Sleep Apnoea and its Relationship with Cardiovascular, Pulmonary, Metabolic and Other Morbidities

Abstract:

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F Khan, C Walsh, SJ Lane, E Moloney
Peamount Hospital, Newcastle, Co Dublin

Abstract

Sleep apnoea (OSAS) is a multisystem disorder. There is a high prevalence of cardiovascular and metabolic morbidities in patients investigated for sleep apnoea. We aim to evaluate any association between cardiovascular, metabolic and pulmonary co morbidities in patients investigated for OSAS and whether clinical findings based on Epworth sleep score (ESS) and snoring helps in diagnosing sleep apnoea. 258 consecutive patients who were electively admitted for sleep assessment in Peamount Hospital, Dublin from Sept 2009 to Aug 2011 were retrospectively reviewed. 139/258 were diagnosed as OSAS. Cardiovascular, metabolic and pulmonary co morbidities were 46.12%, 37.2% and 29% respectively. There is no correlation found between ESS, Snoring with Apnoea Hypopnoea Index in OSAS group. Screening for OSAS should be considered in patients with certain cardiovascular and metabolic disorders. PSG is so far considered the gold standard investigation to diagnose OSAS and better clinical evaluating tools need to be formulated.

Introduction

Obstructive sleep apnoea syndrome (OSAS) is characterized by recurrent episodes of apnoeas and hypopnoeas due to complete or partial collapse of the upper airway during sleep respectively. Different screening programmes in America, Europe and Australia have shown that there is a remarkable proportion of the adult population suffering from mild-to-moderate sleep-disordered breathing.[1,2] The foremost common risk factor of rising prevalence of OSAS is obesity. Studies have consistently shown that body mass index (BMI) is the strongest risk factor for OSAS. Almost 70% of those with OSAS are obese and its prevalence in obese men and women is about 40%.[3] A large neck circumference is also associated with an increased risk of OSAS. Infact, neck circumference of 15.7 in (40 cm) or greater may have a greater sensitivity and specificity than BMI in predicting OSAS, regardless of the person's sex.[4]

OSAS affects multiple organs and systems particularly the cardiovascular system. Several conditions associated with OSAS are also present in obese individuals including hypertension, insulin resistance, systemic inflammation, visceral fat deposition and dyslipidaemia. Weight loss has been accompanied by improvement in characteristics related not only to obesity but to OSAS as well; suggesting that weight loss might be the most vital step in the management of both conditions.[5] Over 5000 European sleep apnoea patientsâ   database suggested high prevalence of cardiovascular and metabolic morbidities among them. It has also been mentioned that sleep-disordered breathing is likely to be a risk factor for hypertension and consequent cardiovascular morbidity in the general population.[6] As we know excessive daytime sleepiness, snoring, and fatigue are the major symptoms of patients with OSAS, there are few scoring systems drawn to quantify those symptoms, Epworth Sleep score (ESS) is one of them. The validity of this questionnaire and its relationship with sleep studies is still questionable.[7]

We sought to determine whether clinical findings based on ESS help in diagnosing sleep apnoea and we also aim to evaluate any association between cardiovascular, metabolic and pulmonary comorbidities in patients investigated for sleep related disorders.

Methods

A retrospective two years review of 258 consecutive patients who were electively admitted for sleep assessment in Peamount Hospital, Dublin from Sept 2009 to Aug 2011 was performed and analysed using statistical software R version 2.12 [cite R Development Core Team (2010). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org/. Patients admitted to the study included all those that were more than 20 yr of age, symptoms of daytime somnolence, fatigue, snoring history, and high ESS. Patients with unstable angina, liver cirrhosis, end-stage renal disease, haematological disease or diagnosed cancer were excluded. Their general characteristics on admission including calculated ESS are shown in Table 1.

All the patients underwent polysomnography (PSG). Standard overnight PSG was performed to document sleep parameters and architecture in each patient in a sleep laboratory. Variables are manually recorded in the quiet and darkened room.

Their PSG variables were calculated to formulate the diagnosis of sleep apnea and categorize it accordingly. Apnoea is defined as more than 90 percent dropping of baseline airflow with continued chest wall and abdominal wall movement for a minimum of 10 sec, regardless of whether or not there was an associated oxygen desaturation or sleep fragmentation; baseline is defined as the mean amplitude of the three largest breaths in the two minutes preceding the onset of the event. The definition of hypopnoea was a 50 percent or greater reduction in airflow for a minimum of 10 seconds, associated with an equal to or greater than a 4 per cent drop in SpO2 or an EEG alpha wave arousal.[8] The definition of desaturation episode was equal or more than a 4 percent drop in SpO2, which was induced by apnoea or hypopnoea events. Apnoea hypopnoea index (AHI) was the number of apnoea plus hypopnoea events per hour of total sleep time, and desaturation index (DI) was the number of desaturation episodes per hour of total sleep time. AHI helps in defining and grading the severity of OSAS. An AHI of less than 5 is considered normal; 5-15 is mild; 15-30 is moderate; and more than 30 events per hour characterises severe sleep apnea.

The medical notes of all 258 patients, who had PSG, were reviewed. Among them, we further analyzed the prevalence of cardiovascular diseases including Hypertension (HTN), Ischaemic Heart Disease (IHD), Valvular Heart Disease, Arrhythmias; Pulmonary diseases including Asthma, Chronic Obstructive Pulmonary Disease (COPD); Hyperlipidaemia; Endocrinological diseases including Hypothyroidism, Diabetes; Gastroenterological diseases including Gastritis, Gastroesophageal Reflux Disease (GORD), Hiatus Hernia (HH), Peptic Ulcer Disease (PUD) and Depression.

Results

The patients were divided in Sleep apnoea (OSAS) and non sleep apnoea (NON OSAS) group on the basis of their PSG variables as shown in Table 2. Of 258 patients, 139 (77.6% males, 22.3% females) are OSAS and 119 (47% males, 54% females) are NON OSAS. As per AASM criteria[9] for scoring sleep apnoea, our OSAS group was further divided in mild (56%), moderate (24%) and severe (20%) sleep apnoea. In OSAS group, there are strong correlations found between age ($p=0.045$, $r=0.162$), sex ($p=0.0002$, $r=0.296$), BMI, and smoking history showing an increased prevalence of sleep apnoea in elderly, obese, male smokers but there is no correlation found between ESS ($p=0.743$, $r=0.026$), with AHI. As sleep experts know, females with OSAS exhibit a lower AHI, less severe hypoxaemia and greater BMI. Similarly in NON OSAS group, there is no correlation found between ESS ($p= 0.965$, $r= -0.003$) with AHI as shown in the Table 3. It reconfirms the statement that all snorers are not sleep apnoeic and sleep apnoea can not entirely be diagnosed with clinical evaluation sleep scores.

In addition, the prevalence of co-morbidities was split into two major stems of OSAS and NON OSAS. It showed higher prevalence of cardiovascular diseases in OSAS group (51% vs 40%) especially HTN, metabolic disorders including diabetes (13% vs 8%), hyperlipidaemia (27.3% vs 25%) and hypothyroidism (8.6% vs 5.8%) in comparison to NON OSAS group as shown in Table 4. It is also found that respiratory diseases including COPD and asthma are also slightly more prevalent in OSAS group than NON OSAS but less frequently as compared to metabolic and cardiovascular diseases.

A statistician has been consulted and a multivariate model has been fitted to identify factors jointly associated with OSAS. In order to determine the factors that influence the presence of OSAS in a multivariate model, a backwards stepwise logistic regression was fitted. Factors entered included ESS, Smoking, Age, BMI and Gender. In the final model Age (p=0.001), Gender (p<0.0001) and BMI (p<0.0001) were statistically significantly associated with OSAS.

It is also analyzed that there is a relatively higher prevalence of depression 28/258, (10.8% vs 8.5%)[10] in all patients enrolled for PSG, as compared to the general population, who do not have exhibiting risk factors for PSG enrolment. In addition, 54/258 (21%) of all high risk sleep apnoea patients suffer from gastrointestinal disorders. Sleep apnoea cannot only be diagnosed clinically; PSG is so far considered the gold standard investigation to diagnose OSAS. In general, OSAS is more common in elderly and obese, male smokers. There is a higher prevalence of cardiovascular, pulmonary and metabolic co-morbidities in high risk sleep apnoea subjects.

Discussion

A large proportion of adult patients who are referred to sleep disorder centres have excessive daytime sleepiness. ESS is a simple, self administered questionnaire which provides a measurement of personâ s day time somnolence. The majority of older adults (almost 60%) are unable to answer all of the ESS question stems. It may underestimate sleepiness severity in older subjects.[11] In order to confirm the presence of upper-airway closure during sleep and to assess the patient’s level of risk of OSAS, we need to perform a full PSG.[12] OSAS is an independent risk factor for hypertension[13] with 30% prevalence of occult sleep apnoea among middle-aged males with so called â primary hypertensionâ . The results of our study identified similar results in the Irish population, showing a 33.1% prevalence of hypertension in OSAS group.[14] Peppard describes the more severe the sleep apnoea, the higher the prevalence of hypertension.[6] OSAS-related hypertension is predominantly diastolic and nocturnal, affect non-dippers, treatment resistant and high risk of the formation of arterial lesions.[15] Further described Continuous Positive Airway Pressure [CPAP] ventilation not only plays an important role in treating OSAS but also appears to be significant for refractory HTN.

Metabolic disorders in OSAS has been studied and shown a close relationship between OSAS and increasing prevalence of hyperlipidaemia.[16] There is 33.8% prevalence of hyperlipidaemia in OSAS population and it is independent of gender difference, likewise in our study a 27.3% prevalence is identified.[17] There is 10.6% prevalence of more than one metabolic disorder including HTN, hyperlipidaemia and diabetes in patients suffering from OSAS[18], as compared to 13.1% in our Irish cohort.

Considering pulmonary complications in OSAS, Flenley described combination of COPD and OSAS as Overlapping syndrome [OS] which is characterised by hypoxia, hypercapnia, pulmonary arterial hypertension and nocturnal hypoxemia.[21] It is estimated in general population that about 325,000 (7.3%) people suffer from COPD in Ireland.[19] In the European Union, general prevalence of COPD lies in the range of 4 â 10% as per EUPHIX summary in December 2009.[20] COPD prevalence, in our sleep apnoea patients is 13.6%, which correlates closely to international findings. OSAS is an independent risk factor for asthma exacerbations. Likely explanation of increased frequency of asthma exacerbations and poor control in OSAS are neuromechanical reflex bronchospasm, gastroesophageal reflux disease, local and systemic inflammation and OSAS-induced cardiac dysfunction. There is a higher prevalence of OSA symptoms in an asthmatic population (39.5%) when compared to a primary care population (27.2%).[22] Interestingly, in comparison to our study prevalence of asthma in OSAS patients is much lower than international standards at 17.2%. Justification of this may be due to diagnosis of sleep apnea masking asthma diagnosis. Also, COPD may be over diagnosed instead of asthma as both are overlapping obstructive ventilatory defects.

Negative intrathoracic pressure in OSAS patients have been suggested as the underlying mechanisms of nocturnal gastro-oesophageal reflux diseases (GORD). Obesity is a common factor and a cause of the high prevalence of GORD in OSAS patients.[23] It has also been described that the treatment of OSAS with nasal CPAP helps in improving nocturnal GORD and decreases the frequencyof symptoms by 48%. There is greater improvement in GORD expected with higher nasal CPAP.[24] As we know, there is a high frequency of nocturnal arousals, movements and reflux symptoms in OSAS patients. Nasal CPAP corrects negative intrathoracic pressure which corrects these predisposing factors and reduces nocturnal GORD symptoms.[25]

Despite the large number of cross-sectional or case-controlled epidemiological studies, the issue of whether OSAS independently increases the risk of mentioned systemic diseases have been contentious. The development of sophisticated animal models will be required to explore pathophysiological mechanisms, and the collaboration of respiratory, cardiovascular, epidemiological, and clinical trials experts to examine the clinical consequences of diagnosing and treating sleep apnoea. In conclusion, the diagnosis and treatment of sleep-related breathing disorders can improve health outcomes in patients suffering from or at risk for cardiovascular, metabolic, endocrinological, gastroenterological and respiratory diseases.

Correspondence: F Khan
AMNCH, Tallaght, Dublin 24
Email: drfaheemkhan@gmail.com

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