DOI Number: 10.5958/2320-608X.2019.00058.1

Assessment of Neurocognitive Impairment in Obstructive Sleep Apnea

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Abstract

Sleep apnea is usually reported in south Indian population. The indications of obstructive sleep apnea (OSA) comprise of breathing difficulties particularly owing to obstruction in the upper airway tract. The present study investigated the effect of the syndrome, the patients documented with OSA, by categorizing the patients into mild, moderate and severe OSA groups depending on apnea-hyponea index (AHI), derived from sleep study (polysomnographic findings). The comparative evaluation of various outcomes considered in this study included healthy individuals (control group, AHI < 5), mild OSA (AHI 5-15), moderate (OSA 15-30) and severe (AHI > 30). Investigations were conducted on the subjects which evaluated baseline characteristics, polysomnographic data and neuro-cognitive performances by Mini-Mental State Examination (MMSE). The results revealed significantly higher body mass index (BMI), snoring and decresed sleep efficiency in patients with sleep apnea syndrome when compared with control group. OSA patients further exhibited compromised neuro-cognitive. The intensity of the impairments and difficulties increased with upsurge in severity of the syndrome among all patients. The findings of this work strongly indicated that impaired executive functioning; neuro-cognitive abnormalities exit in a heightened state among OSA patients, than in the normal healthy individuals, the control group. These findings in aggregate would help clinicians in diagnosis and in understanding the disease prognosis.

Keywords: *Obstructive Sleep Apnea, apnea-hyponea index (AHI), Mini-Mental State Examination (MMSE), Polysomnographic findings.*

Introduction

Sleep is a vivacious part of good health and wellbeing. Pathologic disruption of sleep is related with a number of adverse health and safety outcomes[1-2]. Episodic cessation of breathing during sleep is referred as sleep apnea[3]. Sleep apnea is broadly classified into three principal types: obstructive, central and mixed. Obstructive sleep apnea, is caused by collapse of the soft tissues of upper airway during sleep whereas, Central apnea, which occurs when brain does not send proper signals to the muscles that controls breathing. Additionally some people have complex sleep apnea which is a combination of both The distinctive features of obstructive sleep apnea (OSA) includes repeated episodes of high-resistance breathing, reduced breathing (hypopnea events), and breathing pauses (apnea events) during a single night of sleep[4-5]. OSA is generally defined as five or more apneas and/or hypopnic events as per hour of sleep [(apnea-hypopnea index (AHI)>5)]. The severity of OSA is measured by the apnea-hypopnea index (AHI), obtained by counting the total number of apneas and hypopneas during sleep and dividing that by the hours of sleep. An AHI lower than 5 per hour is considered as normal; an AHI of 5 to 15 is mild OSA, 15 to 30 is moderate OSA, and greater than 30 events per hour is severe disease. The common symptoms of OSA is excessive daytime sleepiness, which may be mild or severe enough to interfere with employment or driving an automobile, day to day activities and could also leads

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to cognitive decline[6-7].

OSA is being progressively renowned as a cause of substantial medical, social and psychological morbidity as well as an increased mortality[8-9]. The concerns of OSA are diverse and in most of the cases are often serious; nevertheless the syndrome remains largely under-diagnosed. Early recognition and treatment are essential to alleviate the symptoms and consequence of sleep related disorders. The aim of this study was to determine the strength of association of OSA and its sequelae of events to morbidity in a representative sample and to assess the neurocognitive functioning in patients with OSA and its correlation with the severity of OSA.

Material and Method

Study protocol

100 OSA patients and 50 control subjects of both the genders were recruited for the study. Prior to the study, informed consent will be obtained from the patients and the ethical clearance was obtained from Institutional Ethics Committee of Deccan College of Medical Sciences and allied hospitals. Data on demographic characteristics, sleep pattern, medical history, medication use, and habits was obtained with the use of a standardized questionnaire administered by a trained technologist before the initiation of overnight polysomnography (PSG); the questionnaires was reviewed by a physician. Patients on continuous positive airway pressure (CPAP) therapy, oral appliances or any other treatment for OSA, Diabetics and any other disorders such as Parkinson's disease which are known to affect peripheral neuropathy, smokers, pregnant and lactating female were excluded from the study.

Assessment of Sleep apnea

Based upon the symptoms the patient's undergone full-night polysomnographic study within the premises of a sleep lab. Continuous polygraphic recordings was acquired applying electroencephalographic, electrocardiographic, electro-oculographic and actigraphic leads. Total cessation of airflow for at least 10 seconds was classified as apnea and partial airway closure, resulting in a reduction of airflow by more than 30% for at least 10 seconds and associated with oxygen desaturation of 4% or more, was termed as hypopnea. Calculated polysomnographic variable was including the apnea–hypopnea index[15].

Cognitive function test

The Mini-Mental State Examination (MMSE) is a well-validated screening tool and was used for appraisal of cognitive impairment. The test measures orientation to time and place, attention, immediate recall, short-term verbal memory, calculation, language, and the ability to follow simple verbal and written commands. The division of scores were according to the task allotted in each part of the test such as for orientation (10 points), registration (3 points), attention and calculation (5 points), recall (3 points) and 9 pints for language and praxis. The scores were summed and the interpreted. An aggregate score in the range of 24-30 showed no cognitive impairment, 18-23 mild cognitive impairment and 0-17 severe cognitive impairment

Statistical Analysis

Student's t-test was used to compare mean values at baseline among OSA patients with those in the control group. The data will be analyzed by an analysis of variance (ANOVA), chi-square, t-tests, correlation and regression analysis and other necessary statistical analysis wherever necessary. The differences was considered significant if $p < 0.05$. All the analysis was processed by the software's; SPSS 18.0 and Origin 8.

Observations and Results

The average time for administration of the OSA questionnaire and cognitive test was 30 minutes. A total of 123 patients were enrolled to the sleep center during the study period, of whom, 100 (M/F, 1/0.27) were considered eligible to participate in the sleep study and underwent polysomnography. Based on the past history, 23 patients were deemed ineligible as they were taking Continuous positive airway pressure (CPAP) treatment for OSA. A total of 100 of the 123 study participants (71%) were identified as having obstructive sleep apnea. Table 1 shows the demographic data of the study group and controls. Apnea-hypopnea index (AHI) was acquired by including the total number of apneas and hypopneas during sleep and dividing that by the hours of sleep. Among all the OSA patients 26% were having mild OSA, 16% moderate and 48% were having severe OSA (with respect to the AHI criteria discussed above) respectively.

Table 1: Socio- demographic characteristics of participants.

Characteristics	OSA patients (n=100)	Controls (n=50)	Significance (P value)
Age (Yr) (Mean ± SD)	51 ± 12	62 ± 3	0.836
Male Sex (%)	52	36	0.04
Habitual Snoring (%)	29	11	<0.001
Body Mass Index (Mean ± SD)	36 ± 5	21 ±3	<0.001
Obesity (%)	23	08	<0.001
Apnoea-Hypopnea Index (AHI)	34.6±16.5	1.4±0.8	<0.001
Current Consumption of Alcohol (%)	15	9	0.12

Table 2 shows the evaluation of MMSE for cognitive assessmentin both OSA patients and control. We observed a significant decrease in MMSE score in OSA patients when compared to control.Orientation 3.2±0.8 was low in OSA patients whereas it was found to be 3.9±1.1in controls. Memory (immediate and delayed recall), registration, attention and calculation skills, language and constructive praxis was observed to be 7.9± 1.3, 2.2±0.6, 3.7±1.2 and 2.2±0.6 respectively in OSA patients which was found to significantly low in contrast with controls.

Table 2: Cognitive performance of OSA patients and controls .

Cognitive test	Patients with OSA (n=100)	Controls (n=50)	Significance (P value)
MMSE	26.7 ±1.6	28.9 ± 0.9	0.01
Orientation	3.2±0.8	3.9±1.1	0.042
Registration	2.2±0.7	2.6±0.4	0.038
Attention and Calculation	3.7±1.2	4.2±0.7	0.046
Recall	7.9± 1.3	8.7± 1.0	0.02
Language and Praxis	2.2±0.6	2.7±0.3	0.041

Discussion

OSA syndrome, estimated to occur in about 1 in 20 of all adults, is usually unrecognized, undiagnosed and results in behavioral, metabolic and cardiovascular morbidity. The patients with OSA have difficulty with attention, task learning and performing any task at work compared with the general population[16]. As such cognitive impairment can also disrupt a patient's ability to gain or maintain employment because their behaviour may be misunderstood as laziness or a lack of motivation[17]. The present study, included adults from Hyderabad, South India, attempted to examine the epidemiological and cognitive status of obstructive sleep apnea, particularly its relationship with AHI, obesity and cognitive parameters.

Executive and cognitive functioning are integral parts of daily life. The data suggested serious impairment by day time sleepiness, sleep fragmentation on cognitive abilities in OSA patients. The negative effects of these attributes have also been extensively discussed in research findings of other researchers as well, such as impaired cognitive function reduced attention, vigilance,

memory, executive dysfunction, with worsening effects with increase in severity; resulting in a global cognitive impairment..

Our results demonstrated that, sleep disordered breathing was strongly associated with the impaired cognitive functioning. The Mini-Mental State Examination (MMSE), a well-validated selection tool was used for evaluation of cognitive impairment. In our study while assessing attention, memory, language and executive functions, we found that the performance of OSA patients was impaired in comparison to healthy controls in. The impact of OSA on cognitive performance provided insight into important parameters in ascertaining the degree of damage in OSA subjects. Low attention, loss in memory and low executive function capabilities are useful indicators in understanding the symptoms of OSA. MMSE, being a global measure of cognitive functioning, showed significant categorical changes in various aspects of executive function, and the overall score indicated the implication of the score.

Hence, a variability of cognitive fields seems to be exaggerated in this condition and brief cognitive testing may detect such changes which are in consistent with the previous findings by Bawden CF et al 2011[10].

Our analysis suggests that OSA of reasonable severity may be associated with moderate to large impairments. While assessing the cognitive performance in patients with mild OSA, a noteworthy impairments may not be evident at low levels of sleep disordered breathing and symptomatology.

One of the probable reason could be either of nocturnal hypoxaemia or severe sleepiness in the impairment to cognitive performance both reported by [18,19] and measured patients with OSA[20,21]

As revealed previously, cognitive dysfunction may be an important denominator in the increased risk of occurrence of road accidents in patients with OSA. We believe that the assessment of cognitive impairment, even being of mild severity, is enough to persuade further studies targeting at explicating the etiology of these deficits.

Conclusion

In conclusion, we found that OSA was responsible for inconsistencies in attention, memory and executive functioning. We observed cognitive impairment in patients with OSA, which is a significant factor in averting road accidents and may help the patient to improve or maintain employment. The early medical treatment may help to prevent such symptoms in patients with OSA and can improve the quality of life.

Summary

In summary, the results of this study provide compelling evidence that OSA is related with cognitive decline. Although hypoxemic stress and sleep disruption are likely the key players in the pathogenetic mechanisms behind such derangements, the role of an underlying common denominator needs to be scrutinized. Further studies are needed to define the driving mechanisms through which sleep-disordered breathing promotes many of these consequences.

Funding: No funding was received for this research.

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial in the subject matter or materials discussed in this manuscript.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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