Obstructive Sleep Apnea-hypopnea Syndrome Patients with Overweight and Hypertension in a Japanese Workplace

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Abstract: Obstructive Sleep Apnea-hypopnea Syndrome Patients with Overweight and Hypertension in a Japanese Workplace: Ken Okabayashi, et al. JR East Health Promotion Center, East Japan Railway Company—The objective of this study was to determine the relationship between obstructive sleep apnea-hypopnea syndrome (OSAHS) and overweight combined with hypertension and to examine whether OSAHS in conjunction with overweight and hypertension is associated with daytime sleepiness. In a Japanese workplace of 28,636 employees, 368 men (19–62 yr old), who were anxious regarding their OSAHS symptoms, underwent home pulse oximetry. Of these, 153 men subsequently underwent all-night polysomnography (PSG), and OSAHS was diagnosed in 149. We next classified these 149 men into the following groups: A [Overweight (–)/Hypertension (–), n=41], B [Overweight (–)/Hypertension (+), n=15], C [Overweight (+)/Hypertension (–), n=46], and D [Overweight (+)/Hypertension (+), n=47]. The Epworth Sleepiness Scale (ESS) was used to evaluate daytime sleepiness and the apnea-hypopnea index (AHI) was used to evaluate the severity of OSAHS. The averages of the ESS score and the AHI were compared in each group. Both the average ESS scores and the percentage of ESS scores ≥11 were not significantly different among the groups. The average AHI of group D was the highest among all of the groups and that of group C was significantly higher than those of groups A and B. In all the groups, the OSAHS patients with overweight and hypertension in this study had the highest AHI. The level of daytime sleepiness evaluated by the ESS in this study was almost the same in the OSAHS patients regardless of the degree of overweight or hypertension. These observations suggest that it is necessary to positively recommend PSG to men who are suspected of having OSAHS with overweight and hypertension, even if they do not have daytime sleepiness.


Key words: Epworth Sleepiness Scale (ESS), Home pulse oximetry, Hypertension, Overweight, Polysomnography, Sleep apnea

Accumulating evidence has suggested that obstructive sleep apnea-hypopnea syndrome (OSAHS) is not only a phenomenon of the cessation of breathing during sleep but also the cause of sleepiness during the day and various other physical disorders1–3). Moreover, neurocognitive sequelae, such as daytime sleepiness and impaired executive function, are important factors implicated in motor vehicle accidents and probably contribute to the loss of work-related productivity4). The true prevalence of OSAHS in Japan has not been established. A community-based study of sleep apnea in middle-aged Chinese men (30–60 yr old) residing in Hong Kong used full polysomnography (PSG) and demonstrated an estimated 4.1% prevalence of OSAHS5). Most population-based studies that have estimated the sex-specific prevalence have indicated a greater risk of OSAHS in men than in women6). Thus, OSAHS is common in adult males and remains an important public health problem. However, many people with OSAHS remain undiagnosed and untreated because the symptoms of OSAHS, such as snoring and cessation of breathing, are not necessarily
recognized.

While screening for OSAHS, it is necessary to look for various objective symptoms such as overweight and hypertension rather than rely on subjective symptoms. Overweight and obesity are known to be risk factors for the development of OSAHS. Several studies have demonstrated that OSAHS is related to the development of hypertension. However, to our knowledge, few epidemiological studies have examined the relationship between OSAHS and overweight combined with hypertension. We have initiated an OSAHS awareness program in a Japanese workplace from the viewpoint of preventing traffic and labor accidents and with respect to health promotion and preventive medicine. The purpose of this study was to determine the relationship between OSAHS and overweight combined with hypertension and to examine whether OSAHS in conjunction with overweight and hypertension is associated with daytime sleepiness in a Japanese workplace.

Materials and Methods

Subjects and measurements

The study population comprised 28,636 employees (male, 26,111; female, 2,525) in a workplace in Japan. In March 2003, we produced pamphlets and an educational video on OSAHS and distributed these to each section in the workplace. The participants watched the video and read the pamphlets. In these pamphlets and the video, persons with symptoms such as snoring or cessation of breathing when sleeping as identified by family members, and who experienced drowsiness during the daytime, were particularly encouraged to undergo home pulse oximetry. In this study, 368 male subjects (19–62 yr old), who were anxious regarding their OSAHS symptoms, were recruited from a workplace in Japan and underwent home pulse oximetry once over a 2-yr period (April 2003–March 2005). Since there were only 4 females subjects with similar symptoms, females were excluded from this study.

The subjects volunteered to undergo home pulse oximetry as a screening test for OSAHS. Next, the use of a pulse oximeter was explained to these subjects. They answered several questions regarding their OSAHS symptoms, including those scored by the Epworth Sleepiness Scale (ESS), underwent physical examinations, including the measurement of height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP); and also underwent an oropharyngeal examination. The ESS is a questionnaire on daytime sleepiness. It consists of 8 questions each allocated a score from 0 to 3 according to the subjects daytime sleepiness; an excessive daytime sleepiness is defined as an ESS score ≥11. Blood pressure was measured twice in the left arm during the daytime using a manual mercury sphygmomanometer. The measurements were taken by a physician or nurse after the subjects had rested for ≥5 min in a seated position in a quiet area. Subsequently, the means of 2 separate SBP and DBP measurements were calculated in order to derive the blood pressure values that are reported in this study. The subjects underwent pulse oximetry at home during their sleep. A PULSOX-3Si (Minolta Co. Ltd., Japan) pulse oximeter was used for this purpose. The internal memory of this device stored the values of blood oxygen saturation by performing a moving average for the last 5 s and updated the data every second. This sampling time was sufficiently short to avoid underestimating oxygen desaturation. The data thus obtained were fed into a personal computer and used to calculate the desaturation cycles per hour as an oxygen desaturation index (ODI).

The study protocol was approved by the Ethics Committee of the JR East Health Promotion Center and informed consent was obtained from all subjects prior to the commencement of this study.

Polysonnmography

Based on the results of the home pulse oximetry, we judged that the subjects with a 2% ODI ≥5 dips/h were those suspected of suffering from OSAHS. The subjects with a 2% ODI ≥5 dips/h were advised to undergo all-night PSG for a detailed examination of OSAHS. The reason for selecting a 2% ODI instead of either a 3% or 4% ODI was to avoid, as far as possible, overlooking apneas that were not accompanied by oxygen desaturation. Those subjects with a 2% ODI <5 dips/h, who were anxious regarding their OSAHS symptoms, were advised to undergo PSG.

PSG was performed at a sleep unit in the JR Tokyo General Hospital between 8 p.m. and 6 a.m. by using a Sleep-Watcher-P (Teijin Co. Ltd., Japan) as a digital PSG system. Oronasal airflow measured by a thermistor sensor, 4 channels of electroencephalogram, bilateral electro-oculogram, submental electromyography, electrocardiogram, movements of the chest and abdominal walls, arterial oxygen saturation, and snoring sounds were all recorded. Among the subjects undergoing PSG, OSAHS was diagnosed in those with an apnea-hypopnea index (AHI) ≥5 per hour, but was ruled out in those with an AHI <5 per hour. Apnea was defined as the complete cessation of airflow lasting more than 10 s, and hypopnea as a 50% visual reduction in airflow associated with a decrease of 3% or more in the arterial oxygen saturation of hemoglobin lasting more than 10 s. The AHI was defined as the number of apneas and hypopneas per hour of sleep.

Classification by a combination of overweight and hypertension

After establishing the baseline PSG, subjects in whom OSAHS was diagnosed were classified into group A

Classification by a combination of overweight and hypertension

After establishing the baseline PSG, subjects in whom OSAHS was diagnosed were classified into group A
[Overweight (–)/Hypertension (–)], group B [Overweight (–)/Hypertension (+)], group C [Overweight (+)/Hypertension (–)], and group D [Overweight (+)/Hypertension (+)]. Overweight (+) was defined as a body mass index (BMI) \( \geq 25 \) kg/m\(^2\) and Overweight (–) as a BMI <25 kg/m\(^2\). Hypertension (+) was defined as an SBP \( \geq 140 \) mmHg or a DBP \( \geq 90 \) mmHg. The subjects for whom hypertension had previously been diagnosed at hospital and who were under treatment were also included in group B (n=9) or D (n=19). Hypertension (–) was defined as an SBP <140 mmHg and a DBP <90 mmHg.

Data analysis

All groups were compared with respect to the average ESS score for the evaluation of sleepiness and the average AHI. The Mann–Whitney U test was used for the comparison of these averages among the groups. An analysis of covariance was used to compare the influence of BMI on the AHI among the groups. A chi-squared test was used to compare the percentages of ESS scores \( \geq 11 \) among the groups. A \( p \) value <0.05 was considered to be significant. Moreover, we analyzed the correlation of the AHI with the BMI of the subjects who underwent PSG. Correlations were tested by calculation of Pearson’s correlation coefficient (r). All analyses were performed using the statistical software SPSS (version 10.0).

Results

Baseline characteristics of the subjects classified by home pulse oximetry

The baseline characteristics of all the 368 male subjects classified on the basis of a 2% ODI, including sex, age, BMI, SBP, DBP and ESS, are shown in Table 1. Among the 368 subjects, 313 exhibited a 2% ODI \( \geq 5 \) dips/h. The remaining 55 subjects exhibited a 2% ODI <5 dips/h. Although 292 subjects (79.3%) were more than 40 yr of age and the remaining 76 subjects (20.7%) were less than 39 yr of age, all subjects were analyzed together as follows. In this study, 151 of the 313 subjects with a 2% ODI \( \geq 5 \) dips/h and 2 of the 55 subjects with a 2% ODI <5 dips/h underwent PSG. The reason why the 2 subjects with a 2% ODI <5 dips/h underwent PSG is that cessation of breathing during sleep was noted by family members and the subjects expressed a strong desire to undergo PSG. All the 313 subjects with a 2% ODI \( \geq 5 \) dips/h were advised to undergo all-night PSG; however, 162 of the 313 subjects did not undergo PSG either because of their work schedules or for economic reasons. Concerning the subjects with a 2% ODI \( \geq 5 \) dips/h, the averages of BMI and the ESS score, and the percentages of the ESS score \( \geq 11 \), were not significantly different between the 151 subjects who underwent PSG and the 162 subjects who did not undergo PSG (Table 1). The respective \( p \) values were not significant. Moreover, we analyzed the correlation of the AHI with the BMI of the subjects who underwent PSG. Correlations were tested by calculation of Pearson’s correlation coefficient (r). All analyses were performed using the statistical software SPSS (version 10.0).

Table 1. Baseline characteristics of the 368 subjects classified on the basis of a 2% ODI

| Pulse oximetry | Subjects (number) | Age (yr) | BMI (kg/m\(^2\)) | SBP (mmHg) | DBP (mmHg) | ESS (score) | ESS score \( \geq 11 \) (number) (%)
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</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>Total</td>
<td>55</td>
<td>43.0 ± 1.5</td>
<td>23.5 ± 0.4</td>
<td>127 ± 1.6</td>
<td>79.4 ± 1.4</td>
<td>8.0 ± 0.6</td>
</tr>
<tr>
<td>PSG (+)</td>
<td>2</td>
<td>39.5 ± 9.5</td>
<td>23.3 ± 3.6</td>
<td>128 ± 0.5</td>
<td>80.0 ± 5.0</td>
<td>8.5 ± 1.5</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>2% ODI (dips/h)</td>
<td>Total</td>
<td>313</td>
<td>46.2 ± 0.5</td>
<td>26.2 ± 0.2</td>
<td>132 ± 1.0</td>
<td>83.6 ± 0.7</td>
<td>8.3 ± 0.2</td>
</tr>
<tr>
<td>( \geq 5 )</td>
<td>PSG (+)</td>
<td>151</td>
<td>46.0 ± 0.7</td>
<td>26.7 ± 0.4</td>
<td>133 ± 1.6</td>
<td>84.0 ± 1.1</td>
<td>8.7 ± 0.4</td>
</tr>
<tr>
<td>PSG (–)</td>
<td>162</td>
<td>46.5 ± 0.7</td>
<td>25.8 ± 0.3</td>
<td>131 ± 1.4</td>
<td>83.3 ± 0.9</td>
<td>8.0 ± 0.3</td>
<td>41 (25.3)</td>
</tr>
<tr>
<td>Total</td>
<td>368</td>
<td>45.7 ± 0.5</td>
<td>25.8 ± 0.2</td>
<td>131 ± 0.9</td>
<td>83.0 ± 0.6</td>
<td>8.3 ± 0.2</td>
<td>108 (29.3)</td>
</tr>
</tbody>
</table>

ODI, oxygen desaturation index; PSG, polysomnography; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth sleepiness scale. Age, BMI, SBP, DBP and ESS are represented as mean ± SEM.

Table 2. Baseline characteristics of the 153 subjects who underwent all-night PSG

| PSG | Subjects (number) | Age (yr) | BMI (kg/m\(^2\)) | SBP (mmHg) | DBP (mmHg) | ESS (score) | ESS score \( \geq 11 \) (number) (%)
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</thead>
<tbody>
<tr>
<td>AHI (per hour)</td>
<td>&lt;5</td>
<td>4</td>
<td>33.5 ± 7.2</td>
<td>25.6 ± 1.4</td>
<td>125 ± 11</td>
<td>83.5 ± 7.0</td>
<td>9.3 ± 2.5</td>
</tr>
<tr>
<td>( \geq 5 )</td>
<td>Total</td>
<td>149</td>
<td>46.2 ± 0.7</td>
<td>26.7 ± 0.4</td>
<td>133 ± 1.6</td>
<td>83.9 ± 1.1</td>
<td>8.7 ± 0.4</td>
</tr>
</tbody>
</table>

PSG, polysomnography; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth sleepiness scale; AHI, apnea hypopnea index. Age, BMI, SBP, DBP and ESS are represented as mean ± SEM.
Table 3. Baseline characteristics of the 149 subjects who underwent all-night PSG and in whom OSAHS was diagnosed

<table>
<thead>
<tr>
<th>Group</th>
<th>Subjects (number)</th>
<th>Age (yr)</th>
<th>BMI (kg/m²)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>ESS (score)</th>
<th>ESS score ≥11 (number) (%)</th>
<th>AHI (per hour)</th>
<th>AHI corrected for BMI (per hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>41</td>
<td>45.6 ± 1.3</td>
<td>22.8 ± 0.3</td>
<td>120 ± 1.7</td>
<td>74.7 ± 1.2</td>
<td>8.6 ± 0.6</td>
<td>12</td>
<td>29.3</td>
<td>27.6 ± 3.0</td>
</tr>
<tr>
<td>B</td>
<td>15</td>
<td>53.2 ± 1.4</td>
<td>22.9 ± 0.4</td>
<td>141 ± 2.7**</td>
<td>88.6 ± 1.8**</td>
<td>9.1 ± 1.2</td>
<td>5</td>
<td>33.3</td>
<td>24.7 ± 2.7</td>
</tr>
<tr>
<td>C</td>
<td>46</td>
<td>45.0 ± 1.4</td>
<td>27.4 ± 0.4***</td>
<td>123 ± 1.3</td>
<td>77.8 ± 0.9</td>
<td>9.4 ± 0.7</td>
<td>17</td>
<td>37.0</td>
<td>40.0 ± 3.0***</td>
</tr>
<tr>
<td>D</td>
<td>47</td>
<td>45.7 ± 1.3</td>
<td>30.4 ± 0.6***</td>
<td>151 ± 2.7***</td>
<td>96.4 ± 1.9***</td>
<td>7.9 ± 0.6</td>
<td>13</td>
<td>27.7</td>
<td>54.2 ± 3.6***</td>
</tr>
<tr>
<td>Total</td>
<td>149</td>
<td>46.2 ± 0.7</td>
<td>26.7 ± 0.4</td>
<td>133 ± 1.6</td>
<td>83.9 ± 1.1</td>
<td>8.7 ± 0.4</td>
<td>47</td>
<td>31.5</td>
<td>39.5 ± 1.9</td>
</tr>
</tbody>
</table>

Group A, Overweight (−)/Hypertension (−); Group B, Overweight (−)/Hypertension (+); Group C, Overweight (+)/Hypertension (−); Group D, Overweight (+)/Hypertension (+); PSG, polysomnography; OSAHS, obstructive sleep apnea-hypopnea syndrome; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ESS, Epworth sleepiness scale; AHI, apnea hypopnea index. Age, BMI, SBP, DBP, ESS and AHI are represented as mean ± SEM. *p<0.05 vs Group A, †p<0.05 vs Group B, #p<0.05 vs Group C.

Fig. 1. (A) The effects of overweight and hypertension on the Epworth Sleepiness Scale (ESS; score). None of the groups exhibited significant differences. (B) The effects of overweight and hypertension on the apnea-hypopnea index (AHI; per hour). Group D exhibited the highest AHI average of all the groups and the average AHI of group C was higher than those of groups A and B; these observations were statistically significant (*p<0.05). In particular, the average AHI of group D was higher than that of group C. The number presented is the total number of patients in each group.

<5 dips/h. Thus, OSAHS was diagnosed in 149 subjects, but ruled out in the remaining subjects (n=4) with an AHI <5 per hour. Table 2 shows the baseline characteristics of these 153 subjects who were classified on the basis of the AHI.

The relationship between ESS and AHI with the combination of overweight and hypertension

The subjects (n=149) in whom OSAHS was diagnosed were classified into groups A, B, C and D according to their BMI, SBP and DBP values. The baseline characteristics of these subjects are shown in Table 3. The average BMI of group D was significantly higher than that of group C. The range of the ESS among all groups was between 7.9 and 9.4. Although these ESS scores were relatively high, the average ESS score was not significantly different among all groups (Fig. 1A). Furthermore, the percentage of the ESS score ≥11 was also not significantly different among these groups (Table 3). Group D exhibited the highest AHI average among all the groups and the average AHI of group C was higher than those of groups A and B; these observations were statistically significant (p<0.05) (Fig. 1B). In particular, the average AHI of group D was higher than that of group

values were 0.063, 0.130 and 0.163.

Subjects who underwent all-night PSG

OSAHS was diagnosed in 147 of the 151 subjects with a 2% ODI ≥5 dips/h, and in the 2 subjects with a 2% ODI
However, the average AHI corrected for BMI was not significantly different among all the groups (Table 3).

A plot of BMI against AHI for those subjects (n=149) in whom OSAHS was diagnosed is shown in Fig. 2. The BMI and AHI were observed to be significantly correlated (r=0.568, p for slope <0.001) without the consideration of hypertension.

Discussion

The present study has demonstrated the relationship between OSAHS and overweight combined with hypertension. It is noteworthy that the level of daytime sleepiness evaluated by the ESS in this study was virtually the same in all the OSAHS patients regardless of the degree of overweight or hypertension.

The National Institutes of Health (NIH) and World Health Organization (WHO) guidelines define obesity as a BMI ≥30 kg/m², and overweight as a BMI ≥25 kg/m². OSAHS is an increasingly common disorder that is strongly related to overweight and obesity. Therefore, overweight and obesity are major risk factors for OSAHS. This study demonstrated that the average AHI of the groups with BMI ≥25 kg/m² (groups C and D) was higher than that of the groups with BMI <25 kg/m² (groups A and B). The exact underlying mechanisms that render the overweight or obese at risk of OSAHS are still unclear; however, it may be related to airway narrowing as a result of excessive soft tissue in the neck and around the uvula. In several other case-control studies, weight loss in OSAHS patients led to a significant decrease in the frequency of apnea. Further, it has been demonstrated that weight loss is associated with a decrease in upper airway collapsibility in OSAHS.

To our knowledge, there is no clinical evidence suggesting that hypertension causes OSAHS in humans. On the contrary, epidemiological and animal experimental studies have strongly supported the possibility that OSAHS could be one of the important factors contributing to hypertension. These studies have used various study designs; however, most of them had large sample populations, and all the studies have attempted to strictly account for confounding factors such as BMI and sex. Moreover, the Joint National Commission on Hypertension lists OSAHS first among treatable causes of hypertension. OSAHS causes the daytime elevation of blood pressure apparently due to multifactorial mechanisms. OSAHS also causes acute nocturnal surges in blood pressure in response to chemoreflex-mediated hypoxic stimulation of sympathetic activity with a resultant increase in peripheral vascular resistance and circulating catecholamine levels associated with sympathetic nerve activity. Further, it enhances vasoconstrictor sensitivity partly due to vascular remodeling by the nocturnal blood pressure surges. Moreover, the effective treatment of OSAHS with continuous positive airway pressure (CPAP) leads to a significant decrease in both nocturnal and diurnal blood pressure. The uniformity of these positive results has led some researchers to conclude that OSAHS is an important risk factor for hypertension that is independent of excess weight and other potential confounding factors and should be considered as a cause of secondary hypertension.

The relationship between overweight and hypertension is complex and probably represents an interaction of several factors; however, the interaction has been strongly supported by the epidemiologic data. As discussed above, considered individually, overweight and OSAHS are very strongly associated with hypertension. Furthermore, in this study, we observed that overweight and OSAHS coexist and that overweight may be conducive to OSAHS. Various putative pathophysiological mechanisms are involved in the interaction between overweight, OSAHS, and hypertension. These mechanisms are as follows:
Excessive daytime sleepiness is a cardinal feature of OSAHS and several studies have demonstrated an improvement in daytime sleepiness after the treatment of OSAHS. Sleep fragmentation due to repeated arousals from apneas and hypopneas is thought to be the cause of excessive sleepiness in patients with OSAHS. Because asymptomatic individuals are less likely to be evaluated for the presence of OSAHS than those who complain of sleepiness, patients presenting for evaluation and treatment of OSAHS may not be representative of the subjects with an elevated AHI in the general population. However, despite the strong association of the AHI with self-reported sleepiness, the majority of subjects for whom OSAHS was diagnosed did not report excessive sleepiness. The observed variation in the resultant sleepiness was not explained; however, the perception and reporting of daytime sleepiness appear to vary greatly among individuals. The ESS is widely used as a valid measure to evaluate the degree of daytime sleepiness. In this study, the OSAHS patients with overweight and hypertension did not necessarily have the highest ESS score. However, this result needs careful consideration as the ESS is thought of as a valid measure of daytime sleepiness. Therefore, the necessity of explaining the factors underlying the individual differences in susceptibility to daytime sleepiness has been suggested.

The present study has 3 limitations. First, we did not include a large community-based sample population. Instead we recruited only subjects from a Japanese workplace who were anxious regarding their OSAHS symptoms. This might have resulted in the elevation of the average BMI or ESS scores. Second, pulse oximetry inherently underestimates apnea during sleep compared with full PSG, particularly in a non-obese population, and overestimates apnea by picking up artifacts caused by body movements and vasoconstriction. The reasons for the lower sensitivity of pulse oximetry among lean subjects have been considered to include the functional reserve of lung volume sufficient to maintain normal blood oxygen levels and the difficulty in detecting hypopneic events that do not cause oxygen desaturation. In fact, in this study, 2 subjects with a 2% ODI < 5 dips/h were diagnosed as having OSAHS by PSG. Third, the passage of screening in this study was not uniform. Consequently, 162 of the 313 subjects with a 2% ODI > 5 dips/h did not undergo PSG. Because of this we could not prove the validity of home pulse oximetry for the screening test of OSAHS.

In conclusion, the OSAHS patients with overweight and hypertension in this study had a higher AHI than those with only overweight, with only hypertension, or with neither overweight nor hypertension. The level of daytime sleepiness evaluated by the ESS in this study was virtually the same in all OSAHS patients regardless of the degree of overweight or hypertension. Based on these observations, it is suggested that it is necessary to positively recommend PSG to men who are suspected of having OSAHS with overweight and hypertension even if they do not suffer from daytime sleepiness.

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