Transient Increase in Epileptiform Discharges after the Introduction of Nasal Continuous Positive Airway Pressure in a Patient with Obstructive Sleep Apnea and Epilepsy

Takefumi Hitomi, Toru Oga, Tomomasu Tsuboi, Chikara Yoshimura, Takeo Kato, Akio Ikeda, Ryosuke Takahashi and Kazuo Chin

Abstract

In patients with obstructive sleep apnea (OSA) and epilepsy, the frequency of generalized spike and wave complexes (GSWCs) usually decreases after the initiation of nasal continuous positive airway pressure (nCPAP) therapy. However, we herein report a patient who had a transient increase in GSWCs following nCPAP treatment. A woman with epilepsy underwent polysomnography, who showed severe OSA and 30 GSWCs during the sleep study. Polysomnography at the introduction of nCPAP showed that the GSWCs increased to 94 times during the monitoring period, despite improvement of her OSA. Polysomnography was again performed four months later, and the GSWCs had decreased to 23 times. Physicians should therefore be cautious regarding a possible increase in epileptiform discharges and seizures immediately after the introduction of nCPAP.

Key words: transient increase in epileptiform discharges, epilepsy and obstructive sleep apnea, nasal continuous positive airway pressure (nCPAP) introduction

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Introduction

Both sleep disordered breathing (SDB) and epilepsy are common disorders. SDB was observed in 24% of adult men and 9% of adult women (1) and the prevalence of epilepsy in the general population is approximately 1% (2). Therefore, epilepsy is often accompanied by SDB, mainly obstructive sleep apnea (OSA). In one study, one-third of medically intractable epilepsy patients had a respiratory disturbance index greater than 5 (3), and another study showed that about 10% of the adult epilepsy patients had OSA (4). In patients with SDB and epilepsy, the frequencies of seizures (5-7) and epileptiform discharges (8) are usually decreased after the treatment of SDB, such as by nasal continuous positive airway pressure (nCPAP) and other means.

This secondary beneficial effect of SDB treatment on epilepsy may be associated with a decrease in sleep fragmentation, sleep stage transition, and desaturation, since focal and generalized seizures are more likely to occur during light sleep or soon after awakening (9) and epileptiform discharges tend to be activated by sleep in some epilepsy patients.

As mentioned above, treatment for SDB usually ameliorates not only SDB, but also epilepsy, in patients with both conditions. However, we herein report a patient who experienced a transient increase in epileptiform discharges immediately after beginning nCPAP treatment.

Case Report

An 18-year-old woman began to have monthly complex
Table. Polysomnogram Analysis of the Effect of Introducing nCPAP on OSA and GSWCs

<table>
<thead>
<tr>
<th></th>
<th>Before nCPAP</th>
<th>Just after nCPAP</th>
<th>4mo after nCPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep duration (min)</td>
<td>399</td>
<td>336</td>
<td>414</td>
</tr>
<tr>
<td>Sleep onset (min)</td>
<td>11</td>
<td>14</td>
<td>36</td>
</tr>
<tr>
<td>Sleep efficacy (%)</td>
<td>84.1</td>
<td>75.6</td>
<td>88.2</td>
</tr>
<tr>
<td>Stage I (%)</td>
<td>13.4</td>
<td>3.6</td>
<td>6.2</td>
</tr>
<tr>
<td>Stage II (%)</td>
<td>36.7</td>
<td>36.3</td>
<td>49.1</td>
</tr>
<tr>
<td>SWS (%)</td>
<td>39.0</td>
<td>55.2</td>
<td>35.4</td>
</tr>
<tr>
<td>REM (%)</td>
<td>10.9</td>
<td>4.9</td>
<td>9.3</td>
</tr>
<tr>
<td>Arousal index/h</td>
<td>19.7</td>
<td>22.0</td>
<td>15.8</td>
</tr>
<tr>
<td>Awakenings/h</td>
<td>5.6</td>
<td>8.4</td>
<td>2.5</td>
</tr>
<tr>
<td>Micro arousals/h</td>
<td>14.1</td>
<td>13.6</td>
<td>13.3</td>
</tr>
<tr>
<td>AHPI/h</td>
<td>52.2</td>
<td>5.7</td>
<td>3.0</td>
</tr>
<tr>
<td>Obstructive apneas/h</td>
<td>13.7</td>
<td>0.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Mixed apneas/h</td>
<td>0.3</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Central apneas/h</td>
<td>0.6</td>
<td>0.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Hypopneas/h</td>
<td>38.5</td>
<td>4.1</td>
<td>0.7</td>
</tr>
<tr>
<td>REM-AHI</td>
<td>53.8</td>
<td>3.6</td>
<td>0.0</td>
</tr>
<tr>
<td>NREM-AHI</td>
<td>52.0</td>
<td>5.8</td>
<td>3.4</td>
</tr>
<tr>
<td>Minimum SpO2 (%)</td>
<td>80</td>
<td>89</td>
<td>91</td>
</tr>
</tbody>
</table>

nCPAP: nasal continuous positive airway pressure, OSA: obstructive sleep apnea, GSWCs: generalized spike and wave complexes, SWS: slow wave sleep, REM: rapid eye movement sleep, NREM: non-rapid eye movement sleep, AHPI: hypopnea index, SpO2: percutaneous oxygen saturation.

The patient experienced partial seizures at the age of 13. Her seizure semiology consisted of a loss of awareness and motion arrest lasting for 1 minute; thereafter, the seizure sometimes evolved into a secondarily generalized tonic clonic seizure. Interestingly, a seizure was once induced by hyperventilation. Her developmental milestones were normal, and she had no cognitive impairment. Interictal electroencephalogram (EEG) showed 2-3 Hz generalized spike and wave complexes (GSWCs) that were sometimes maximal at the right frontal area but not on the left side, and intermittent rhythmic slow waves at the right frontal area. Magnetic resonance imaging (MRI) of the head showed no apparent abnormality. Interictal electroencephalogram (EEG) showed 2-3 Hz generalized spike and wave complexes (GSWCs) that were sometimes maximal at the right frontal area but not on the left side, and intermittent rhythmic slow waves at the right frontal area. Magnetic resonance imaging (MRI) of the head showed no apparent abnormality. Valproic acid, which was the first treatment administered, was not effective, but her seizures were well controlled after switching to carbamazepine (CBZ). Based on these findings, she was diagnosed as having focal epilepsy arising from the right frontal area despite the appearance of GSWCs. We consider that the GSWCs were a result of secondary bilateral synchrony. At least 1 year before and 1 year after the introduction of nCPAP, she was seizure-free and the dose of CBZ (800 mg/day) and its serum concentrations (8.5-13.3 μg/mL) were consistent.

The patient experienced excessive daytime sleepiness and had exhibited loud snoring at the age of 18. She was therefore referred to our clinic. At that time, her height and weight were 159.3 cm and 99.5 kg, respectively, and her BMI was 39.2 kg/m². The results of an arterial blood gas analysis were pH, 7.39; PaCO₂, 43.5 mmHg; PaO₂, 88.1 mmHg; and HCO₃⁻: 26.2 mmol/L with room air. The Epworth Sleepiness Scale score was 9 (reference value ≤10) points. She was suspected to have OSA and underwent polysomnography (PSG) (Somnostar Pro System, Fukuda Denshi, Tokyo, Japan). The sleep stages were defined according to the criteria of Rechtschaffen and Kales (10). Apnea was defined as the cessation of airflow for ≥10 seconds, and hypopnea was defined as a >50% decrease in a valid measure of airflow in association with oxygen desaturation of >4% or an arousal (11). The apnea and hypopnea index (AHI) was calculated as the number of episodes of apnea and hypopnea per hour over the total sleep time. The number of GSWCs during PSG recording was counted with respect to each sleep stage and the total sleep time. The PSG showed severe OSA with an AHI of 52.2 (Table) and also showed that GSWCs occurred 30 times (6 during stage 1; 14, stage 2; 3, stage 3; 5, stage 4; and twice during rapid eye movement (REM) (Figure).

Two weeks after the first PSG, the patient was introduced to nCPAP. The PSG that was performed on the second night of nCPAP treatment showed a reduction in the AHI to 5.7 (Table). However, the GSWCs increased, to 94 times during the study period, which was more than three times the number detected during the first PSG (9, during stage 1; 66,
stage 2; stage 1; stage 3; 5, stage 4; and once during REM) (Figure). With respect to the patient’s sleep architecture, slight decreases in the total sleep time and sleep efficacy, an increase in the arousal index, a decrease in stage 1 and REM and increased slow wave sleep were observed in comparison to findings of the baseline PSG (Table). Despite these findings by PSG, the patient did not experience any clinical seizures and her daytime sleepiness improved.

A follow-up PSG was performed four months after the introduction of nCPAP, which revealed a normalized AHI of 4.3 (Table). There were 23 GSWCs during the sleep study, thus indicating a return to close to the baseline level (6 during stage 1; 13, stage 2; 3, stage 3; 0, stage 4; and once during REM). Regarding her sleep architecture, a slight increase in sleep efficacy, a slight decrease in the arousal index, decreased stage 1 and increased stage 2 were observed in comparison with the baseline PSG (Table).

**Discussion**

We herein reported a patient who experienced a transient increase in epileptiform discharges after the introduction of nCPAP. With regard to the worsening effect of the treatment for SDB on epilepsy, one previously reported OSA patient had a new-onset seizure due to frontal lobe epilepsy after the introduction of nCPAP (12). This report, in addition to our experience with our patient, suggests that treatment for OSA can provoke either new-onset seizures or an increase in epileptiform discharges. However, our examination of the literature did not yield any previous reports showing an increase in epileptiform discharges immediately after the introduction of nCPAP.

Although the mechanism responsible for the worsening of epilepsy following SDB treatment remains unknown, several possible mechanisms can be considered. Acute defragmentation in the sleep architecture, acute improvement in the arterial blood gases, and acute reversal of regional cerebral hyper- or hypoperfusion can be caused by the acute release of airway collapse in OSA by nCPAP (13, 14). These drastic changes usually induce favorable clinical results, but they could rarely cause a transient increase in epileptiform discharges, as was the case in our patient. This short-term adverse effect might have been related to the lack of beneficial effects of CPAP on the early mortality rate in patients with central sleep apnea and heart failure (15). In addition, the contribution of instability in slow wave sleep was suggested by analyzing the cyclic alternating pattern in sleep EEGs (12). The authors of that study also mentioned that

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**Figure.** The number of generalized spike and wave complexes (GSWCs) observed during polysomnography (PSG) recorded before, immediately after and four months after the introduction of nCPAP. The gray line indicates the temporal change in the number of GSWCs recorded during stage 1, the black small dotted line the GSWCs during stage 2, the black large dotted line stage 3, black line stage 4, gray small dotted line rapid eye movement (REM), and the gray large dotted line represents the total number of GSWCs recorded during the sleep study. Immediately after the introduction of nCPAP, the GSWCs increased to 94 times (9, stage 1; 66, stage 2; 13, stage 3; 5, stage 4; and once for REM), which was more than three times the number before CPAP (total of 30; 6, stage 1; 14, stage 2; 3, stage 3; 5, stage 4; and twice for REM), and then the value returned to the baseline level (total of 23 times; 6, stage 1; 13, stage 2; 3, stage 3; 0, stage 4; and once for REM).
nCPAP might force the EEG synchronization, which may trigger the epileptiform discharges. Since REM sleep deactivate generalized seizures and generalized discharges (16), a decreased REM sleep percentage following CPAP introduction is also a possible mechanism underlying the increase in epileptiform discharges.

The most plausible mechanism in this particular patient is the acute change in arterial blood gases, since she had experienced a seizure induced by hyperventilation in the past. Indeed, upon the introduction of nCPAP treatment, the number of awakening times increased from 5.6/h to 8.4/h, while the numbers of microarousals did not change significantly, from 14.1/h to 13.6/h. In general, awakening from sleep induces relative hyperventilation, which may have evoked epileptiform discharges in this particular patient (Table). A follow-up PSG showed a decrease in the number of awakenings to 2.5/h with stable microarousals. These decreased awakenings resulted in decreased relative hyperventilation, and thus, the GSWC frequency returned to the approximate baseline level. These findings were consistent with the fact that seizures are provoked by hyperventilation in some patients with generalized and focal epilepsy (17).

Physicians should therefore be aware of a possible increase in epileptiform discharges or the new appearance of seizures immediately after treatment for SDB in patients with epilepsy and SDB, although the incidence of such a worsening effect of SDB treatment on epilepsy may be very low.

There is a limitation associated with our report. The variability in the night-to-night GSWC frequency could also be a possible mechanism underlying the transient increase in GSWCs after nCPAP introduction, although the variability of GSWCs in this particular patient were relatively small. Nevertheless, this should be kept in mind by physicians when evaluating epileptic patients being introduced to nCPAP treatment.

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

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References

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