Original Article

The Clinical Predictors of Hypertension and Sleepiness in an Asian Population with Sleep-disordered Breathing

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Abstract

Introduction: The objective of this study was to identify the clinical predictors for hypertension and sleepiness in an Asian population with sleep-disordered breathing (SDB). Materials and Methods: This is a retrospective, consecutive case series of 228 patients with symptoms of SDB referred to a tertiary level sleep disorders unit. A full sleep history, body mass index (BMI), Epworth Sleepiness Score (ESS), apnoea-hypopnoea index (AHI) and lowest oxygen saturation were recorded. All patients had an in-hospital polysomnogram. AHI ≥5 defined SDB. ESS >8 defined sleepiness. Results: A BMI of 25 had a positive and negative predictive value of 75% and 56%, respectively, for predicting AHI ≥5, area ROC (receiver operating curve) = 0.668. Patients with AHI >5 had 3 times the risk of developing hypertension compared to the population with AHI <5. Using stepwise multivariate analyses with constant, age, BMI and lowest oxygen desaturation were predictors for hypertension. Patients with AHI≥5 were 1.88 times more likely to have ESS >8. After stepwise multivariate analyses, the subjective complaint of sleepiness and lowest oxygen saturation during sleep were predictors of ESS >8. Conclusion: The lowest oxygen saturation attained during sleep was the common factor for hypertension and sleepiness in our Asian SDB population. Mild obesity predisposes to AHI ≥5 in our population, the threshold at which the risk of hypertension is 3-fold compared with AHI <5. The subjective complaint of sleepiness predicted an ESS of >8.

Ann Acad Med Singapore 2006;35:6-10

Key words: Apnoea, Blood pressure, Singapore, Somnolence

Introduction

Sleep physicians have only recently began to learn much about the epidemiology of sleep-disordered breathing (SDB) from large, well conducted prospective community-based studies.[1] These studies have helped identify the risk factors for identifying sleep apnoea, particularly in the Western population. In the recent Joint National Commission for the Detection and Treatment of Hypertension, sleep apnoea was an important cause of secondary hypertension.[2] The impact of SDB on the heart includes impaired left ventricular function, which can be improved with positive airway pressure therapy.[3] Mild-to-moderate SDB has also been linked to cardiovascular diseases.[4,5]

The issue of evaluating sleepiness is more complex. While sleep disruption leads to sleepiness, or a tendency to sleepiness, the perception of sleepiness may vary from one individual to another, making the objective assessment of sleepiness difficult. This is in part related to the lack of sensitivity of the tools that we currently use to measure sleepiness. Also, there are yet mechanisms of sleepiness that we fail to understand and discover.

There is a paucity of data from Asian countries on the epidemiology of SDB, particularly the risk factors for predicting hypertension and sleepiness in an SDB population. In a population survey on snoring and sleep-related breathing disorders done in Singapore, Malays and Indians had a higher prevalence of SDB, obesity and hypertension.[6] Another study done in Singapore showed that 87% of loud habitual snorers had significant SBD on polysomnogram (using and cut-off of apnoea index >5) and

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72% had excessive daytime sleepiness.[7] A study on Hong Kong bus drivers suggested that body mass index (BMI) and witnessed apnoeas were independent predictors of SDB. In this study, 20% of the sample had respiratory disturbance index of more than 5 and sleepiness.[8] In another study from Hong Kong, BMI, habitual snoring, sleep latency and age were identified as predictors for apnoea-hypopnoea index (AHI) ≥5 in a middle-aged Chinese male population.[9] These data indicate the presence of a significant degree of SDB in the Asian population with serious consequences.

With this background in mind, we attempt to define the predictive factors for SDB and its sequelae – hypertension and sleepiness – in our multiracial population at a tertiary referral sleep disorders centre.

Materials and Methods

Our study is a retrospective consecutive case series analysis of medical records and overnight polysomnograms done at the National University Hospital in Singapore. It is a tertiary referral centre with a 2-bed sleep laboratory facility for predominantly sleep breathing disorders. We included all patients from October 2001 to March 2003.

All patients were referred for an evaluation of sleep-related breathing disorder. They all had full in-house overnight polysomnograms. The Epworth Sleepiness Score (ESS) was also recorded. An Epworth score of >8 was considered an objective marker for sleepiness.[10] Clinic notes had a detailed inquiry into the main sleep complaints and past medical and surgical histories. The presence of hypertension was defined as a history of being diagnosed with hypertension, with or without treatment. When no history of hypertension was available, we used the published Joint National Commission VI guidelines for the diagnosis of hypertension.[11] BMI and largest neck circumference were measured for all patients.

The overnight studies were performed on the Alice 3 Sleepware System, Healthdyne, Respironics, Pennsylvania, USA, with 16-channel recordings and in accordance with standardised 10-20-20 EEG electrode placement. Sleep epochs were scored according to the standardised Rechtschaffen and Kales criteria.[12] Apnoea was defined as a cessation of breathing for >10 seconds, with discernible thoracoabdominal movement and this was detected by using a thermocouple. Hypopnoea was defined as a reduction in airflow seen on the thermocouple, accompanied by an oxygen desaturation of ≥4%.[13] The total number of apnoea and hypopnoeas were counted and divided over total sleep time to give the AHI. An AHI of ≥5 was the minimal threshold value for defining SDB.[14] Lowest oxygen saturation was the lowest recording noted on the pulse oximeter that was artifact-free.

Statistical Analysis

All statistical analyses were performed using SPSS 11.5 (SPSS Inc, Illinois, USA). Normality assumption for quantitative response variables was checked using the Komolgorov-Smirnov 1-sample test. ANOVA was performed to determine the differences amongst the 4 severity groups of SDB based on AHI if normality (and homogeneity) assumptions were satisfied; otherwise the Kruskall-Wallis test was applied. Two sample *t*-test (or Mann-Whitney U test) was applied when SDB was defined into a 2-group category of AHI ≥5 or not. Associations of SDB with categorical responses were assessed using chi-square or Fisher's Exact tests. Receiver operating curve (ROC) analyses were also performed to determine the appropriate cut-off values of BMI and neck circumference for AHI ≥5. A multiple logistic regression model was used to determine the risk factors for predicting hypertension and sleepiness. Statistical significance was set at P <0.05.

Results

There were a total of 228 patients. The sample population demographics are summarised in Table 1.

Epidemiologic Data

When the sample population was categorised into 4 groups based on severity of AHI (<5 normal, 5-15 mild, >15 to 30 moderate and >30 severe), BMI, neck circumference, ESS, lowest oxygen saturation (Kruskal-Wallis test) and being of male gender were all significant predictors for increasing severity of SDB based on AHI.

Categorising SDB into AHI≥5 or not, the above predictors were still significant: males (P = 0.01; OR = 2.5; 95% CI, 1.2 to 5.1), BMI (median, 29.3 versus 26.3; P <0.001, Mann-Whitney U), neck circumference (median, 42 versus 39; P <0.001, Mann-Whitney U), ESS (median, 12 versus 10; P = 0.013, Mann-Whitney U) and lowest oxygen saturation (median, 73 versus 89; P <0.001, Mann-Whitney U). Also, AHI ≥5 were older (46.1 ± 12.6 versus 41.5 ± 12.2; P = 0.01, 2-sample *t*-test).

A BMI of 25.1 (mild obesity category) had a positive and negative predictive value of 75.0% and 56.0%, respectively, for predicting AHI ≥5, area ROC = 0.668. A neck circumference of 35 cm had a positive and negative predictive value of 71.7% and 77.8%, respectively, for predicting AHI ≥5, area ROC = 0.71.

Hypertension and SDB (AHI ≥5)

Patients with AHI ≥5 were more likely to develop hypertension (OR = 3.1; 95% CI, 1.6-6.1; P = 0.001, chi-square test). Performing a multiple logistic regression with the following variables included in the model: AHI ≥5, age, sex, complaint of unrefreshing sleep, daytime sleepiness,

Table 1. Patient Demographics Including Both Clinical and Polysomnographic Data

Variables (n = 228)	Values*
Patient demographics	
Age (y)	44.6 ± 12.6
Sex	
Male [No. (%)]	190 (83)
Female [No. (%)]	38 (17)
Race [No. (%)]	
Chinese	172 (76)
Malay	23 (10)
Indian	23 (10)
Others	10 (4)
BMI (kg/m^2)	29.9 ± 7.2
Neck circumference (cm)	41.5 ± 4.4
Epworth Sleepiness Score	11.6 ± 4.9
Hypertension [No. (%)]	79 (34.6)
Sleep history [No. of positive response (%)]	
Snoring	211 (92.5)
Excessive daytime sleepiness	129 (56.6)
Witnessed apnoeas	35 (15.4)
Choking during sleep	43 (18.9)
Unrefreshing sleep	32 (14.0)
Nocturnal awakenings	21 (9.2)
Polysomnogram parameters	
Sleep latency (min)	13.5 ± 34.4
REM latency (min)	153.2 ± 83.9
Sleep efficiency (%)	80.3 ± 14.9
Total AHI (events/h)	24.7 ± 26.3
Lowest oxygen saturation (%)	74 ± 17
Severity based on AHI [No. (%)]	
AHI <5	73 (32)
AHI 5-15	46 (20.2)
AHI >15-30	37 (16.2)
AHI >30	72 (31.6)

AHI: apnoea-hypopnoea index; BMI: body mass index;
SD: standard deviation
* Values represent Mean ± SD unless indicated otherwise

witnessed apnoea, choking, nocturnal awakening, BMI, ESS, sleep latency, rapid eye movement (REM) sleep latency, sleep efficiency and lowest oxygen saturation achieved during the overnight polysomnogram; age (*P* = 0.001; OR = 1.07; 95% CI, 1.03 to 1.12) and BMI (*P* = 0.027; OR = 1.09; 95% CI, 1.01 to 1.19) were the only significant predictors for hypertension.

Using a forward stepwise multivariate analysis with constant, age (*P* <0.001; OR = 1.08; 95% CI, 1.03 to 1.12), BMI (*P* = 0.026; OR = 1.09; 95% CI, 1.01 to 1.17) and lowest oxygen saturation (*P* = 0.024; OR = 0.967; 95% CI, 0.939 to 0.995) were significant predictors of hypertension.

Sleepiness and SDB

The patients with AHI ≥5 were 1.88 times (95% CI, 1.024 to 3.471, *P* = 0.04, Pearson's chi-square test) more likely to have ESS >8 compared with those having AHI <5.

Table 2. Predictive Factors for Hypertension After Adjusting for AHI ≥5

	P value, significance	SE	OR	95% CI
Age	0.0001	0.020	1.075	1.034-1.118
BMI	0.026	0.037	1.086	1.010-1.168
Lowest O_2 saturation	0.024	0.015	0.967	0.939-0.995

AHI: apnoea-hypopnoea index; BMI: body mass index; 95% CI: 95% confidence interval; OR: odds ratio; SE: standard error

When applying the same variables, as described in the above paragraph for hypertension, in a multiple logistic regression model, daytime sleepiness (*P* <0.001; OR = 6.2; 95% CI, 2.5 to 15.6) was the only significant predictor. Performing a forward stepwise analysis, both daytime sleepiness (*P* <0.001; OR = 5.6; 95% CI, 2.4 to 13.1) and lowest oxygen saturation (*P* = 0.046; OR = 0.97; 95% CI, 0.941 to 0.999) were predictors of ESS >8.

Discussion

In this study, we have sought to determine the epidemiology and risk factors for hypertension and sleepiness in an Asian population with SDB at a tertiary referral centre. To our knowledge, such associations are poorly defined in Asians. The racial distribution of our study population is reflective of the general population of Singapore. The limitations of our study include studying a very select sample population at a tertiary centre which may lead to sample bias. However, 43% of our referral base were either self or general practitioner referrals. In addition, the use of thermocouple can underdetect airflow limitation.[15] Arousal index was not included in our study as no criteria for scoring arousals was determined at the beginning of the study period. A previous study by one of the authors (PHL) did not reveal an association of arousals with sleepiness in a similar population as in this study.[10] In another study done in Singapore, severe snoring, higher sleep efficiency and increased total arousals predicted excessive daytime sleepiness.[16] We have chosen to analyse the data based on cut-off AHI ≥5 to investigate these risk factors based on data from previous studies, which showed that the cardiovascular consequences of SDB may be present even at mild-to- moderate AHI.[4,5]

For the same BMI, there were differences in body fat proportion among different races i.e, Malays and Indians have a higher proportion of body fat given the same BMI when compared to the Chinese population.[17] A BMI of 25 (obese category)[18] had a positive predictive value of 75% for AHI ≥5, area ROC = 0.668, suggesting that even mildly obese Asians are predisposed to SDB. Neck circumference was one of the predictors for increasing severity of SDB, based on AHI criteria. While the BMI is a useful tool to measure obesity, the inclusion of upper airway cephalometric data in our Asian population may be important in improving our multivariate modelling for other predictors of SDB.

With regard to hypertension, a previous study by Young et al[19] showed that the odds ratio for hypertension was 1.8 when the AHI cut-off was 15 versus 0. Significantly, with AHI ≥5, one is 3 times more likely to develop hypertension in our study. This finding has implications for initiating treatment for patients with borderline sleep studies, especially when sleepiness is not the primary complaint. The data would suggest that AHI ≥5 is a reasonable threshold for initiating therapy, particularly in the presence of cardiovascular risk factors.

In the logistic regression analysis, 3 factors were predictive of hypertension in our SDB patients – age, BMI and lowest oxygen saturation – when adjusted for AHI ≥5. A comparative study by Ong et al[20] did show that for the same AHI, Asians had a lower oxygen saturation than Caucasians. Worsening nocturnal hypoxaemia, and not AHI, also correlated with impaired vascular endothelial function and left ventricular filling in a study by Kraiczi et al.[21] The above derangements in physiology as a result of hypoxaemia can explain, in part, our finding of lowest oxygen desaturation as a predictor of hypertension.

The complaint of sleepiness may be expressed in many ways, for example, tiredness, fatigue, lethargy and lack of energy.[22] Previous work done by one of the authors (PHL)[10] have shown that the ESS score could predict sleepiness in this population when compared with the sleep latency on the multiple sleep latency test (MSLT), although this correlation is only a modest one ($P = 0.039$). An ESS of 8 or above predicted a mean MSLT of <10 minutes with a sensitivity of 73.9% and specificity of 50.0%.[10] Thus, we have used an ESS of 8 and above as an objective marker of sleepiness in this study. Two consistent predictors for an ESS >8 have emerged in our study – the subjective complaint of sleepiness and lowest oxygen desaturation during sleep. This finding is similar to the results from a study done by Chervin and Aldrich,[23] where they found that the lowest oxygen saturation was at least as predictive for sleepiness as the total AHI.

In conclusion, the lowest oxygen saturation attained during sleep appeared to be the single common predictive factor for both hypertension and sleepiness in our study. Perhaps, sleep physicians should reduce the threshold for treating such patients and not rely entirely on AHI for initiating therapy, particularly in Asians. Increasing recognition of risk factors for sleep apnoea and its consequences would help physicians decrease morbidity and perhaps, mortality from sleep disordered breathing in our population.

All the work in this study was performed at the National University Hospital Sleep Laboratory.

All authors have no financial conflict of interest whatsoever in the participation and execution of this study.

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