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Original article

Excessive daytime sleepiness in obstructive sleep apnea: prevalence, severity, and predictors☆

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Abstract

Objectives: To assess prevalence, severity, and predictive factors of excessive daytime sleepiness (EDS) in obstructive sleep apnea (OSA) in an Asian population.

Methods: A retrospective, cross-sectional study of data from patients diagnosed with OSA over a period of three years and having had overnight polysomnography (PSG) followed by daytime multiple sleep latency test (MSLT). Respiratory disturbance index (RDI) was used for diagnosis and assessment of severity. OSA was classified as mild (RDI 5–20), moderate (RDI 20–40), and severe (RDI > 40). EDS was objectively assessed using MSLT. According to MSLT, patients were categorized into two groups; EDS (mean sleep latency:MSL < 10) and no EDS (MSL > 10). PSG, MSLT and demographic data were subjected to univariate and multivariate analyses to ascertain predictive factors of EDS.

Results: There were 195 patients comprising 89.4% males and 10.6% females. The severity of OSA was mild in 35.9%, moderate in 27.2%, and severe in 36.9%. EDS was demonstrated in 87.2%. Sleep onset REM periods were detected in the MSLT of 28.2% patients. Univariate analysis demonstrated age, RDI, sleep efficiency, total arousals, arousals with apnea, arousal index, number of desaturations, and severity of snoring as significant predictors of EDS. However, stepwise logistic regression analysis identified only sleep efficiency, total arousals, and severity of snoring as significant predictive factors.

Conclusions: OSA causes EDS in the majority of patients. Severe snoring, higher sleep efficiency and increased total arousals in polysomnography seem to predict EDS.

Keywords: Obstructive sleep apnea; Excessive daytime sleepiness; Snoring; Multiple sleep latency test

1. Introduction

Excessive daytime sleepiness (EDS) is a well recognized consequence of obstructive sleep apnea (OSA), increasingly considered an important health problem leading to accidents, psychosocial morbidity and poor quality of life [1–4]. However, the subjective evaluation of EDS is complicated by the fact that patients may complain of fatigue, tiredness, and lack of energy rather than sleepiness itself [5]. Therefore, objective assessment of prevalence, severity, and predictors of EDS in OSA would be useful in understanding the magnitude of the problem and identifying high risk groups.

Several studies have looked into the predictive factors of EDS in OSA patients from predominantly Caucasian populations [6–10]. A study from Singapore has indicated prevalence of snoring and OSA syndrome to be around 77 and 15%, respectively, in that country [11]. In this context, we were interested in determining prevalence, severity, and predictors of EDS in the local OSA population of Singapore.

2. Materials and methods

2.1. Sample and acquisition of data

A total of 195 consecutive patients diagnosed with OSA at the Sleep Disorders Unit of Singapore General Hospital

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between January 2000 and December 2002, having gone through both overnight polysomnography (PSG) and multiple sleep latency test (MSLT) were included in the study. All patients were seen by a single clinician (KP), who routinely performed MSLT and PSG in every case. The vast majority of cases were referred because of snoring, and a few for the complaint of daytime sleepiness. Clinical, demographic, PSG and MSLT data were collected retrospectively from case records. Only pre-treatment data were considered for analysis.

2.2. Overnight polysomnography

Overnight polysomnography consisted of continuous recordings from four electroencephalographic (EEG) leads (C4A1, C3A2, O1A2, O2A1 of international 10–20 system), two electro-oculographic leads (ROC A1, LOC A2), four electromyographic (EMG) leads (two sub mental and bilateral tibialis anterior), thermistors for nasal and oral airflow, strain gauges for thoracic and abdominal excursion, finger pulse oximetry and electrocardiography (ECG). Thirty-second epochs were analyzed and sleep stages were scored according to the international criteria of Rechtschaffen and Kales [12]. All patients had maintained sleep logs, which were scrutinized prior to PSG to ensure adequate sleep hygiene. Those who were on concurrent medications for underlying medical problems were advised to discontinue sedative drugs at least one week before the test.

An apnea was defined as more than 90% reduction in airflow for at least 10 s [13], hypopnea as 50–90% reduction of airflow for at least 10 s associated with 4% or more reduction in oxygen saturation and/or arousal. The respiratory disturbance index (RDI) was defined as the total number of apneas and hypopneas per hour of total sleep time. The diagnosis and assessment of severity of OSA were based on RDI. We defined RDI of 5–20, 20–40, and >40 as mild, moderate, and severe OSA, respectively.

EEG arousals were scored according to the criteria of American Sleep Disorders Association [14]. Arousal index was defined as total number of EEG arousals per hour of total sleep time. When the arousal occurred within 3 s after a leg movement, it was counted as leg movement associated arousal.

Other PSG sleep variables considered in the statistical analysis were sleep efficiency, percentage of delta sleep, percentage of rapid eye movement (REM) sleep, number of oxygen desaturations, maximum desaturation, and periodic limb movement (PLM) index.

The degree of snoring, assessed using audio recording during PSG, was classified into mild, moderate, and severe groups by loudness. Although the signal strength was not quantified in terms of decibels or frequency, a second technician listened to all the recordings and re-checked classification in order to avoid observer bias. Around 95% concordance was seen between the two observers. Each degree of snoring was given a score to indicate severity for statistical analysis. No snoring was scored as 0, and mild, moderate and severe snoring as 1, 2, and 3, respectively.

2.3. Multiple sleep latency test

The MSLT, conducted on the morning following PSG according to the American Sleep Disorders Association guidelines [15], consisted of four 20-min nap trials at intervals of 2 h. The recording montages were similar to that of the PSG, except that chest and abdominal strain gauges and thermistors were not included. The nap trial was terminated at 20 min if the subject did not achieve sleep, and was continued for 15 min after sleep onset if sleep occurred within 20 min. Epochs were scored according to the rules of Rechtschaffen and Kales [12].

Sleep latency was defined as the duration in minutes from lights-out to the first epoch of sleep in each nap trial. Mean sleep latency was calculated from all four trials of each MSLT. Sleep onset REM periods (SOREMPs) were defined as REM sleep occurring within 15 min of sleep onset. Mean sleep latency was used for objective assessment of EDS. Those with mean sleep latency of >10 were categorized as non-sleepy/no EDS (group A). The sleepy/EDS group (group B), with mean sleep latency of <10, were further classified into two subgroups: moderate EDS (group C) with mean sleep latency 5–10, and severe EDS (group D) with mean sleep latency <5.

2.4. Statistical analysis

All variables between groups A and B were subjected to univariate analysis using chi squared test or Mann–Whitney U test in order to delineate significance; P value of 0.05 or less was defined as statistically significant. Stepwise logistic regression analyses were performed between groups A and B to define variables independently associated with sleepiness. Severe snoring was compared to mild and moderate snoring to determine whether severity is significantly associated with EDS.

3. Results

3.1. Demographic characteristics

The study population consisted of 89.4% males and 10.6% females, with a mean age distribution of 45.5 ± 11.1 years, median of 45 years and range of 20–74 years.

3.2. Polysomnographic characteristics

Mild OSA was determined in 35.9% of cases, with 27.2 and 36.9% falling into the moderate and severe OSA groups, respectively. Descriptive statistics for both the EDS

Table 1
Univariate analysis of patients with and without EDS

Variable	Group A (no EDS) $n = 25$		Group B (EDS) $n = 170$		P value
	Mean	SD	Mean	SD	
Age	52.7	8.8	44.4	11	<0.005
RDI	25.9	18.7	37.1	24.9	0.038
Sleep efficiency	76	14.6	86.7	10.3	<0.005
Total arousals	119.7	54.7	210.4	134.8	0.001
Arousal with apnea	74.1	46	157.6	139.5	0.005
Arousal index	32.3	49.7	34.9	23.5	0.032
Number of desaturations	109.5	140.4	197.2	177.6	0.007
Degree of snoring	1.9	0.6	2.4	0.7	<0.005
Delta sleep %	8.9	7.8	8.7	7.4	0.950
REM sleep %	13.1	7.7	13.0	5.9	0.802
Arousals with PLM	1.5	5.2	8.3	23.6	0.398
Maximum desaturation	77.7	12.6	71.8	14.9	0.053
PLM index	1.7	5.6	4.4	16.3	0.587
Number of SOREMPs	0.2	0.6	0.5	0.9	0.061

95% CI, 95% confidence interval; SD, standard deviation.

and no-EDS groups are presented in Table 1. The majority of snorers (86.8%) belonged to the EDS groups (Table 2).

3.3. MSLT characteristics

EDS proved to be highly prevalent (87.2%) among OSA patients, among whom 52.3% had severe and 34.9% moderate EDS. Mean value for mean sleep latency was 4.5 ± 2.4 for the EDS group and 13.5 ± 2.6 for the no-EDS group. SOREMPs were reported in 28.1% of patients. The numbers of SOREMPs recorded per MSLT were 1 in 13.8%, 2 in 9.7%, 3 in 4.1%, and 4 in 0.5%.

3.4. Statistical analysis of predictors of EDS

Univariate analysis showed age, RDI, sleep efficiency, total arousals, arousal index, arousals caused by apnea/hypopnea, arousals caused by leg movements, number of oxygen desaturations, maximum desaturation, and PLM index as variables significantly different between groups A and B (Table 1). Higher sleep efficiency, increased number of total arousals, and severity of snoring were found to be independent predictors of EDS by the stepwise logistic regression analysis (Table 3).

Table 2
Number of snorers in EDS and no-EDS groups

Degree of snoring	Group A (no EDS) $n = 25$	Group B (EDS) $n = 170$
Mild	5	12
Moderate	16	63
Severe	4	89
No snoring	0	2
Data unavailable	0	4

Table 3
Stepwise logistic regression: variables in the equation

		P value	Odds ratio (OR)	95% CI for OR	
				Lower	Upper
Step 1*	Sleep efficiency	0.001	1.062	1.026	1.100
	Constant	0.029	0.041		
Step 2	Sleep efficiency	0.000	1.084	1.041	1.129
	Snoring:severe vs mild and moderate	0.002	13.551	2.581	71.142
	Constant	0.002	0.004		
Step 3	Sleep efficiency	0.000	1.094	1.045	1.144
	Total arousals	0.011	1.011	1.002	1.019
	Snoring:severe vs mild and moderate	0.008	11.169	1.883	66.247
	Constant	0.000	0.000		

* variables entered on step 1, sleep efficiency; step 2, snoring; step 3, total arousals.

4. Discussion

The number of studies published on possible predictors of EDS in OSA underscores the clinical importance of this subject [6–10]. However, the studies are not absolutely homogeneous. There are some differences evident in the study design, statistical methodology, and tools used to evaluate EDS among different studies. Yet they provide a useful insight into this phenomenon.

Various tools such as Epworth Sleepiness Scale (ESS) and MSLT have been used to evaluate and quantify sleepiness. It is argued that ESS and MSLT measure different aspects of sleepiness; ESS reflects an individual's subjective assessment of sleepiness in relation to day-to-day life whereas MSLT is an objective measure in a laboratory. However, MSLT has been well validated scientifically and is considered to be the gold standard [15]. The use of ESS is debatable, as some studies favour it [16,17] while others have found poor correlation between ESS and MSLT scores [18,19]. Accordingly, we selected MSLT as our objective measure of sleepiness for correlation with predictive factors.

Guilleminault and colleagues conducted a study of determinants of daytime sleepiness among 100 patients with OSA. Using Student's t test, they demonstrated mean percentages of stage 1 sleep to be significantly higher and stages 3 and 4 to be significantly lower in the severely sleepy group compared with the non-sleepy group. The sleepy patients also had significantly higher RDI, percentage of stage 1, percentage of stages 3-4, number of awakenings and lower percentage of REM sleep. Cluster analysis showed nocturnal total sleep time and SOREMPs (in MSLT) to be higher in the sleepy group. However, covariate and multiple stepwise regression analysis failed to demonstrate any statistically significant relation. [6].

Other reported associations of EDS include sleep disordered breathing during NREM sleep [7], RDI, degree

of sleep fragmentation and severity of nocturnal hypoxemia [8], reduced nocturnal slow wave activity [9], and sleep fragmentation indices [10].

In the current study, a MSLT score of >10 was categorized as no-EDS and <5 as severe EDS. Our decision to include mean sleep latency of 8–10 in the EDS group may be controversial. Van den Hoed et al. considered this score to be a 'grey zone' [20]. In our study protocol, mean sleep latencies of 5–10 were classified as 'moderately sleepy' in order to include sleepy patients falling within the grey zone.

In the final stepwise logistic regression analysis only three variables emerged as independent predictors of EDS. Increased number of total arousals as a predictor of EDS can be explained on the basis of sleep fragmentation, as observed in previous studies [10]. Sleep efficiency was found to be significantly higher in the EDS group, probably indicating longer, though fragmented, sleep as the total time in bed was standardized for all cases. Guilleminault and colleagues also found the severely sleepy patients (with MSLT <5 min) to have the greatest sleep fragmentation and longest total sleep time [6]. These findings probably indicate that OSA patients experience sleep related problems throughout 24 h, with EDS during the day and prolonged yet fragmented sleep at night. This observation is of particular importance in understanding the impact of OSA on sleep and wake states.

Degree of snoring is the third independent predictor. An interesting analogy can be drawn from a study of community-dwelling adults published by the Sleep Heart Health Study Research Group, in which a significant association was found between snoring and sleepiness, independent of the effect of elevated RDI [21]. A potential drawback in our study is that the method of quantifying snoring is not foolproof. The ideal method would be to quantify audio signals in terms of decibels and frequency, yet we believe we have provided reasonably dependable data on snoring. Snoring as an independent risk factor for EDS in OSA merits further research.

Of particular interest is the presence of SOREMPs in the MSLT of 28.1% cases. Although not analyzed in this study, all OSA patients underwent subsequent repeat PSG and MSLT with continuous positive airway pressure (CPAP) titration that demonstrated abolition of SOREMPs. In the analysis of clinical data none of the patients revealed features of narcolepsy. It is therefore reasonable to infer that SOREMPs were caused by OSA rather that other associated sleep disorders such as narcolepsy.

The vast majority of studies on OSA and EDS have been conducted in Western countries. There is paucity of data from the Asia. The Singapore population predominantly consists of ethnic Chinese. In a previous study from our centre in Singapore, involving a healthy adult population, the prevalence of OSA was estimated to be 20.8% [11]. Of this, 72% had EDS, with a prevalence of OSA syndrome (OSA + EDS) estimated to be 15%. Our current study also demonstrates a high prevalence (87.2%) of EDS among patients with OSA. It is of great value to compare these two studies with a similar study from the West in order to note geographical differences. Using data from the Wisconsin Sleep Cohort study, Young et al. found the prevalence of sleep-disordered breathing (defined as apnea-hypopnea score of 5 or more) in a population of 30–60 year-old adults to be 16.5%, with EDS among these estimated at 19% [22]—a figure very much lower than the two Singapore studies. The prevalence of OSA in Singapore (20.8%) is slightly higher than in the Wisconsin study (16.5%). However, in interpreting the discrepancy of these values it should be taken into account that the Wisconsin study used a questionnaire to assess EDS, whereas it was validated by MSLT in the Singapore studies.

Our study is an attempt to objectively evaluate sleepiness and predictors in OSA in an Asian population. To our knowledge, this is the largest study of EDS in OSA conducted in an Asian country, and it shows a similar trend to that seen in other studies: disturbed night sleep leads to excessive daytime sleepiness.

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