Changes in Blood Pressure Levels in Patients with Obstructive Sleep Apnoea

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ABSTRACT

BACKGROUND

Obstructive sleep apnoea (OSA) is characterised by recurrent episodes of upper airway obstructions during sleep. Recent studies suggest that OSA is independently associated with hypertension. So, the current study was done to analyse the relationship between OSA and blood pressure changes and to determine as to what extent OSA is independently contributing to those changes. This was to highlight the importance of the need for early diagnosis and prompt treatment of patients with OSA.

METHODS

97 patients with symptoms of OSA were selected. Following polysomnography, patients were grouped into two: OSA patients with Apnoea-Hypopnea Index (AHI) ≥ 5 and controls (AHI < 5). Linear regression analysis was done to find out the independent effect of exposure variables (age, body mass index (BMI), AHI etc.) on the outcome the variable (blood pressure).

RESULTS

Systolic BP was significantly high in OSA patients (154.84 ± 15.89) compared to control group (132.00 ± 11.45). Diastolic BP was significantly high in OSA patients (90.63 ± 7.87) compared to control group (85.13 ± 5.95). Linear regression analysis showed that for each unit change in AHI, systolic blood pressure changed by 0.406 independent of other factors and for each unit change in desaturation index, diastolic blood pressure changed by 0.111 independent of other factors.

CONCLUSIONS

The blood pressure levels both systolic and diastolic were significantly elevated in patients with OSA. Increase in AHI was independently associated with increase in systolic blood pressure and the increase in desaturation index was independently associated with increase in diastolic blood pressure. Since OSA is a highly prevalent and highly underdiagnosed condition, the current study emphasises the importance of screening for OSA, so that with early diagnosis and prompt treatment the development and progression of cardiovascular risk factors like hypertension can be reduced.

KEYWORDS

OSA, Sleep Apnoea, Hypertension, Blood Pressure, Sleep Fragmentation

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BACKGROUND

Obstructive sleep apnoea (OSA) is characterised by recurrent episodes of upper airway obstructions during sleep. OSA develops when there are elevated mechanical loads on the upper airway along with defects in compensatory neuromuscular responses.[1] Several studies across various geographical regions and ethnic groups have established the high prevalence of OSA. Wisconsin Sleep Cohort Study conducted in USA had estimated a prevalence of 9 % in women and 24 % in men. Sharma S.K. et al., in a population of Delhi, reported a prevalence of 7.4 % in women and 19.7 % in men.[2] In spite of adequate access to health care, up to 80 % of cases of moderate or severe OSA have gone undiagnosed.[3,4]

The recurrent episodes of upper airway obstruction in OSA patients cause episodic oxyhaemoglobin desaturation. This leads to recurrent arousals during sleep resulting in sleep fragmentation. The arousals cause increased sympathetic activity during sleep, which persist even during the wake period.[5] The sleep fragmentation and sympathetic over activity leads to dysfunction of many systems, the most commonly affected being the cardiovascular system. OSA is associated with markedly increased change in blood pressure during sleep, which in normal subjects is a period of lower blood pressure with less changes in blood pressure.[5] This poses great cardiovascular morbidity to OSA patients. Many studies with daytime blood pressure measurements have shown that hypertension is prevalent in OSA patients.[6,7] Recent studies suggest that OSA is independently associated with hypertension.[8]

Objectives

The current study was done to analyse the relationship between the polysomnographic (PSG) parameters of respiratory disturbance in OSA patients (viz. apnoea-hypopnea index (AHI), desaturation index (DI) etc.) and the blood pressure changes and to what extent OSA is independently contributing to those changes. This was to highlight the importance of the need for early diagnosis and prompt treatment of patients with OSA.

METHODS

Study Design

The present study was an observational-analytical study done to determine the relationship between polysomnographic parameters of respiratory disturbance (AHI and desaturation index) and the changes in blood pressure in patients with OSA. Ethical clearance was obtained from institutional ethics committee.

Selection of Subjects

97 consecutive patients who attended the pulmonary medicine outpatient department, over the study period (2 years), with symptoms suggestive of OSA were selected, after getting informed consent. All of them were in the age group 25 - 75 years. OSA symptoms included the following

1. Those reported by patient are excessive daytime sleepiness, nocturnal awakenings, gasping or chocking episodes during sleep, unrefreshing sleep, difficulty in driving long distances, poor concentration, decreased libido and morning headache.
2. Those reported by partner are loud & intermittent snoring, witnessed apnoea and irritability.

Inclusion Criteria

Subjects were grouped into two, following polysomnography (PSG).

- Group I – OSA patients: Those who had only obstructive apnoea (i.e.) continued thoraco-abdominal respiratory effort in the setting of partial (hypopnea) or complete (apnoea) cessation of airflow and an AHI ≥ 5.
- Group II – Controls: Subjects with an AHI < 5.

Total number of subjects in Group I were 67 and Group II were 30. Patients with other types of sleep apnoea – central or mixed apnoea were excluded from the study.

Data Collection

The patients presented in Out Patient Department with symptoms suggestive of OSA were evaluated in detail in the form of clinical examination which consisted of detailed history taking and physical examination including BMI, calculated as weight in kg / height in meter^2 and blood pressure measurement in right arm in supine position after 10 minutes rest. These patients were made to undergo polysomnography (PSG). The patients who were diagnosed to have OSA after PSG were taken as group I (OSA patients) and others without sleep apnoea were grouped as controls.

Polysomnography

Each patient underwent an attended overnight polysomnography in the sleep laboratory between 9:00 pm to 6:00 am. It was done with Vincent Polygraph, Medcare, TMS International, Netherlands. Each study consisted of continuous polygraphic recording from surface leads of electroencephalography (EEG), electromyography (EMG), electrooculography (EOG) and electrocardiography (ECG). Chest and abdominal movements and body position was measured by inductance plethysmography, airflow and snores detected via a nasal-pressure sensors and oxygen saturation (SaO_2) by a pulse oximeter. EEG electrodes were placed at C3 and A1 positions and a ground electrode on the forehead. The electromyogram was recorded from chin-muscle activity with the two electrodes placed just beneath the tip of the chin. For electrooculogram, the electrodes were attached to the outer canthus of each eye to record eye movements. Results were analysed with software and were also scored manually.[9]

Parameters of Respiratory Disturbance Studied

Apnoea-Hypopnea Index (AHI)

Number of apnoea and hypopnea cycles per hour of total sleep time. (apnoea: cessation of airflow for > 10 sec and hypopnea: decrease in airflow with a desaturation of at least 3 %). Total apnoea index (TAI): Number of apnoea cycles per hour of total sleep time.

Total Hypopnea Index (THI)

Number of hypopnea cycles per hour of total sleep time.

Lowest Desaturation (LD)

Lowest desaturation attained during sleep.

Desaturation Index (DI)

Number of desaturations (≥ 3 %) per hour of total sleep time.

Patient was diagnosed with OSA if an apnoea-hypopnea index was ≥ 5.

Collection of Blood Samples

On the morning, after sleep study, blood samples were collected in the fasting state by venous puncture method using disposable syringes with needles under aseptic precautions and transferred into clean dry bottles. The parameters assayed were total cholesterol (TC) and fasting blood sugar (FBS). Total cholesterol levels in the serum were estimated with reagent kits using the cholesterol oxidase phenol 4-aminoantipyrine peroxidase (CHOD-PAP) method and fasting blood sugar using glucose oxidase- peroxidase method.[10]

Statistical Analysis

All quantitative variables were compared between the two groups with independent sample t-test. Proportions of gender were compared between the two groups using chi-square test. Correlations between the variables were studied by determining the Pearson correlation coefficients. Linear regression analysis was done to find out the independent effect of exposure variables (age, BMI, AHI etc.) on the outcome variables (blood pressure). All the above analyses were done using Statistical Package for the Social Sciences (SPSS) software version 16. For all statistical tests a P-value of ≤ 0.05 was taken as level of significance.

RESULTS

Mean age of OSA patients (49.45 ± 10.72) was high compared to control group (45.33 ± 10.60). But it was not statistically significant (P value = .083). In OSA group, proportion of males was more 80.6 % (N = 54) compared to the control group 63.3 % (N = 19) and proportion of females was less in OSA group 19.4 % (N = 13) compared to the control group 36.7 % (N = 11). But it was not statistically significant (P-value = 0.069). No significant difference was noted in BMI between the OSA patients (31.90 ± 5.21) and control group (30.68 ± 2.07) (P value = .220).

Polysomnography parameters viz. apnoea-hypopnea index, desaturation index, total apnoea index and total hypopnea index were significantly high in OSA patients compared to control group, whereas the lowest desaturation value was significantly low in OSA patients. But no significant difference was noted in mean oxyhaemoglobin saturation between the two groups (Table 1).

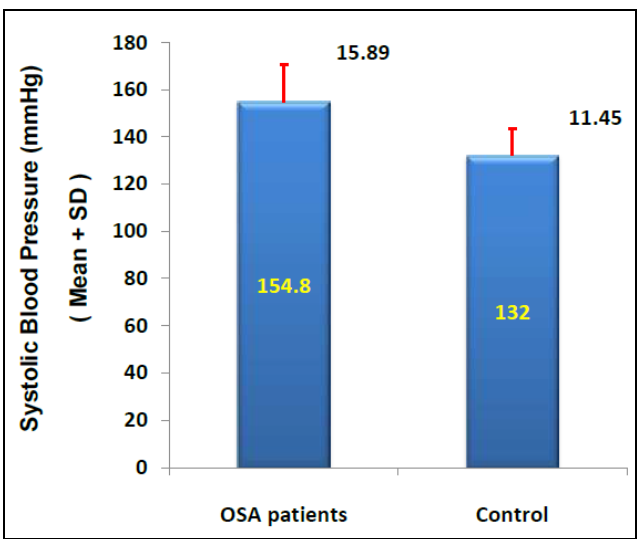

Figure 1. Comparison of Systolic Blood Pressure between the Study Groups

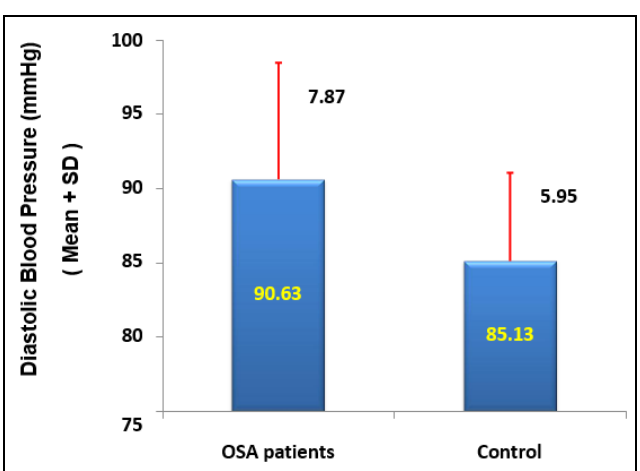

Figure 2. Comparison of Diastolic Blood Pressure between the Study Groups

Variable	Mean ± SD OSA Patients (N = 67)	Control (N = 30)	P-Value
AHI	33.79 ± 23.07	2.55 ± 1.21	.001
DI	28.92 ± 24.62	6.46 ± 7.97	.001
TAI	12.03 ± 15.95	.31 ± .34	.001
THI	21.75 ± 14.79	2.26 ± 1.21	.001
MS	93.43 ± 5.34	94.51 ± 5.63	.371
LD	74.93 ± 14.28	81.40 ± 15.56	.048

Table 1. Comparison of Polysomnographic Parameters between the Study Groups

(N = 97) AHI: Apnoea Hypopnea Index, DI: Desaturation Index, TAI: Total Apnoea Index, THI: Total Hypopnea Index, MS: Mean Saturation, LD: Lowest desaturation

Variable	Mean ± SD OSA Patients (N = 67)	Control (N = 30)	P-Value
SBP	154.84 ± 15.89	132.00 ± 11.45	.001
DBP	90.63 ± 7.87	85.13 ± 5.95	.001
TC	184 ± 42	202 ± 40	.046
FBS	129.13 ± 38.52	97.17 ± 21.36	.001

Table 2. Comparison of Basic Parameters between the Study Groups

SBP: Systolic BP, DBP: Diastolic BP, FBS: Fasting Blood Sugar, TC: Total Cholesterol.

	SBP	DBP	TC	FBS
AGE	.262**	.153	.066	.212*
SEX	- .155	.012	.201*	- .111
BMI	.350**	.081	.119	.159
AHI	.719**	.273**	.126	.354**
DI	.580**	.342**	.198	.217*
TAI	.545**	.262**	.138	.374**
THI	.621**	.184	.070	.206*
MS	- .199	- .163	- .042	- .109

Table 3. Pearson's Correlation Coefficients

**. Correlation is Significant at the 0.01 level (2-tailed) *. Correlation is significant at the 0.05 level (2-tailed)

BMI: Body Mass Index, AHI: Apnoea Hypopnea Index, DI: Desaturation Index, TAI: Total Apnoea Index, THI: Total Hypopnea Index, MS: Mean Saturation.

Exposure Variable	For Each Unit Change in Exposure Variable Systolic Blood Pressure Changes by	P Value	For Each Unit Change in Exposure Variable Diastolic Blood Pressure Changes by	P Value
AGE	.213	.088	.030	.670
SEX	1.507	.635	.995	.584
BMI	- .010	.975	- .132	.495
AHI	.406	.001	- .023	.699
DI	.017	.864	.111	.026
FBS	.033	.378	.062	.005

Table 4. Strength of Association between Exposure Variables and Systolic and Diastolic Blood Pressures

FBS: Fasting Blood Sugar, AHI: Apnoea Hypopnea Index, BMI: Body Mass Index. DI: Desaturation Index.

Systolic blood pressure (SBP) was significantly high in OSA patients (154.84 ± 15.89) compared to control group (132.00 ± 11.45) with P value = 0.001 (Figure 1). Diastolic blood pressure (DBP) was significantly high in OSA patients (90.63 ± 7.87) compared to control group (85.13 ± 5.95) with P-value = 0.001 (Figure 2). OSA patients (184 ± 42) had significantly lower total cholesterol (TC) levels compared to control group (202 ± 40) (P-value = 0.046). OSA patients (129.13 ± 38.52) had significantly higher fasting blood sugar (FBS) levels compared to control group (97.17 ± 21.36) P-value = 0.001 (Table 2). There was significant positive correlation between AHI and various parameters like systolic BP, diastolic BP (Table 3, shown in bold). There was significant positive correlation between desaturation index (DI) and various parameters like systolic BP, diastolic BP (Table 3, shown in bold). Linear regression analysis showed that for each unit change in AHI, systolic blood pressure changes by 0.406 independent of other factors, P-value = 0.001 and that for each unit change in desaturation index, diastolic blood pressure changes by 0.111 independent of other factors, P-value = 0.026 (Table 4).

DISCUSSION

Obstructive sleep apnoea is a highly prevalent and underdiagnosed condition.[2] Recent evidence show that OSA patients form a high-risk group for cardiovascular morbidity and mortality, due to their increased association with hypertension.[5] The present study was done to determine the relationship between OSA and the changes in blood pressure and it highlighted the cardiovascular risk in these patients. The most common cardiovascular disease associated with OSA is hypertension. In the current study, daytime blood pressure was measured and analysed. It showed that systolic blood pressure and diastolic blood pressure were significantly high in OSA patients compared to the control group (Figures 1 and 2). There was significant positive correlation between polysomnographic parameters of respiratory disturbance (AHI and desaturation index) and both the systolic and diastolic blood pressure values (Table 3). Linear regression analysis showed that AHI was independently associated with systolic blood pressure, whereas diastolic blood pressure was independently associated with desaturation index (Table 4). These findings were consistent with the earlier studies done by JT Carlson et al.[11] and S.R. Coughlin et al.[8]

Episodes of apnoea and hypopnea in OSA patients cause temporary elevations in blood pressure in association with blood oxygen desaturation and arousal. This may cause elevated blood pressure during the daytime also and ultimately sustained hypertension.[12] Pathophysiological mechanisms by which OSA increases blood pressure are not yet well defined. Several mechanisms have been postulated to be involved like abnormal peripheral sympathetic nerve activity, abnormal chemoreflex sensitivity and baroreceptor reflex response and endothelial dysfunction.[5] Microneurographic studies have demonstrated that recurrent apnoeic episodes cause sudden rise in peripheral (muscle) sympathetic nerve activity and associated elevated blood pressure levels during sleep. These changes in blood pressure and increased muscle sympathetic nerve activity are abruptly inhibited by resumption of breathing.[13] Increased sympathetic nerve activity persists during wakefulness and is reduced by treatment with nasal continuous positive airway pressure (CPAP).

Abnormal peripheral chemoreflex sensitivity has been demonstrated in OSA patients. Markedly abnormal blood pressure responses to hypoxia during the day have been reported in patients with OSA. Narkiewicz et al. showed that these patients developed a marked pressor response to hypoxic breathing (exposure to a hypoxic gas mixture-10 % oxygen (O_2) in nitrogen (N_2) with carbon dioxide (CO_2) titrated to maintain isocapnia when compared to the response in normal subjects.[14] The magnitude of this pressor response increased with the severity of OSA.[5] Ventilatory responses to hypoxia were also increased and correlated with the magnitude of this pressor response. Even though both increased blood pressure and increased ventilation act as powerful restraints on the sympathetic response to hypoxia, peripheral sympathetic activity remained high during the hypoxic breathing. Thus, in OSA

patients, the enhanced peripheral chemoreflex sensitivity appears to be a potent mechanism for sympathetic activation.[14]

Impairment of baroreflex function may be another potential mechanism linking OSA to an increased risk for hypertension. Study done by Narkiewicz et al. showed that the baroreflex regulation of sympathetic activity for similar blood pressure changes was diminished in patients with sleep apnoea compared to normal control subjects. The blood pressure profile during sleep in patients with OSA is dominated by responses to obstructive apnoeic events that occur repetitively throughout sleep. In a subject who is normotensive during wakefulness, the sympathetic–mediated blood pressure surge at the end of the apnoeic event can reach levels as high as 250 / 120 mm Hg. The repetitive blood pressure increases during the night may also decrease the baroreflex gain.[15] A role for endothelial dysfunction in the pathogenesis of hypertension in OSA has been observed in various studies. M. Kato et al. and H. Kraiczi et al. had reported an impairment in endothelium-dependent vasodilatation.[16,17] Intermittent hypoxia activates pro-inflammatory transcription factors such as nuclear factor kappa B that promote the activation of various inflammatory cells with the downstream consequence of expression of pro-inflammatory mediators like tumour necrosis factor alpha (TNF-α) that may lead to endothelial dysfunction.[18] TNF-α induces activation of xanthine oxidase and production of O_2, leading to endothelial dysfunction.[19] Furthermore, treatment with nasal CPAP has been reported to reverse endothelial dysfunction.[20] Recent studies have revealed a high prevalence of obstructive sleep apnoea as well as obstructive sleep apnoea syndrome in Indian population,[21] which is closely related to current obesity epidemic.[2] Since the present study was able to demonstrate an independent association between OSA and cardiovascular risk factor viz. hypertension, it highlights the importance of early diagnosis by screening for OSA especially in the obese and those having snoring or excessive day time sleepiness and to provide them prompt treatment, so that the cardiovascular morbidity and mortality can be minimised.

CONCLUSIONS

Blood pressure levels both systolic and diastolic were significantly elevated in patients with OSA. Increase in AHI was independently associated with increase in systolic blood pressure and the increase in desaturation index was independently associated with increase in diastolic blood pressure. From the observations and results of the present study, it can be concluded that OSA affects the control of blood pressure independent of the effects of co-existent obesity. This may increase the risk for the development of hypertension either additively or synergistically. Since OSA is a highly prevalent and highly underdiagnosed condition, the current study emphasises the importance of screening for OSA, especially in obese people and those having snoring or excessive daytime sleepiness. This would help to reduce the development and progression of cardiovascular risk factors like hypertension.

Limitations of the Study

Even though the present study demonstrated an independent association of OSA with hypertension, a long-term prospective study with more number of OSA patients free from risk factors like obesity, diabetes and dyslipidemia is necessary to establish the independent role of OSA in the development of cardiovascular diseases.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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