocturia, although his Epworth Sleepiness Score (ESS) which represented objective sleepiness was 4. Therefore, we conducted polysomnography (PSG) after the improvement in HF. On admission, the patient (154.7 cm in height; 64.5 kg in body weight; 92/74 mmHg in blood pressure; and 80 bpm in pulse rate) showed jugular engorgement, systolic murmurs in the apical area, and marked edema of the lower extremities. Blood gas analysis (under atmosphere), that was performed prior to conducting PSG, revealed hypoxemia and hypocapnia as evidenced by 7.47 in pH, 35.1 torr in PCO₂, 68.7 torr in PO₂, and 25 mEq/l in HCO₃⁻. The plasma brain natriuretic peptide (BNP) level was as high as 233 pg/ml. Plain chest X-ray indicated a cardiothoracic ratio of 72%, and echocardiography exhibited a left ventricular ejection fraction (LVEF) of 14%, a decrease in diffuse hypokinesis of the left ventricular wall, severe mitral regurgitation, and severe tricuspid regurgitation.

A polysomnogram, that was obtained after the improvement in HF, is shown in Fig. 1. The patient showed severe SDB as indicated by an apnea–hypopnea index (AHI) of 93.5/h. Among the episodes, the central apnea index (CAI)—mostly showing the waveforms of CSR-CSA—accounted for 37.9/h. The minimum SpO₂ level was 82%. Furthermore, the arousal index (ArI) was 94.2/h, indicating marked sleep fragmenta-
tion associated with hyperventilation. Consequently, sleep quality was noticeably impaired. Furthermore, the patient had eight nocturnal micturitions, also indicating sleep fragmentation by these episodes.

PSG indicated typical CSR-CSA. A beta-adrenergic receptor blocker was difficult to be used for our patient because he was hypotensive. Therefore, we considered nonpharmacotherapy for CSR-CSA. The patient presented possible difficulty in undergoing positive pressure ventilation therapy because of old age and underlying disease. First, we conducted titration by nocturnal oxygen therapy (3 L/min). Consequently, SDB improved as indicated by an AHI of 51.4/h, with a CAI of 3.1/h. However, hypopnea considered to be residual central and/or changing obstructive, and an elevated ArI (66.1/h) associated thereto persisted, and the number of nocturnal micturitions did not reduce.

Oxygen therapy failed to sufficiently improve respiratory sleep parameters and sleep quality. Therefore, we conducted titration with HEART PAP™ (Fig. 2). Time was required to set initial pressures. Therefore, apnea persisted as evidenced by an AHI of 37.6/h and a CAI of 2.6/h. However, the ArI reduced to 38.2/h, and slow-wave sleep and REM sleep—that had not been observed during oxygen therapy—occurred. Furthermore, the patient had no nocturnal micturition and noticed, after the titration, a feeling of sound sleep and alleviated drowsiness during daytime hours. HEART PAP™ improved respiratory sleep parameters and sleep quality and was also well-tolerated by the patient. Therefore, the device was implemented under the following conditions: 24 cmH2O in the maximum inspiratory positive airway pressure (IPAP max); 10 cmH2O in the minimum inspiratory positive airway pressure (IPAP min); 10 cmH2O in expiratory positive airway pressure (EPAP); and 15 breaths/min in respiratory rate. Subsequent follow-up on an outpatient basis revealed excellent adherence to loading the device. The mean duration of device use was 6.5 h/day. Edema of the lower extremities, nocturnal pollakiuria, a feeling of sound sleep, and exertional breathlessness during daytime hours improved.

At 3 months after implementation of HEART PAP™, PSG was conducted in the patient who loaded HEART PAP™ under the same conditions as those for outpatient care. Consequently, the AHI reduced to 16.3/h and the minimum SpO2 was 91%; hence, the patient showed improvement in hypoxemia. Furthermore, the ArI also showed a marked reduction to 13.0/h, and the improvement of both sleep depth and REM sleep persisted from the time of implementing HEART PAP™. In addition, the patient showed no nocturnal micturition during the testing. During these 3 months, there was no change in medications for heart failure. LVEF evidenced by echocardiography slightly improved from 14% to 21%. However, the patient’s impression about usage is excellent, and he is under continuing treatment on an outpatient basis without readmission for 2 years.

![Figure 2](image_url)

**Figure 2** Polysomnogram under HEART PAP™ titration. Ventilatory volume on a breath-by-breath basis is averaged by auto inspiratory positive airway pressure (IPAP) (1), desaturation is improved (2), and arousal reactions are reduced.
Discussion

CSR-CSA is concurrently associated with approximately 30—40% of patients with chronic HF, and the following events are considered to be involved in its pathogenesis: (1) hyperventilation due to the stimulation of lung stretch receptors induced by chronic pulmonary congestion associated with decreased cardiac output; (2) enhanced sensitivity of central chemoreceptors; and (3) a delay in circulation time associated with decreased cardiac output. Namely, CSR-CSA is considered to be the consequence of HF. However, Lanfranchi et al. [2] have reported that the presence of CSR-CSA itself is an independent prognostic factor for HF. Moreover, Carmona-Bernal et al. [3] have demonstrated that HF patients with CSR-CSA had a worse QOL than those with HF alone. Consequently, CSR-CSA currently attracts attention as a new therapeutic target for chronic HF.

To date, oxygen therapy [4], continuous positive airway pressure (CPAP) [5], bi-level positive airway pressure (BiPAP) [6], ASV [7], and other modalities have been reported as nonpharmacologic therapies for CSR-CSA. However, an improvement in long-term prognosis has never been reported, and no established therapeutic modality is currently available. However, beta-adrenergic receptor blockers and cardiac resynchronization therapy (CRT) (in patients for whom the modality is indicated). However, our patient could not receive these treatments for HF because of hypotension, severe tricuspid regurgitation, and high age, so we had to choose nonpharmacologic therapies for CSR-CSA.

ASV (HEART PAP™), noninvasive positive pressure ventilation (NPPV) that was developed for the purpose of treating SDB, which is concurrently associated with chronic HF, is principally characterized by its function of assisting IPAP that automatically allows the sustainment of proper ventilation volume in proportion to the patient’s respiratory condition (auto IPAP). Furthermore, HEART PAP™ can set EPAP—that deletes the components of OSA which is present frequently in a concurrent fashion—and is theoretically capable of addressing all levels of SDB in HF. We surmised since the beginning of the present admission that NPPV was difficult to be implemented for our patient because of age, underlying disease, and other factors. First, we conducted nocturnal oxygen therapy. Although desaturation improved, sleep quality failed to be improved due to the frequent occurrence of arousal reactions induced by persisting CSR-CSA. Nocturnal oxygen therapy (3 L/min) for outpatients with chronic HF, whose respiratory disturbance index (RDI) in arterial blood was ≥5 episodes/h and whose LVEF was ≤45%, improved their QOL [4]. However, this study examined principally patients with mild chronic HF and did not conduct nocturnal PSG in all the patients examined. Therefore, sleep quality was not assessed. Furthermore, they considered the improvement of oxygen saturation due to oxygen therapy as improvement in respiratory parameters; therefore, they possibly underestimated respiratory events involving arousal reactions. On the other hand, HEART PAP™ indicated increases in deep sleep and REM sleep and was tolerated by the patient rather better than oxygen therapy. Table 1 shows the results of PSG which was performed before treatment for CSR-CSA, under titration by nocturnal oxygen therapy, titration with HEART PAP™, and after 3 months after implementation of HEART PAP™. Our patient was a very elderly with low cardiac function, for whom NPPV is generally considered difficult to be implemented. Therefore, we considered that HEART PAP™ is a potentially effective therapeutic option also for patients for whom positive pressure therapy has been difficult to be implemented because of its low tolerability. Moreover, a study [5] reported that excessive preload reduced by CPAP might be one of the causes for the fact that the therapy had not improved prognosis. Our patients received extraordinary high IPAP pressure because obstructive component did not diminish even 10 cmH2O of EPAP during titration. Avoiding the excessive EPAP pressure, therefore, high IPAP max pressure was needed. During follow-up, however, our patient showed reduced edema of the lower extremities without a decrease in blood pressure. Therefore, we regard that ASV is an effective therapy when conducted at pressures that were set by titration under nocturnal observation. Kasai et al. reported that HEART PAP™ significantly improved respiratory sleep parameters and sleep parameters for chronic HF patients with CSR-CSA which had persisted also under the use of CPAP and BiPAP [10]. However, they studied only one night and did not evaluate the long-term effectiveness of HEART

<table>
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<th>Table 1</th>
<th>PSG findings of before and after treatment for CSR-CSA.</th>
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<tbody>
<tr>
<td></td>
<td>Before treatment</td>
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<tr>
<td>AHI (episodes/h)</td>
<td>93.5</td>
</tr>
<tr>
<td>CAI</td>
<td>37.9</td>
</tr>
<tr>
<td>OAI</td>
<td>4.9</td>
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<tr>
<td>% of TST SpO2 &lt;90%</td>
<td>17.2</td>
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<tr>
<td>Lowest SpO2 (%)</td>
<td>81</td>
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<tr>
<td>ArI (episodes/h)</td>
<td>94.2</td>
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<tr>
<td>Sleep stage (% of TST)</td>
<td></td>
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<tr>
<td>1 and 2</td>
<td>100</td>
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<tr>
<td>SWS</td>
<td>0</td>
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<td>REM</td>
<td>0</td>
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AHI: apnea–hypopnea index; CAI: central apnea index; OAI: obstructive apnea index; TST: total sleep time; SpO2: arterial oxyhemoglobin saturation; ArI: arousal index; SWS: slow-wave sleep; REM: rapid eye movement; ASV: adaptive-servo ventilation.
PAP™ for sleep quality and QOL. Unfortunately, we did not evaluate his QOL objectively. However, subjective symptoms such as exertional dyspnea and nocturia were dramatically improved. Therefore, we considered that the treatment with HEART PAP™ dramatically improved subjective symptoms and this device potentially improved patient’s QOL and was well-tolerated even in very elderly HF patients, who did not receive any other treatments for CSR-CSA. We expect that the application criteria for ASV, method of titration, and other conditions be established in the future and that a large-scale clinical trial of ASV be conducted in which life prognosis and QOL of patients with chronic HF complicated by CSR-CSA should also be examined.

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References


