Adaptive Servo-Ventilation in Patients With Idiopathic Cheyne-Stokes Breathing

Katsuhisa Banno, M.D.; Kuniyuki Okamura, M.D.; Meir H. Kryger, M.D.

Sleep Disorders Center, St. Boniface General Hospital, Section of Respiratory Diseases, University of Manitoba, Winnipeg, Manitoba, Canada

Background: Cheyne Stokes Breathing (CSB), a form of central sleep apnea is often found in medical illnesses such as heart failure, stroke or renal failure. Adaptive servo-ventilation (ASV) has been reported to be an effective treatment of CSB in heart failure. However, there are no reports about using ASV for idiopathic CSB, which is not associated with heart failure or other serious medical problems.

Case summary: We evaluated three patients with idiopathic CSB and examined the feasibility of using ASV to treat them. The patients had a periodic breathing pattern resembling Cheyne-Stokes Breathing. During polysomnography, the abnormal breathing pattern was present while patients were both awake and asleep. The patients were first tested on continuous positive airway pressure (CPAP) and/or oxygen; however they did not respond well to either of these treatments. They were then assessed on ASV. The mean abnormal breathing events index decreased from 35.2 to 3.5 per hour of sleep on ASV. There was a significant reduction in the mean number of arousals caused by abnormal breathing events: from 18.5 to 1.1 per hour of sleep. After six to twelve months of using ASV, the patients had maintained significant improvement in subjective daytime alertness and mood.

Conclusion: A trial of ASV for patients with idiopathic CSB is recommended if they do not have improvement in sleep respiration or daytime performance on CPAP and/or oxygen.

Keywords: Adaptive servo-ventilation, central sleep apnea, Cheyne-Stokes respiration, daytime sleepiness, periodic breathing, sleep


Central sleep apnea syndrome, a disorder characterized by recurrent apneic episodes in the absence of upper-airway obstruction during sleep, causes nocturnal oxygen desaturations, recurrent arousals, and subjective daytime sleepiness. Central sleep apnea syndrome has been reported to be present in alveolar hypoventilation disorders, heart failure, and neurologic disorders, and some cases are idiopathic. Cyclic breathing with regularly repeating periods of central apneas or hypopneas alternating with periods of hyperpnea in a gradual crescendo and decrescendo pattern is termed Cheyne-Stokes breathing, which is often associated with heart failure or neurologic disorders. Cheyne-stokes breathing is defined as “Other Central Sleep Apnea, including Cheyne Stokes Breathing Pattern” in the International Classification of Sleep Disorders-2. Association with a serious medical illness, such as heart failure, stroke, or renal failure, is usually necessary to document this diagnosis by International Classification of Sleep Disorders-2.

Various respiratory interventions, including continuous positive airway pressure (CPAP), bilevel positive airway pressure, or nasal oxygen have been evaluated in patients with heart failure and Cheyne-Stokes breathing. These treatments may improve sleep respiration. In heart failure, it has been hypothesized that CPAP stabilizes the respiratory pattern by increasing PaCO$_2$ and increasing intrathoracic pressure, which decreases left ventricular afterload. Adaptive servo-ventilation (ASV), a new noninvasive ventilation modality, recently has been reported to be effective in patients with heart failure and Cheyne-Stokes breathing. However, we are not aware of reports about using ASV for Cheyne-Stokes breathing in the absence of heart failure or any other serious medical problem.

We evaluated the efficacy of respiratory interventions, including CPAP, oxygen, and ASV, for the treatment of idiopathic Cheyne-Stokes breathing in 3 patients. The patients were assessed with comprehensive polysomnography, including synchronized digital video recording, the monitoring of neurophysiologic measures (electroencephalogram, chin electromyogram, electrooculogram, anterior tibialis electromyogram) and cardiorespiratory variables: chest-wall motion, abdominal motion, nasal pressure, oronasal PCO$_2$, SpO$_2$ (by ear oximeter), and electrocardiogram. Nasal pressure, oronasal CO$_2$, chest wall, and abdominal motion were used to assess respiratory events. Video records were used for additional assessment of abnormal breathing. The sleep record was analyzed manually for sleep staging using a 30-second epoch. Abnormal breathing patterns were defined using conventional criteria. After a definitive diagnosis was made, the patients were tested with following treatments: CPAP, nasal oxygen, and CPAP and nasal oxygen. The patients were then assessed while on the ASV at the default settings (AutoSet CS; ResMed, Sydney, Australia), described in detail elsewhere. We report our experience in using ASV for the treatment of idiopathic Cheyne-Stokes breathing.
A 51-year-old male insurance executive (body mass index: 24.4 kg/m²) was referred because of observed apneas and excessive daytime sleepiness interfering with his ability to be productive at work. His Epworth Sleepiness Scale score was 20. On average, he slept 7.5 hours every night. He denied hypnagogic hallucinations, cataplexy, or sleep paralysis. He had symptoms of restless legs syndrome. His medical history was noncontributory. The family history revealed that his father died of myocardial infarction at age 52, and his brother also had a myocardial infarction at age 47 with subsequent angioplasty. Physical examination revealed that he had a long uvula and nasal obstruction on his left side. There were no findings suggestive of heart failure or cerebral neurologic disorders.

**BASELINE ASSESSMENT**

The patient was assessed by overnight polysomnography, which confirmed central sleep apneas with an apnea-hypopnea index (AHI) of 30.4 per hour. Almost all of the respiratory events were central apneas, and the breathing pattern had the configuration of Cheyne-Stokes breathing. He spent 0.7% of the sleep time with an SpO₂ < 90%. The arousal index was 22.2; 12.3 arousals per hour of sleep were related to abnormal breathing events. The cause of his subjective daytime sleepiness was considered to be the abnormal breathing pattern. The highest recorded end-tidal CO₂ was 39.8 mmHg. There were 59.7 leg movements per hour; however, only 5.8 arousals per hour were caused by leg movements. Blood was tested to exclude known biochemical causes of movement disorder; no abnormalities in thyroid function, iron stores, or vitamin B₁₂ levels were found. The results of the baseline polysomnographic study are presented in Table 1.

**CONTINUOUS POSITIVE AIRWAY PRESSURE**

The patient was tested on CPAP. However, his periodic breathing worsened after he was started on CPAP. Because of this negative response, the assessment on CPAP was terminated.

**OXGEN**

Because nasal CPAP worsened his apnea, the patient was then assessed on oxygen at 2 liters per minute, which decreased the oxygen desaturation index (3%) from 16.4 to 4.0 per hour of sleep time, although it did not eliminate the central apneas (Table 1). There was no significant change in the arousal index or the sleep structure. He was sent home on nocturnal oxygen.

He stated that there was improvement in his work performance and daytime alertness; however, his sleepiness was not entirely controlled by oxygen. Therefore, modafinil was started for his residual sleepiness. After a few months of using modafinil, he developed atrial fibrillation. Modafinil was discontinued.

**ADAPTIVE SERVO-VENTILATION**

Because the other treatments did not resolve the patient’s problem, another sleep study was done to assess response to ASV. The study showed that the patient still had periodic breathing when he was both awake and asleep. The ASV machine compensated by generating pressure when his ventilation decreased (Figure 1). Although the SpO₂ was oscillating at the beginning of the polysomnographic recording, ASV gradually normalized the SpO₂ level (Figure 2). The arousal index was 9.7 per hour; 1.6 were related to abnormal respiratory events. The abnormal breathing pattern was well controlled by ASV. The AHI was 5.7 per hour on ASV. The patient stated that there was a more significant improvement in daytime alertness with ASV than with any previous treatments that he had tried. It was recommended that he use ASV treatment at home.

---

**Table 1—Results of Polysomnographic Findings in 3 Cases**

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep stage, % of total sleep time</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.4</td>
<td>7.0</td>
<td>4.4</td>
</tr>
<tr>
<td>2</td>
<td>47.2</td>
<td>51.6</td>
<td>50.5</td>
</tr>
<tr>
<td>3</td>
<td>17.0</td>
<td>4.1</td>
<td>8.8</td>
</tr>
<tr>
<td>4</td>
<td>7.4</td>
<td>1.7</td>
<td>0</td>
</tr>
<tr>
<td>REM</td>
<td>27.0</td>
<td>35.7</td>
<td>36.3</td>
</tr>
<tr>
<td><strong>Apnea index, no./h</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30.4</td>
<td>26.5</td>
<td>5.7</td>
</tr>
<tr>
<td>Obstructive</td>
<td>1.4</td>
<td>0.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Mixed</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Central</td>
<td>29.0</td>
<td>25.9</td>
<td>5.5</td>
</tr>
<tr>
<td>Average SpO₂</td>
<td>94.8</td>
<td>95.6</td>
<td>94</td>
</tr>
<tr>
<td>SpO₂ &lt; 90%, % of time</td>
<td>0.7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mean heart rate, bpm</td>
<td>56</td>
<td>54</td>
<td>53</td>
</tr>
<tr>
<td><strong>Arousal index, no./h</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22.2</td>
<td>23.3</td>
<td>9.7</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>4.1</td>
<td>2.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Respiratory</td>
<td>12.3</td>
<td>13.8</td>
<td>1.6</td>
</tr>
<tr>
<td>PLM</td>
<td>5.8</td>
<td>7.5</td>
<td>4.0</td>
</tr>
</tbody>
</table>

ASV refers to adaptive-servo ventilation; REM, rapid eye movement; PLM: periodic limb movement.

*The continuous positive airway pressure (CPAP) was terminated shortly because of the worsening of apneic episodes.

*The patient could not tolerate CPAP.
FOLLOW-UP

After the patient had been using ASV at home every night for 1 month, he stated that subjective daytime sleepiness was completely diminished. In addition, his subjective mood and cognitive function were dramatically improved, which made him feel like a new person. The improvement was still noted after 6 months.

Case 2

A 58-year-old male lawyer (body mass index=26.6 kg/m²) was referred because of snoring, observed sleep apneas, and daytime sleepiness (Epworth Sleepiness Scale score = 11). He napped daily because of sleepiness, which substantially interfered with his work performance. He denied hypnagogic hallucinations, cataplexy, sleep paralysis, and symptoms of restless legs. There was no other major medical history except for hypertension and occasional palpitations. His father died of a heart attack at age 64. Physical examination revealed that there were no remarkable findings. He had mild retrognathia. There were no findings of heart failure or neurologic disorders. Biochemical evaluations for thyroid disease were negative.

BASELINE

The patient was assessed by overnight polysomnography, which confirmed sleep apneas of primarily the central type with an AHI of 35.6 per hour; 53.7% of the abnormal respiratory events were central apneas (Table 1). These had the configuration of Cheyne-Stokes breathing. The arousal index was 48.6 per hour; 20.2 were related to abnormal breathing events. There were 60.5 leg movements per hour of sleep, which were also observed on synchronized digital video.

CONTINUOUS POSITIVE AIRWAY PRESSURE

We tested the patient on CPAP, which did not eliminate his abnormal breathing events (AHI=21.0 per hour). He had 25.7 arousals and 22.7 leg movements per hour of sleep.

OXYGEN

The patient was then tested with nasal oxygen at 2 liters per minute. The AHI decreased from 35.6 to 13.5 per hour. The percentage of time with an SpO² < 90% decreased from 4.3% to 0.1%. The arousal index decreased from 48.6 to 34.5 per hour; 18.9 were related to abnormal leg movements. The patient continued to have leg movements at 41.5 per hour. He was started on oxygen at 2 liters per minute at home. However, his subjective daytime sleepiness continued, and impaired concentration in the work place was still problematic.

CPAP AND OXYGEN

Because his apneas did not resolve with the use of CPAP or
Case 3

A 69-year-old male farmer (body mass index = 27.1 kg/m²) was referred for assessment of sleep-related breathing disorder due to observed apneas. The patient had a history of snoring for 60 years. Although he did not complain of pathologic daytime sleepiness, his wife stated that he was very irritable. He denied hypnagogic hallucinations, cataplexy, sleep paralysis, or symptoms of restless legs. He did not awaken with an acid taste in his mouth, a feeling of choking, palpitations, or headaches. There was no peripheral edema in the lower limbs. His pharyngeal airway was within normal limits. He had retrognathia. There was no history of cardiovascular diseases or stroke.

Baseline

The sleep study showed central sleep apneas with periodic breathing, which were observed during sleep and wakefulness. These had the configuration of Cheyne-Stokes breathing. These apneic episodes were in the range of about 50 seconds in duration, during which time his oxygen saturation decreased from the high 90s to the low 80s. Once he fell asleep, he continued to have periodic breathing, with episodes at a rate of 39.5 per hour of sleep. He spent 10.9% of time below an SpO₂ of 90%. Synchronized digital video revealed that there were times during the night when he had periodic breathing with ventilation increasing and decreasing with no evidence of obstruction. At other times, the patient had some evidence of obstruction, with loud snorts occurring before the resumption of ventilation. The sleep structure was abnormal, with 32.2 arousals per hour of sleep; 22.9 episodes were related to abnormal respiratory events. There was no rapid eye movement sleep. There were 48.3 leg movements during sleep; 3.9 episodes per hour of sleep were related to arousals. The sleep efficiency was 74.1%. The baseline polysomnographic findings are presented in Table 1. It was concluded that he had combination of periodic breathing and upper-airway obstruction.

Continuous Positive Airway Pressure

Although he was assessed on CPAP, he could not tolerate CPAP at all. Thus oxygen was tried on him as part of a split-night study.

Oxygen

The patient was then tested on oxygen at 1 liter per minute. The percentage time of with an SpO₂ < 90% was decreased from
10.9% to 0% on oxygen; however, he still had 16.9 episodes of periodic breathing per hour of sleep.

**Adaptive Servo-Ventilation**

We repeated another sleep study because neither CPAP, oxygen, or a combination of CPAP and oxygen were sufficiently effective to improve his abnormal breathing and symptoms. He still had problems with mood and daytime alertness; therefore, he wanted to pursue another treatment for his abnormal breathing. His wife mentioned that his irritability continued, and this has been causing a problem for them.

We tested the patient while using an ASV machine. The number of abnormal breathing events decreased to 1.3 per hour of sleep. He had a sleep efficiency of 81.3%. There were now normal amounts of slow-wave sleep and rapid eye movement sleep. The patient had an improvement in his overall sleep, and he fell asleep in 11 minutes. Leg movements per hour of sleep decreased from 48.3 (baseline) to 28.1. The following morning, he stated that he felt much improved having been on the ASV device for an entire night. Since the most appropriate treatment for him was ASV at this point, he was recommended to start ASV at home.

**Follow-up**

The patient had been using ASV at home every night for 6 month since ASV was prescribed. At the 1-month and 6-month follow-up visits, he stated that he felt much better on ASV than on CPAP and oxygen, and his sleep quality substantially improved on ASV. His wife also mentioned that his mood significantly improved.

**Discussion**

To our knowledge, this is the first report of patients with idiopathic Cheyne-Stokes breathing who were successfully treated with ASV. The mean abnormal breathing events decreased from 35.2 to 3.5 per hour of sleep on ASV. In addition, the mean number of arousals related to abnormal breathing was also reduced: 18.5 to 1.1 per hour of sleep. The 3 cases all had had disturbed work performance or mood problems caused by idiopathic Cheyne-Stokes breathing, which were most improved by using ASV. The elimination of abnormal breathing causing nocturnal arousals or sleep disruption may be a key issue for improved daytime cognitive function in patients with idiopathic Cheyne-Stokes breathing.

Topfer et al.

reported that ASV improved quality of life in patients with Cheyne-Stokes breathing and heart failure. Abnormal breathing or arousals have been reported to be reduced more by ASV than by CPAP or oxygen. It has been recently reported that ASV is a more efficacious treatment for Cheyne-Stokes breathing caused by heart failure than is CPAP, in that ASV corrects more abnormal breathing events than does CPAP, and patients on ASV are more compliant than those on CPAP at 6 months. Although our 3 cases did not have heart failure or cerebral neurologic disorders, they demonstrated repetitive central apneas that are best characterized as Cheyne-Stokes breathing. Also, their mean heart rate was in the low 40s to the high 50s. The abnormal breathing was found while they were both awake and asleep. Thus, the patients may have had abnormal control of ventilation. The ASV device did the opposite of what the patients did with respect to breathing. When tidal volume decreased, the computerized system increased ventilatory support; when ventilation was normal or increased, the ventilatory support decreased (see Figure 1). The compensation of ventilation improved sleep respiration and, thus, reduced nocturnal arousals. In this study, the reason why ASV was more effective than the other treatments in resolving abnormal breathing and sleep structure was unclear.

Another noteworthy finding was a significant reduction in leg movements and arousals related to leg movements with ASV. The leg movements were significantly decreased in Case 3 without medications to suppress leg movements. The mechanism of improvement in the abnormal movements on ASV is not clear.

On the surface, ASV seems to an efficacious treatment for idiopathic Cheyne-Stokes breathing when breathing periodicity is present. However, due to the methodologic issues (small sample, no control group, no randomization), another study comparing the outcome of ASV and other treatments is warranted to see which approach is the most appropriate in cases with idiopathic Cheyne-Stokes breathing.

**Conclusions**

Short-term treatment by using ASV improved sleep structure, sleep respiration, subjective daytime sleepiness, and mood problems in patients with idiopathic Cheyne-Stokes breathing (Cheyne-Stokes breathing without heart failure or other serious medical problem). Clinicians should consider the use of ASV in patients with idiopathic Cheyne-Stokes breathing who do not respond well or fail to tolerate CPAP, oxygen, or both CPAP and oxygen.

**References**

K Banno, K Okamura, and MH Kryger
