Clinical Research

Effect of continuous positive airway pressure ventilation on nocturnal ST-segment changes in patients with sleep-disordered breathing

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Objective To determine whether sleep-disordered breathing (SDB) may lead to nocturnal myocardial ischemia and whether the severity of this ischemia may be relieved by nasal continuous positive airway pressure (CPAP). Methods Overnight polysomnogram examination and simultaneous 3-channel Holter monitoring were performed on 76 patients with moderate to severe SDB and no history of coronary heart disease. All the cases were treated with CPAP for one night. ST depression was defined as a ST segment decrease of more than 1 mm from baseline and lasting 1 min or more. The total duration (minutes) of ST depression was indexed to the total sleep time (minutes per hour of sleep). Results Twenty-eight patients (37%) showed ST segment depression during their sleep. Before CPAP treatment, the respiratory disturbance index (RDI) and arousal index were significantly higher during periods of ST depression than when ST segments were isoelectric, whereas no significant difference was found in blood oxygen saturation (SaO2). After the CPAP treatment of patients with ST depression, the duration of ST depression was significantly reduced from 36.8±18.9 to 11.4±13.2 min/h (P<0.05). ST depression-related indexes, including RDI, arousal index and the percentage of sleep time spent at SaO2 below 90% (TS90/TST), were all significantly decreased, with RDI from 63.4±23.8 to 8.1±6.6 /h, arousal index from 51.2±18.9 to 9.6±5.4 /h, and TS90/TST from 50.6±21.4 to 12.9±14.7% (P<0.05). Conclusion ST-segment depression is rather common in patients with moderate to severe SDB, and CPAP treatment can significantly reduce the duration of ST depression. ST depression in these patients may reflect the myocardial ischemia that really exists and the non-ischemic changes associated with recurrent SDB. (J Geriatr Cardiol 2007;4:101-4.)

Key Words ST-segment depression; myocardial ischemia; sleep-disordered breathing; continuous positive airway pressure

Sleep-disordered breathing (SDB) and coronary artery disease (CAD) often coexist and they have many similar risk factors. Some retrospective studies proved that the correlation exists between SDB and myocardial infarction, but the pathophysiological mechanism of their interaction is not yet clear. This study was aimed at determining whether SDB might lead to nocturnal myocardial ischemia reflected by ST-segment depression and whether this ischemia could be corrected after SDB is stopped by continuous positive airway pressure (CPAP).

Methods

Subjects After a diagnosis was made with clinical assessment and overnight polysomnogram (PSG) monitoring, 76 patients with moderate (20 < RDI < 40) to severe SDB (RDI ≥ 40) were enrolled in the study. Respiratory disturbance index (RDI) was defined as the number of apnea and hypopnea events per hour of sleep. Fifty-five patients were men and 9 were women, with a mean age of 50.4 ± 13.6 years and mean body mass index (BMI) of 30.6 ± 4.4 kg/m2. Through clinical questionnaire, no history of CAD (i.e. no symptoms and abnormal electrocardiogram) was found among patients. During the first night, overnight PSG examination and simultaneous 3-channel Holter monitoring were performed on all the patients in a sleep monitoring laboratory. During the second night, sleep and Holter monitoring were performed when they were treated with CPAP.

Sleep studies Patients were monitored overnight by polysomnography (Alice 3, Respironics Corp., USA). The recorded indexes included electroencephalogram (EEG, C3-A2, C4-A1), electro-oculogram (EOG), genioglossus electromyogram (EMG), electrocardiogram (ECG), thoracic
breathing, abdominal breathing, airflow at the nose and mouth, blood oxygen saturation (SaO₂), snore, body position, movement of limbs, etc. Data were recorded continuously, stored in the computer and analyzed on the following day.

Sleep apnea was defined as the absence of airflow at the nose and mouth for longer than 10 seconds; sleep hypopnea was defined as a reduction in airflow by at least 50% associated with a corresponding SaO₂ decrease. Blood oxygen desaturation was measured as the percentage of sleep time spent at SaO₂ below 90% (TS₉₀/TST) and mean blood oxygen saturation (MSaO₂). Arousal was defined as sustained waking state from sleep lasting for greater than 5 seconds. It was characterized by the distinctive δ wave on EEG, accompanied by eye movement and the activity on EMG. Arousal index is expressed as the number of arousal events per hour of sleep. Real-time recording of ECG was made by computer, and ST-segment depression, if preceded for less than 2 min by a disordered breathing event, was considered related to disordered breathing.

A clinical questionnaire was given to all patients on their general condition, present history, past history, and clinical symptoms.

Holter monitoring

PSG examination and simultaneous Holter monitoring were performed on all the patients during the same night. The time of Holter monitoring was adjusted similarly to that of PSG. ECG leads included II, V₅, and V₆, with frequency ranging from 0.05 to 100 Hz. On the following day, data were analyzed by Oxford Excel 2 system on the computer and manually adjusted by experienced technicians. ST segment was measured from 0.06 sec after J point. A ST segment drop more than 1 mm from baseline lasting 1 min or more was considered an ischemic episode. After the integration of PSG and Holter monitoring data, the total duration (minutes) of ST depression was indexed to the total sleep time (minutes per hour of sleep).

Treadmill exercise test

Patients with abnormal ST-segment depression in Holter ECG recording underwent a treadmill exercise testing to evaluate the presence of inducible myocardial ischemia. The criterion is horizontal or downsloping ST-segment depression of more than 1 mm which appears in three continuous heartbeats 0.06 second after the J point.

Statistical analysis

Data were analyzed with statistic software (SPSS 10.0). All data were given as mean ± SD. The t-test was used to analyze the difference between two groups. The difference between before and after treatment was analyzed with paired t-test. Chi square test was employed to analyze the difference in constituent ratio. A P < 0.05 was regarded as statistically significant.

Results

Study population

All 76 patients had moderate to severe SDB, without history of CAD. Twenty-eight patients showed significant ST segment depression during their night sleep and the other 48 patients did not show any ST segment change. There were no significant differences in age, BMI, heart rate, and the severity of nocturnal sleep apnea/hypoxia between the two groups (Table 1).

Table 1. General conditions of patients in two groups

<table>
<thead>
<tr>
<th>Index</th>
<th>ST depression(n=28)</th>
<th>Normal ST(n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (year)</td>
<td>51.2±12.9</td>
<td>49.6±11.8</td>
</tr>
<tr>
<td>BMI</td>
<td>31.4±4.9</td>
<td>30.2±3.8</td>
</tr>
<tr>
<td>heart rate (time/min)</td>
<td>79±16</td>
<td>80±11</td>
</tr>
<tr>
<td>RDI (/h)</td>
<td>63.4±23.8</td>
<td>61.2±28.9</td>
</tr>
<tr>
<td>arousal index (/h)</td>
<td>51.2±18.9</td>
<td>48.8±14.6</td>
</tr>
<tr>
<td>TS90/TST (%)</td>
<td>50.6±21.4</td>
<td>50.7±23.9</td>
</tr>
<tr>
<td>MSaO₂(%)</td>
<td>86±8</td>
<td>87±6</td>
</tr>
</tbody>
</table>

BMI= body mass index; RDI= respiratory disturbance index; TS90/TST= the percentage of sleep time spent at SaO₂ below 90%; MSaO₂= mean blood oxygen saturation.

Twenty-eight patients in the ST depression group underwent treadmill exercise test. Three patients showed typical asymptomatic ischemic ST segment depression which was confirmed as reversible myocardial ischemia by nuclear scan. Other patients had negative results in the treadmill exercise test.

Effects of CPAP on ST-segment depression

Table 2 shows the changes in parameters of the ST depression group before and after CPAP treatment. Although great variation existed in the duration of ST depression that ranged from 6 min/h to 63 min/h among these patients, CPAP treatment significantly reduced each patient’s duration of ST depression. The mean duration of ST depression was reduced from 36.8 ± 18.9 min/h to 11.4 ± 13.2 min/h, with 5 patients showing no ST depression after treatment. CPAP treatment significantly decreased RDI and TS₉₀/TST, increased mean blood oxygen saturation and also improved the quality of sleep. The proportion of nonrapid eye movement (NREM) I and II sleep was significantly decreased, while the proportion of rapid eye movement (REM) sleep was significantly increased. In addition, the proportion of slow wave sleep (i.e. NREM III and IV sleep) were also increased (without statistical significance). By analyzing the whole distribution of ST segment depression,
we found that 75 ± 21 percent of ST depression occurred in NREM I and II sleep, 4 ± 7 percent in slow wave sleep, and 22 ± 16 percent in REM sleep.

Since sleep architecture, SaO₂, RDI and arousal index were ameliorated with the amelioration of ST segment depression, we further compared the values of above parameters during periods of ST depression with those during the periods when ST segments were isoelectric. No significant difference was found in sleep architecture and MSaO₂ between the two conditions, whereas the RDI and arousal index were significantly higher during periods of ST depression than when ST segments were isoelectric. Under these two conditions, RDI was 65.8 ± 38.6/h and 33.2 ± 20.7/h, and arousal index 47.9 ± 22.3/h and 23.2 ± 14.4/h, respectively. These results suggested that amelioration of ST depression after CPAP treatment is possibly related to the decrease in RDI and arousal index.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before CPAP treatment</th>
<th>After CPAP treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST depression (%)</td>
<td>13.6±8.8</td>
<td>3.8±5.4*</td>
</tr>
<tr>
<td>RDI/(h)</td>
<td>63.4±23.8</td>
<td>8.1±6.6*</td>
</tr>
<tr>
<td>Arousal index (/h)</td>
<td>51.2±18.9</td>
<td>9.6±5.4*</td>
</tr>
<tr>
<td>TS90/TST (%)</td>
<td>50.6±21.4</td>
<td>12.9±14.7*</td>
</tr>
<tr>
<td>Total sleep time (h)</td>
<td>4.9±0.8</td>
<td>4.6±0.7</td>
</tr>
<tr>
<td>I sleep (%)</td>
<td>18.2±7.6</td>
<td>8.3±5.4*</td>
</tr>
<tr>
<td>II sleep (%)</td>
<td>57.3±18.3</td>
<td>30.2±13.4*</td>
</tr>
<tr>
<td>Slow wave sleep (%)</td>
<td>8.4±10.3</td>
<td>22.9±17.6*</td>
</tr>
<tr>
<td>REM sleep (%)</td>
<td>15.7±13.3</td>
<td>38.6±14.3*</td>
</tr>
</tbody>
</table>

*P<0.05 compared with before treatment ST depression; the percentage of duration of ST depression in total sleep time; RDI= respiratory disturbance index; TS90/TST= the percentage of sleep time spent at SaO₂ below 90%; REM=rapid eye movement

Discussion

Our results showed that 37% of patients with moderate to severe SDB without history of CAD had asymptomatic ST-segment depression in their sleep. After SDB was ameliorated by CPAP treatment, the duration of ST depression was significantly reduced. To our knowledge, possible reasons might be nonspecific changes unrelated to sleep apnea, myocardial ischemic changes, or nonischemic changes associated with sleep apnea.

All cases had no history of angina and myocardial infarction. Only three patients had positive results in the treadmill exercise test, and nuclear scan proved that they had reversible ischemia. These results indicated that the incidence of latent CAD was 3.9% in this group of patients, which is consistent with reported incidence of 2.5%-5.0% in the population at large. 5-6 ST-segment depression during sleep in these patients probably represented true myocardial ischemia, 7 and significant amelioration of ST-segment depression after CPAP treatment suggested that this kind of myocardial ischemia is caused by recurrent sleep apnea during sleep.

In this study, among 28 patients with ST-segment depression during sleep, 25 showed no evidence of myocardial ischemia in the exercise test. This could not exclude the possibility that the ST depression in these patients was caused by myocardial ischemia during sleep. 8 Recurrent apnea can result in great change in intrathoracic pressure and severe hypoxemia, which leads to an increase in the preload and afterload, in the oxygen requirement, and subsequent myocardial ischemia. All these may not occur during the exercise test that is limited by symptom. Intrathoracic pressure is decreased when SDB occurs. This causes the increase in the preload and afterload of left ventricle, thus increasing the pressure on left ventricular wall and the oxygen requirement of cardiac muscle. 9 Previous animal experiments showed that periodic hypoxia could cause the partial occlusion of anterior descending branch of coronary artery in the dog, thus resulting in myocardial ischemia. 10 SDB was often accompanied by hypoxia, which can cause myocardial ischemia in patients with CAD. 11 Decrease in oxygen supply and simultaneous increase in oxygen requirement elevate the risk of patients with CAD. Myocardial ischemia will further develop on the base of previous coronary artery disease.

Besides reducing the duration of nocturnal ST-segment depression, CPAP treatment can also improve the sleep architecture, relieve the hypoxemia and decrease the frequency of apnea and related arousal (Table 2). To prove whether the amelioration of ST depression can be attributed to these simultaneous changes, we compared the sleep architecture, MSaO₂, RDI, and arousal index during periods of ST depression with those during the time when the ST segments were isoelectric. When the patients were not on CPAP, no significant difference was found in sleep architecture and MSaO₂ between the two conditions, whereas the RDI and arousal index were significantly higher during periods of ST depression. These results indicate that ST depression is possibly caused by the changes associated with recurrent arousals. Arousals can stop apnea and are accompanied by excessive ventilation. Research has shown that excessive ventilation can lead to ST depression and abnormal T waves. 12 Patients with SDB exhibit increased activity of the sympathetic nervous system, and CPAP treatment can ameliorate this abnormality. 13, 14 Therefore, ST depression during sleep may be caused by the arousal-related intermittent excessive ventilation and increased activity of the sympathetic nervous system. These abnormal changes can be ameliorated through CPAP treatment.
When apnea occurs, change in intrathoracic pressure can cause esophageal reflux and spasm. These factors may lead to the abnormal changes of ST segment and T wave. CPAP treatment can reduce the esophageal reflux and the associated ST segment and T wave changes. Moreover, it has been reported that apnea can increase intracranial pressure and decrease cerebral perfusion, both of which are corrected by CPAP. Once again, ST segment and T-wave changes may accompany these neurological symptoms. This can explain the ST depression of some patients with CAD in our study. Further research is needed to confirm all these potential factors.

Whether ST-segment depression in these patients is caused by myocardial ischemia or by non-ischemic changes associated with SDB, the influence from SDB should be taken into account for the ST depression in Holter monitoring. Especially when ST depression mainly occurs during sleep, the importance of SDB should be given full consideration. Rational treatment of SDB may have a great clinical prospect for reducing the occurrence of myocardial ischemia.

Acknowledgement

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References