Sleep-disordered Breathing and Hypertension in Japanese Steel Workers

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Abstract: Sleep-disordered breathing (SDB) is the major determinants of hypertension. Recent studies indicated sleep duration, in addition to shift work, were also associated with hypertension. But very little attention has been paid to these two factors when looking at the effects of SDB on blood pressure. We conducted the present study to evaluate the relationship between SDB and hypertension adjusting for sleep duration and shift work in a sample of Japanese steel workers. In this cross-sectional study, we measured blood pressure and oxygen desaturations index (ODI) by nocturnal pulse oximetry of 249 male workers aged 20 to 65 yr. SDB was defined by 3% ODI level of 15 or more events per hour. Logistic regression analyses were performed to estimate the associations of SDB with hypertension after adjustment for age, body mass index, alcohol intake, smoking, usual sleep duration, shift work, and occupation. The prevalence of SDB was 18.1%. The adjusted odds ratio of hypertension for high (≥15) vs. low (<15) category of 3% ODI level was 2.86 (95% confidence interval, 1.23–6.66). The significant association between SDB and hypertension suggests that screening for SDB among steel workers is useful for prevention of hypertension.

Key words: Sleep-disordered breathing, Hypertension, Sleep duration, Shift work, Occupation

Introduction

Sleep-disordered breathing (SDB) is one of the major determinants of hypertension. The casual relationship between SDB and hypertension has been supported by both epidemiological and animal experimental studies. Several population-based studies with large sample sizes performed in Western countries have demonstrated a positive association between SDB measured by polysomnography (PSG) and blood pressure levels/hypertension1–3). Nieto et al. have showed independent association between SDB and hypertension especially in middle-aged participants2). An animal experiment using a canine model demonstrated that daytime blood pressure increased after experimentally induced intermittent airway occlusion during nocturnal sleep and fell after a nighttime sleep with quiet breathing4). Thus, the seventh Report of the Joint National Committee (JNC7) included sleep apnea as the first disorder on the list of identifiable causes of hypertension5).

Recently, several epidemiological studies have showed significant association between usual sleep duration and hypertension. Gottlieb et al. have reported that those sleeping less than 6 h per night had adjusted odds ratio for hypertension of 1.66 (95%CI: 1.35–2.04), compared to subjects sleeping 7 to less than 8 h per night6). Gangwisch et al. have reported that sleep durations of ≥5 h per night were associated with a significantly increased risk of hypertension (hazard ratio: 2.10, 95%CI: 1.58–2.79)7).

Two longitudinal studies in Japan reported that shift work was a risk factor for the onset of hypertension8, 9). Oishi et al. conducted a longitudinal study on the relationship between shift work and the progression of hyper-
tension in male Japanese steel workers, and reported that shift work is a significant and independent risk factor for the progression of hypertension\(^{10}\). Kawachi et al. have reported that the multivariate adjusted relative risks of coronary heart disease among US female nurses who worked rotating night shifts were significant higher, compared with women who had never done shift work\(^{11}\).

In Japan, to date, only a few studies have been done to determine the relation between SDB and hypertension. Tanigawa et al. conducted a population-based cross-sectional study of 1,424 men aged 40–69 yr in rural and urban communities, and reported that 3% oxygen desaturation index (ODI) levels was positively associated with systolic and diastolic blood pressure levels after adjustment for age, BMI, ethanol intake, smoking category and community\(^{12}\). Tanigawa et al. also conducted a cross-sectional study among 459 male workers aged 30 to 62 yr at nuclear power plants in Japan, and demonstrated that systolic and diastolic blood pressure levels were correlated with 3%ODI in all subjects after adjustment for age, BMI, ethanol intake, use of antihypertensive medication, and timing of BP measurement\(^{13}\). A population-based cross-sectional study of 1,313 professional truck drivers by his research team showed significant positive associations between the 3%ODI levels and diastolic blood pressure levels\(^{14}\). However, given the potential blood-pressure impact of sleep duration and working shift as mentioned above, we believe that these two factors should be considered simultaneously when exploring how SDB would be associated with blood pressure.

The objective of this study was to examine the relationship between SDB and hypertension after adjustment for sleep duration as well as shift working in Japanese steel workers.

**Participants and Methods**

**Participants**

The study subjects were workers at a steel plant in Japan. Thirty eight point two percent of the workers did shift work. Shift schedules were planned based on a four-team-three-shift and clockwise rotation. Day, evening, and night shifts started at 07:00, 15:00 and 23:00 h, respectively. All shift workers were categorized as blue-collar based on their work contents (e.g., blast-furnace process). The total number of the workers were 2,939.

They were asked to participate in the present study by occupational physicians at the time of annual health check-up from 2004 to 2007 with an explaining the purpose of the study and that this survey was voluntary and even if they did not answer, they did not have disadvantage.

Exclusion criteria included unstable or decompenated cardiopulmonary disease, airway cancers, recent surgery of the upper respiratory tract, current home oxygen therapy, use of continuous positive airway pressure treatment, and use of antihypertensive medication. Participants were also excluded if they undertook overnight pulse oximetry with an inadequate period of sleep (less than four hours), or a history of stroke or cardiovascular disease.

Finally, 249 men (mean age 44.3 yr, range 20 to 65) agreed to participate in the present study.

The study protocol was approved by the Ethical Committee of the Kitasato University.

**Measurement of blood pressure**

Blood pressure levels and body mass index (BMI) were recorded during the annual health check-up at this works. Blood pressure levels were measured by trained nurses using standard automatic sphygmomanometers while the subject quietly seated after a few minutes rest. Hypertension was defined as systolic blood pressure (SBP)≥140 mmHg, and/or diastolic blood pressure (DBP)≥90 mmHg. The time of blood pressure measurement was between 09:00 and 15:00 h throughout the study period.

**Assessment of SDB**

A pulse-oximeter PULSOX-3Si (Minolta Co., Osaka, Japan) was attached to the distal forearm of subjects during one night of sleep at home. The sensor probe was fitted to one fingertip and secured by each subject. No specific limitations on daily life were imposed on the monitoring day.

The internal memory of this device stores the values of blood oxygen saturation by performing a moving average for the last 5 s, updated every second; this sampling time was short enough to avoid underestimation of oxygen desaturation. Data were downloaded to a personal computer via an interface (PULSOX IF-3; Minolta) and analyzed using proprietary software supplied with the equipment (DS-3 ver.2.0a; Minolta). We used the value of oxygen desaturation per hour (oxygen desaturation index, ODI) as an indicator of SDB. A 3%ODI was selected as an index of oxygen desaturation, representing the number of events per hour of recording time in which blood oxygen fell by≥3%. The 3%ODI threshold recorded during an estimated sleep duration of more than 4 h was used for the analysis. The criteria for SDB were defined by 3%ODI level as 15 events per hour, corresponding to moderate-to-severe SDB. All participants who were defined SDB (3%ODI≥15) were advised to consult with their primarily care physicians.

**Confounding variables**

Subjects also completed a self-reported questionnaire...
on confounders that might contribute to or aggravate the incidence of SDB (e.g., the alcohol intake, current smoking, usual sleep duration, work schedule, and type of work). Occupational physicians conducted interviews to confirm the contents. The usually monthly alcohol intake was converted to g of ethanol per day. Persons who smoked one or more cigarettes/day were defined as current smokers.

Statistical analysis
Participants were classified into two groups according to the categories of nocturnal ODI levels (3%ODI: <15, ≥15). Mean values of age, BMI, blood pressure levels, alcohol intake, smoking, and usual sleep duration were calculated, and differences between two groups were evaluated using student t test. Differences in categorical variables were tested by \( \chi^2 \) test.

A logistic regression analyses were performed to estimate the independent associations of the nocturnal ODI levels with hypertension after adjustment for age, body mass index, alcohol intake, smoking, usual sleep duration and form of work. In addition, an analysis of covariance (ANCOVA) was performed to evaluate mean values of SBP and DBP according to categories of 3%ODI levels after adjustment for confounding variables.

All statistical analyses were performed using SPSS 12.0J for Windows. All probability values reported for statistical tests were two-tailed, and values of \( p<0.05 \) were regarded as statistically significant.

Results
The prevalence of a 3%ODI of ≥15 was 18.1% among participants of this study. Table 1 shows physiologic and behavioral characteristics of the subjects according to categories of 3%ODI levels. Of the 37 participants with hypertension, 32 (86.5%) were classified Stage 1 hypertension (SBP=140–159 mmHg or DBP=90–99 mmHg), 5 (13.5%) were classified Stage 2 hypertension (SBP≥160 mmHg or DBP≥100 mmHg) defined by The JNC 7 Report\(^5\). All of them were advised to modify their lifestyle and/or consult with their primarily care physicians. There were significant difference in mean values of age, BMI, SBP, and DBP, and there were no significant difference in mean values of ethanol intake and usual sleep duration.

Table 2 shows the multivariate adjusted odds ratio of hypertension according to categories of 3%ODI levels. Multivariate odds ratio of hypertension for high (≥15) category of 3%ODI level was 2.86 (95% confidence interval, 1.23–6.66), relative to the low (<15%) 3%ODI category.

As summarized in Table 3, both mean SBP and DBP values were found to be significantly greater for the workers with the higher category of 3%ODI than for those with the lower category (\( p<0.01 \)) after adjustment for confounding variables. When we divided the participants by

| Table 1. Characteristics of participants according to 3%ODI levels |
|------------------|------------------|------------------|------------------|
|                  | total (N=249)    | 3%ODI <15 (N=204) | 3%ODI ≥15 (N=45) | \( p \) value |
| Age (yr)         | 44.3 (0.6)       | 43.8 (0.7)       | 46.7 (1.1)       | 0.02          |
| BMI (kg/m\(^2\))| 26.2 (0.2)       | 25.8 (0.2)       | 27.9 (0.5)       | <0.01         |
| SBP (mmHg)       | 125.1 (0.9)      | 123.7 (0.9)      | 131.6 (2.1)      | <0.01         |
| DBP (mmHg)       | 77.3 (0.7)       | 76.1 (0.7)       | 82.9 (1.5)       | <0.01         |
| hypertension (%) | 37 (14.9)        | 24 (11.8)        | 13 (28.9)        | <0.01         |
| alcohol intake (g/day) | 20.8 (1.3)  | 20.5 (1.4)       | 22.3 (3.4)       | 0.6           |
| current smoking (%) | 101 (41.0)     | 80 (39.2)        | 21 (47.0)        | 0.36          |
| usual sleep duration (h/day) | 6.3 (0.1)  | 6.3 (0.1)        | 6.3 (0.1)        | 0.78          |
| shift workers, no. (%) | 95 (38.2)      | 77 (37.7)        | 18 (40.0)        | 0.78          |
| blue-collar occupations, no. (%) | 146 (58.6) | 124 (60.8)       | 22 (48.9)        | 0.14          |

Values are expressed by Means (SE) and Number (%).
work schedule, the shift workers showed only a significant difference in DBP value between the higher and lower categories of 3%ODI (p<0.02). In contrast, the non-shift workers had a significantly greater SBP value (p<0.02) and an almost significantly greater DBP value (p<0.06) associated with the higher category of 3%ODI.

**Discussion**

The present study examined the relationship between SDB and hypertension after adjustment for sleep duration and shift work for employees of a Japanese steel company. The results showed the significant association between oxygen desaturation and hypertension, independent of age, BMI, ethanol intake, smoking, usual sleep duration, shift work, and occupation.

Our results are consistent with previous findings from several-population based studies in Western countries\(^1\)–\(^3\). Wisconsin Sleep Cohort Study reported the relative risk of incident hypertension as 2.89 (95%CI: 1.46–5.64) among subjects with AHI\(\geq 15\) compared with subjects with AHI=0 during a 4-yr follow-up\(^1\). The Sleep Heart Health Study showed the odds ratio for hypertension as 1.37 (95%CI: 1.03–1.83) for the highest category of AHI (\(\geq 30\)), compared with the lowest category (<1.5) after adjustment for BMI, neck circumference, waist-to-hip ratio, alcohol intake and smoking\(^2\).

Tanigawa et al. conducted a population-based cross-sectional study of 1,424 men aged 40–69 yr in rural and urban communities, and reported that multivariate odds ratio of hypertension for the low (3%ODI: 0–4) vs. high (3%ODI\(\geq 15\)) was 1.63 (95%CI: 1.1–2.5) after adjustment for confounding variables age, BMI, ethanol intake, smoking category and community\(^12\). Cui R conducted a population-based cross-sectional study of 1,313 subjects aged 20–69 yr among professional truck drivers, and reported that multivariate odds ratio of hypertension was 2.0(95%CI: 1.1–3.6) for a 3%ODI\(\geq 15\) in reference with a 3%ODI<15\(^14\). Our results are consistent with these previous studies, and odds ratio was slightly higher (OR: 2.82, 95%CI: 1.20–6.60). The reasons for the high odds ratio have been considered that participants were younger (average: 44.3) than those of previous studies. Several studies have reported that the influence of SDB on hypertension is more pronounced in younger and middle aged men than in those above 60 yr\(^13\), \(^14\).

In the cross-sectional study which Tanigawa et al. conducted among 253 male shift workers and 206 male day workers aged 30 to 62 yr at nuclear power plants in Japan, a correlation between SDB severity and diastolic BP levels was more evident among shift workers \(\geq 40\) yr\(^15\). Our ANCOVA results on the BP levels for the shift workers are in line with those presented in this previous paper\(^15\).

Several population-based studies have shown a link between short sleep duration and hypertension\(^6\), \(^7\). Gottlieb et al. have conducted a population-based prospective study, have reported that those sleeping less than 6 h per night had adjusted odds ratio for hypertension of 1.66 (95%CI: 1.35–2.04), compared to subjects sleeping 7 to less than 8 h per night\(^6\). In the longitudinal study which have conducted using data of first National Health and Nutrition Examination Survey, Gangwisch et al. have reported that sleep durations of \(\leq 5\) h per night were associated with a significantly increased risk of hypertension (hazard ratio: 2.10, 95%CI: 1.58–2.79), and the increased risk continued to be significant after controlling for obesity and diabetes\(^7\).

In Japan, the prevalence of hypertension was 12.3%, and the percentage of hypertensive people increased particularly distinct in working men in their 30s–50s\(^17\), \(^18\). Therefore, evaluation of factors that cause hypertension to worsen is necessary.

A meta-analysis of nine prospective studies demonstrated that a long-term difference of 5mmHg in mean diastolic BP was associated with a 34% reduction in risk of stroke and a 21% reduction in risk of coronary heart disease\(^19\). A positive association between SDB and hypertension in the present study suggests that SDB would enhance the likelihood of cardiovascular disease in Japanese steel workers.

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**Table 3. Mean values of SBP and DBP according to categories of 3%ODI levels after adjustment for confounding variables**

<table>
<thead>
<tr>
<th></th>
<th>All workers (N=249)</th>
<th>Shift workers (N=95)</th>
<th>Non-shift workers (N=154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ODI&lt;15</td>
<td>123.7 (13.5)</td>
<td>125.3 (12.4)</td>
<td>122.8 (14.1)</td>
</tr>
<tr>
<td>ODI(\geq 15)</td>
<td>131.6 (14.3)</td>
<td>129.7 (13.1)</td>
<td>132.8 (15.1)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ODI&lt;15</td>
<td>76.1 (10.3)</td>
<td>76.4 (9.9)</td>
<td>75.9 (10.5)</td>
</tr>
<tr>
<td>ODI(\geq 15)</td>
<td>82.9 (10.2)</td>
<td>82.5 (8.4)</td>
<td>83.1 (11.4)</td>
</tr>
</tbody>
</table>

Values are expressed by MEANS (SD).

1) Adjusted for age, BMI, ethanol intake, smoking, short sleep duration and shift work.

2) Adjusted for age, BMI, ethanol intake, smoking, short sleep duration.
With respect to treatment of SDB, Dhillon et al. have reported that long-term use of CPAP in hypertensive patients with sleep apnea is associated with a significant decrease in blood pressure to levels that considerably decrease cardiovascular risk\(^{20}\). Norman et al. have reported that 2 wk of CPAP therapy resulted in a significant reduction in daytime mean arterial and diastolic blood pressure and nighttime systolic, mean, and diastolic blood pressure\(^{21}\). Marti S, et al. have reported that a rise in mortality was found in nontreated sleep apnea/hypopnea syndrome patients compared with the general population, whereas mortality in those treated for sleep apnea/hypopnea syndrome did not differ significantly from that of the general population\(^{22}\). Thus, SDB patients treated by CPAP are considered to reduce cardiovascular risk.

As reported previously\(^{23}\), the pulse oximetry can provide objective measures of breathing status, which help us to determine severe SDB for whom CPAP therapy was indicated. Furthermore, PSG is admitted for the Japanese medical insurance system only after screening using a pulse oximetry. Therefore, the promotion of screening and treatment for undiagnosed SDB among Japanese steel workers would have a substantial impact on the prevention of cardiovascular disease and the decrease in mortality. But at the same time, we need to seek other sorts of interventions to ensure adequate sleep duration, better work schedules, weight reduction, and healthy psychosocial environment at work.

The strength of the present study is to adjust for usual sleep duration and shift work. It showed significant association between oxygen desaturation and hypertension after adjustment for usual sleep duration, and form of work.

Nevertheless, there were several limitations. First, we recognized that a single measure of BP at a single point in the day was not ideal. However, it was practical necessity in this field setting. Second, pulseoximetry inherently underestimates respiratory disturbance events during sleep compared full-PSG, particularly in a non-obese population. However, mean BMI of participants were 25.8 in low (<15%) and 27.9 in high (≥15) category of 3%ODI level, respectively. Nakamata et al. reported that sensitivity of 85% and specificity 100% for detecting an AHI≥20 using a cut-off threshold 3%ODI=15\(^{24}\). The CPAP therapy is admitted for the Japanese medical insurance system on condition that patients with AHI≥20. Third, potential confounding variables for hypertension such as diet or exercise variables were not taken into account. Fourth, the design of this study does deserve careful consideration of possible selection bias. Those choosing to participate in this study may be more likely to have sleep problems other than SDB or have risk factors for SDB, such as obesity (Table 1). Nevertheless, these potential effects should not compromise the internal validity of the study. Fifth, all participants were younger and middle aged male workers. However, the detection of SDB must be of importance especially in middle aged male workers. Sjostrom et al. have found that the influence of SDB on hypertension is more pronounced in younger and middle aged men than in those above 60 yr\(^{13}\). Haas DC, et al. have reported that SDB is associated with systolic/diastolic hypertension in those aged<60yr\(^{14}\). Furthermore, Hedner et al. have reported that the contributions of obstructive sleep apnea to hypertension risk may be sex dependent and higher in males than females\(^{25}\). Sixth, our study was cross-sectional, and sample size was small. Longitudinal studies are needed to determine whether SDB is a risk factor for hypertension in Japanese workers. Seventh, we did not record the timing of BP measurement for each participant. This uncontrolled factor might have affected the present results, but the effects of SDB on BP have been reported to be observed even after adjusting for its measurement timing\(^{13}\).

In conclusion, the present study showed the significant association between oxygen desaturation and hypertension among Japanese steel workers. This finding suggests the need for SDB screening as one of effective approaches toward prevention and treatment of hypertension in the workplace.

Acknowledgements

The authors are grateful to Dr. Toshiaki Miyamoto for his valuable comments on our study. We also thank Dr. Noriaki Kakiuchi, Dr. Kenichiro Nishi, Dr. Makoto Yamamoto, and Dr. Takeshi Kohchi for data collection.

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