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Journal of Nanjing Medical University, 2009, 23(1):59-63
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*Research paper*

# Relationship between obstructive sleep apnea hypopnea syndrome and cardiovascular disorders in adult snorers

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Received 23 September 2008

## Abstract

**Objective:**To investigate the relationship between sleep apnea hypopnea syndrome(OSAHS) and some cardiovascular disorders in adult habitual snorers as well as the effectiveness of nasal continuous positive airway pressure(NCPAP) on those with OSAHS. **Methods:** With the use of polysomnography, 262 adult habitual snorers were examined and divided into the OSAHS group and the Non-OSAHS group (control). Using ambulatory electrocardiogram and blood pressure measurement, daily nocturnal rhythm of blood pressure, hypertension, heart rate variability, some arrythmias and angina pectoris of coronary heart disease were monitored and compared between the two groups, before and after 14 days of treatment with NCPAP in the OSAHS group. **Results:**This study indicated a higher incidence (39.6%) of OSAHS in adult snorers and demonstrated that there was a significantly higher incidence of hypertension, disappearance of the daily nocturnal rhythm of blood pressure, poor effectiveness of nitrate on angina pectoris of coronary heart disease, decreased heart rate variability during sleep, increased arrythmias and lower $SpO_2$ levels in the OSAHS group than in the Non-OSAHS group. After NCPAP treatment during sleep, snoring control, significantly higher $SpO_2$ and lower apnea hypopnea indices were achieved in the OSAHS group; heart rate variability and daily nocturnal rhythm of blood pressure returned to normal levels. **Conclusion:**The results of this research suggested that there was a close relationship between the development of OSAHS and some cardiovascular disorders. Furthermore, NCPAP treatment was effective not only on OSAHS but also on coexisting cardiovascular disorders.

*Key words*: Obstructive sleep apnea hypopnea syndrome; cardiovascular disorder; snoring

## INTRODUCTION

Obstructive sleep apnea hypopnea syndrome (OSAHS) is characterized by apnea and hypopnea during sleep, usually following snoring. It has been reported that the incidence of cardiovascular diseases is usually significantly higher in patients with OSAHS[1-4]. Moreover, it is often found in clinical practice that OSAHS patients with cardiovascular complications usually have a better response to nasal continuous positive airway pressure(nCPAP) treatment[5-7]. To better elucidate this phenomenon, we investigated the association between OSAHS and some cardiovascular disorders, as well as the effectiveness of nCPAP on OSAHS and coexisting cardiovascular disorders in those patients.

## MATERIALS AND METHODS

### Subjects

From October of 2000 to March of 2007, a total of 262 adult habitual snorers(216 males and 46 females, aged 33-66 yrs with a mean age of 49.2 ± 1.4 yrs) were recruited by the hospital's outpatient or inpatient departments of pulmonology or cardiology. Their body mass index(BMI) ranged between 23.8~29.9(26.2 ± 2.1). All of them had obvious snoring during sleep as indicated by complaints by their family members. For better monitoring, all of the observed snorers received a few days hospitalization, beginning from the day of the polysomnography(PSG) examination. Antihypertension drugs were stopped from 3 days before the PSG examination until the end of observation period.

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During the process of subject recruitment, all those with a history or evidence of other chronic respiratory diseases, or cerebral or renal diseases, or diabetes, or BMI ⩾ 30 were excluded from this investigation.

### Diagnosis and group division

A Compumedic PSG(Compumedic Co, Australia) was used to measure and record overnight PSG parameters such as 32 channels' electro-encephalogram, electrocardiogram(ECG), electrooculogram, chin and bilateral anterior tibial electromyogram, chest and abdominal movements by strain gauges, and pulse oxygen saturation($SpO_2$). All tracings were scored manually according to standard criteria. Apnea was diagnosed when cessation of airflow occurred for more than 10s, while hypopnea was identified when there was more than a 50% reduction in airflow and a 3% reduction of $SpO_2$ was observed. The event was considered obstructive when paradoxical chest contraction and abdominal movement were detected. The apnea/hypopnea index(AHI) is defined by the combined number of apnea and hypopnea events per hour of sleep. The mininal criteria for diagnosis of OSAHS is a AHI=5, with the predominant apnea events being obstructive ones[8]. All the snorers were divided into OSAHS group or non sleep apnea hypopnea syndrome(Non-OSAHS) group according to the diagnostic criteria of AHI.

The two groups were compared using the following criteria: blood pressure(Bp) change, conditions related to coronary heart disease(CHD), heart rate variability (HRV), cardiac arrhythmias, and $SpO_2$ levels.

### 24-hours ambulatory ECG and blood pressure monitoring

Subjects' ECGs were monitored continuously with a Marquetter Holter ECG(MARS 8000, MARS Co. Lit, U.S.A.) and their Bps were measured at 30-minute intervals for 24 hrs by an automatic Bp recording system. Nocturnal cardiac arrythmias, day and nocturnal mean arterial pressure average(dMAP and nMAP, MAP=diastolic Bp+1/3 pulse pressure), declined percentage of MAP at night and nMAP, dMAP ratios (nMAP/dMAP × 100%) of all subjects were monitored for comparison between the two study groups.

### Diagnosis of angina pectoris of CHD and evaluation of nitrate's effectiveness on agina pectoris

Angina pectoris of CHD was diagnosed according to the diagnostic criteria of the World Health Organization[9]. Poor effectiveness of nitrate on angina was determined if subjects felt no significant relief of angina after taking nitrate following the occurrence of angina pectoris.

### Analysis of heart rate variability(HRV)

HRV was tested by phase analysis as used by Luigi FS *et al*[10], during different sleep stages in 262 snorers in the OSAHS group, and the Non-OSAHS group before and after 14 days nCPAP treatment in the OSAHS group.

### nCPAP treatment

The nCPAP treatment was performed on 82 confirmed cases of OSAHS. Through use of pressure titration performed with AutoSet T auto-CPAP devices (ResMed Co. Australia), the most optimal treatment pressure for each OSAHS case was established during the first night's nCPAP treatment, and this was followed by 14 days of successive nCPAP treatment during sleep. The treatment lasted 6~8 hrs per night with pressures ranging from 7.4~15.8 $cmH_2O$. All parameters of the OSAHS cases were tested again following the nCPAP treatment.

### Statistical analysis

All parameters were expressed as $\bar{x} \pm s$. u test was used for comparison between the two groups. A $p$ value of less than 0.05 was considered statistically significant.

## RESULTS

After PSG examination on 262 adult snorers, 143 snorers with a AHI=5(21.4 ± 12.3) were diagnosed as OSAHS and assigned to the OSAHS group while the other 119 snorers with a AHI < 5 were assigned to the Non-OSAHS group. The BMI showed no statistically significant difference between the OSAHS and Non-OSAHS groups(26.1 ± 2.0 vs 27.1 ± 2.3, $P > 0.05$).

The comparison of cardiovascular abnormalities between the two groups is shown in ***Table 1***, which indicates that in the OSAHS group, there was a significant increase in the incidence of hypertension, disappearance in daily nocturnal rhythm of Bp, angina pectoris of coronary heart disease(CHD), poor effectiveness of nitrate in relieving angina, nocturnal cardiac arrythmias, average $SpO_2$<95%, and minimal $SpO_2$ < 70%.

As shown in ***Table 2***, there was a significant increase of AHI, nMAP, Bp day nocturnal rhythm and ratio of nMAP to dMAP in the OSAHS group, but a significant decrease in the average and minimal nocturnal $SpO_2$, HRV during non-rapid eye movement sleep(NREM), and percentage decrease from average dMAP to nMAP, compared with Non-OSAHS group.

***Table 3*** indicates that after nCPAP treatment in 82 patients in the OSAHS group, the abnormal high AHI, and the decreased average and minimal nocturnal $SpO_2$ returned to normal. The disappearance of blood pressure day nocturnal rhythm, and the declined HRV

***Table 1*** **Comparison of rates of coexisting cardiovascular disorders between OSAHS and Non-OSAHS groups**

| | OSAHS group case(%)(*n*=143) | Non-OSAHS group case (%)(*n*=119) | *P* value | $x^2$ value |
|---|---|---|---|---|
| Hypertension | 68(47.6) | 27(22.7) | 0.000 | 4.862 |
| Disappearance of Bp day nocturnal rhythm | 143(100) | 6( 5.0) | 0.000 | 4.782 |
| Angina pectoris of CHD | 27(18.9) | 10( 8.4) | 0.000 | 5.682 |
| Poor response to nitrate on angina | 18(12.6) | 4( 3.4) | 0.000 | 6.772 |
| Nocturnal arrhythmia | 56(39.2) | 14(11.8) | 0.000 | 6.742 |
| Brachycardia | 27(18.9) | 6( 5.0) | 0.024 | 2.305 |
| Ⅱ° AVB | 10( 8.4) | 4( 3.4) | 0.037 | 2.147 |
| Ventricular premature complex( > 5/min) | 28(19.6) | 11( 9.2) | 0.007 | 7.024 |
| Average nocturnal $SpO_2$ < 95% | 59(41.3) | 11( 9.2) | 0.000 | 8.129 |
| Lowest nocturnal $SpO_2$ < 70% | 77(53.8) | 0( 0.0) | 0.000 | 8.329 |

Bp: blood pressure, CHD: coronary heart disease, AVB:atrial-ventricular block, $SpO_2$: pulse oxygen saturation.

***Table 2*** **Comparison of AHI, HRV, $SpO_2$ and blood pressure during sleep between OSAHS and NON-OSAHS group**

| | OSAHS group (*n*=143) | Non-OSAHS group (*n*=119) | *P* value | u value |
|---|---|---|---|---|
| AHI | 21.4 ± 12.3 | 2.2 ± 1.1 | 0.000 | 8.312 |
| Average $SpO_2$ | 90.4 ± 2.8 | 96.9 ± 1.3 | 0.024 | −2.374 |
| The lowest $SpO_2$ | 78.3 ± 8.2 | 90.8 ± 5.8 | 0.000 | −6.327 |
| HRV REM | 1.5 ± 0.2 | 1.4 ± 0.3 | 0.073 | 0.312 |
| HRV NREM | 1.2 ± 0.2 | 1.5 ± 0.1 | 0.042 | −2.873 |
| d MAP(mmHg) | 112.2 ± 21.1 | 106.9 ± 15.8 | 0.064 | 0.402 |
| n MAP(mmHg) | 114.2 ± 18.1 | 91.3 ± 14.2 | 0.037 | 1.967 |
| Percentage decrease from dMAP to nMAP | 2.0 ± 1.6 | 16.0 ± 3.2 | 0.000 | −8.317 |
| nMAP/dMAP(%) | 101.8 ± 7.2 | 85.4 ± 6.2 | 0.000 | 4.317 |

Values are presented as mean ± standard deviation.

MAP: mean arterial pressure(diastolic Bp+1/3 pulse pressure).

***Table 3*** **Comparison of parameters before and after nCPAP treatment in OSAHS group[case (%)]**

| | pre-nCPAP case(%)(*n*=82) | post-nCPAP case(%)(*n*=82) | *P* value | $x^2$ value |
|---|---|---|---|---|
| AHI ⩾ 5 | 82(100.0) | 0(0.0) | 0.000 | 8.498 |
| Rhythm disappearance of day-to-night Bp | 82(100.0) | 4(4.9) | 0.000 | 8.169 |
| Average nocturnal $SpO_2$ < 95% | 74( 90.2) | 2(2.4) | 0.000 | 8.542 |
| The lowest nocturnal $SpO_2$ < 70% | 44( 53.7) | 0(0.0) | 0.000 | 8.843 |
| HRV decrease in NREM | 66( 80.5) | 5(6.1) | 0.000 | 7.321 |
| Ventricular extrasystoles( > 5/min) | 23( 30.5) | 11(7.3) | 0.000 | 6.215 |
| Nocturnal angina pectoris | 15( 18.3) | 3(3.7) | 0.000 | 7.022 |
| Poor effectiveness of nitrate to angina | 15( 18.3) | 7(8.5) | 0.026 | 2.241 |

AHI:apnea hypopnea index, HRV:heart rate variability, NREM: non-rapid eye movement sleep.

during NREM greatly recovered, and both the frequency of nocturnal ventricular extrasystoles and the prevalence of nocturnal angina pectoris were significantly reduced.

## DISCUSSION

Our investigation indicated that there was a higher prevalence(39.6%) of OSAHS in adult habitual snorers. The incidences of cardiovascular disorders such as hypertension, CHD and cardiac arrhythmias were significantly higher in our OSAHS group than in the non-OSAHS group. Epidemiological research conducted abroad has suggested a strong correlation between OSAHS and hypertension, and it was considered that in the pathogenesis of hypertension OSAHS could serve as an important risk factor independent of age, body weight, diet, heredity and so on[1-3,11].

Our study demonstrated that there was a significantly higher incidence of hypertension in the OSAHS group than in the Non-OSAHS group and a disappearance of diurnal blood pressure rhythm. The physiological blood pressure day-night rhythm is described as the phenomenon in which the normal nocturnal blood pressure during sleep is about 10% lower than the day-time blood pressure, reaching its minimal level at about 2:00-3:00 a.m. This is considered a protective mechanism in

humans. Disappearance of the diurnal blood pressure rhythm, especially caused by an increase in nocturnal Bp, may lead to a higher occurrence of acute cardiovascular diseases, cerebral stroke and furthermore enhance damage to target organs[12-13]. Elevation in blood pressure is associated with the severe degree of low oxygen saturation and hypoxemia. As a chemoreceptor reflex stimulant of blood pressure, hypoxemia can increase sympathetic tone, thereby increasing heart rate, contractility and vasoconstriction, increasing blood pressure. Upper airway occlusion during apnea can cause an increase in negative intrathoracic pressure and therefore an increased venous return, which, together with arousals, can in turn increase blood pressure. Nocturnal increase of blood pressure and damage to target organs may occur as a result of periodic hypoxemia and neuroendocrine abnormalities such as activated catecholamine, endothelin and other blood pressure increasing substances. After treating OSAHS patients with nCPAP, recovery may take place in the secretion of some hormones involved in blood volume regulation, such as renin-angiotensin-aldosterone and atrial natriuretic peptide[14-15].

OSAHS is also closely associated with CHD[16-17]. In this investigation no cases with myocardial infarction were found in either group. However, there was a significantly higher incidence of angina pectoris of CHD in the OSAHS group. Our observation revealed that all the cases of adult snorers who experienced attacks of nocturnal angina had both OSAHS and angina of CHD, while only 3 out of 10 cases of angina of CHD in the non-OSAHS group suffered such attacks. Compared with those cases with angina of CHD only, the cases with angina and OSAHS displayed poorer relief with nitrates following an angina attack, which seemed to be one of the characteristics of snorers with both OSAHS and angina of CHD. Frequent nocturnal myocardial ischemia has much to do with apnea and the lowering of oxygen saturation during sleep. There is evidence that hypoxemia resulting from obstructive apnea could cause nocturnal myocardial ischemia and this phenomenon could be attenuated or prevented by nCPAP treatment1. We also found that all 15 cases with angina of CHD receiving nCPAP in the OSAHS group showed no occurrence of nocturnal angina during the treatment, even though their day-time angina still occurred. Of the 15 cases, 8 cases showed significant improvement in the effectiveness of nitrate to relieve angina, which may be related to the improved nocturnal myocardial ischemia with nCPAP treatment.

The incidence of nocturnal cardiac arrhythmia during sleep was significantly higher in the OSAHS group than in the non-OSAHS group. Sinus bradycardia, sinus standstill, Ⅱ° AVB and ventricular premature complexes were the main types of arrhythmia. Our investigation of HRV indicated that HRV during NREM sleep was significantly reduced in the OSAHS group, which could be explained as the result of disturbed autonomic neural activity, which is acknowledged to be a significant cause of arrhythmia in OSAHS patients18-19.

nCPAP treatment can stabilize blood gases and ventilation in OSAHS patients due to the enlargement of easily collapsible upper airway, improvement of regulation of breathing through the respiratory centers and an increase in end expiratory lung volume 20. In our study the following improvements during sleep were identified after 7 days of nCPAP treatment in the OSAHS group:① significant decline of AHI, from 21.4 ± 12.3 to 1.1 ±1.0; ②remarkable increase in average and minimal nocturnal SpO2 levels during sleep; ③ notable decrease in nocturnal ventricular ectopic premature complexes; ④recovery of HRV during NREM; ⑤absence of snoring; ⑥ restoration of physiological Bp day nocturnal rhythm. In view of these findings, it should be recognized that OSAHS plays an important role in the etiology and development of cardiovascular disorders. The application of nCPAP can affect not only OSAHS, but also coexisting cardiovascular diseases as well.

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