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Insomnia, Sleep Apnea, and Illness: Does Comorbidity Delay the Diagnosis of Obstructive Sleep Apnea in Patients with Insomnia?

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Abstract

Introduction: About 30% to 70% of those with sleep apnea also exhibited symptoms of insomnia. To date, there are few published reports that study how insomnia and obstructive sleep apnea are assessed in the clinical setting. The purpose of the present research was to investigate the relationships between insomnia, sleep apnea, and comorbid illness and the delay in referral for a sleep study to diagnose obstructive sleep apnea.

Materials and Methods: A retrospective chart review of the medical record of patients diagnosed with insomnia and obstructive sleep apnea was conducted. A Multiple Regression was performed to assess the magnitude of the relationships between the predictor variables; age, gender, ethnic group, body mass index, and number of comorbidities with the outcome variable time to referral for a sleep study in days.

Results: The number of medical records analyzed was 78. Of the predictor variables, BMI was significant and negative (t=-2.701, p=0.009). For the specific comorbidities, endocrine disorders was significant and positive (t=2.124, p=0.037), and contributed the greatest association with time to diagnosis of obstructive sleep apnea.

Discussion: Prompt diagnosis and treatment of obstructive sleep apnea in patients can improve quality of life metrics and potentially stabilize co-existing diseases rather than becoming the focus of treatment.

Conclusions: This study highlights areas where greater awareness regarding the recognition of obstructive sleep apnea symptoms is needed in patients who have insomnia and underlying co-morbid diseases.

Keywords: Insomnia; Obstructive sleep apnea; Sleep medicine

Introduction

Sleep is one of the most important indicators of overall health and well-being. Since the association between insomnia and Obstructive Sleep Apnea (OSA) was first recognized over forty years ago, there has been a growing body of evidence that validates the effort to characterize these two entities as a distinct clinical syndrome [1-3]. For patients treated in sleep disorder clinics, about 30% to 70% of those with sleep apnea also exhibited symptoms of insomnia [4]. Therefore, there does appear to be sufficient support to warrant the conceptualization of comorbid insomnia and OSA as a distinct clinical syndrome [5,6].

The multiple identifiable conditions that adversely affect the quality of sleep may further complicate the diagnosis and treatment of sleep disorders. Ye L, et al. [7] performed a cluster analysis from the Icelandic Sleep Apnea Cohort study. The researchers discovered three discrete patterns of OSA symptoms and comorbidities. Interestingly, the "minimally symptomatic group," were also at higher risk of comorbidity. Hypertension, cardiovascular disease, and diabetes were found among those diagnosed with OSA in this group. A later study conducted by Pien GW, et al. [8] replicated the three-cluster structure and again found that the minimally symptomatic group had higher proportions of reported comorbidities.

Parish noted that those with common medical disorders frequently complain about sleep problems [9]. For example, sleep apnea, or by an obstruction, obstructive sleep apnea is ordinarily associated with obesity. However, the co-occurrence of OSA and type 2 diabetes was found to be not only substantial but independent of obesity as well [10]. Both insomnia and OSA seems to share a significant role in the number of negative consequences to one's health, well-being and quality of life [11]. The heightened awareness of sleep disorders and increasing recognition of its personal and economic costs lends sufficient support to make sleep disorders a major public health concern.

Once insomnia and sleep apnea become viewed as a distinct clinical syndrome, it would then be conceivable that patients complaining of insomnia would be screened regularly for sleep apnea. However, this does not appear to be the case in clinical practice. To date, there are few published reports that have examined if patients being treated for specific medical conditions with complaints of co-morbid insomnia are further assessed for sleep apnea. Thus, the purpose of the present research was to investigate the relationships between insomnia, sleep apnea, and comorbid illness. The objective was to explore whether the specific type of co-morbidity will delay the referral for a sleep study. Our hypothesis was that for specific medical comorbidities there is a delay in referral for a sleep study to assess the presence of OSA in patients diagnosed with insomnia.

Materials and Methods

Participants

Participants for the study were patients referred by their Primary Care Physician to the Jacksonville Pulmonary Sleep Disorders Clinic and Sleep Laboratory between January 01, 2011 and December 31, 2016 for a sleep study. Inclusion criteria were patients aged greater than 18 years of age and older. The participants had a diagnosis of both OSA and insomnia as indicated by either International Classification of Diseases (ICD) Code: ICD 9 and ICD 10 [12,13] respectively. Inclusion also required a complete medical record that allowed all statistical calculations to be performed.

All patients diagnosed with OSA underwent standard overnight Nocturnal Polysomnogram (NPSG) evaluation with assessment of 8 standard Electroencephalogram (EEG) channels, bilateral Electrooculogram (EOG), Electromyography (EMG), 2-lead Electrocardiogram (ECG), oronasal air flow measurement using thermistor, nasal pressure transducer, chest and abdominal movement by respiratory inductance plethysmography, and pulse oximetry including pulse wave form using a commercially available data acquisition system (Twin System Grass Technologies, Natus Neurology RI, USA). The NPSG studies were scored as per the 2013 American Association of Sleep Medicine guidelines for the scoring of sleep and associated events [14]. The diagnosis and severity of OSA was established by full NPSG and were based on the definitions and cutoffs for Apnea-Hypopnea Index (AHI), recommended by the American Academy of Sleep Medicine using the 4% rule for the definition of hypopnea. Apnea-hypopnea index was defined as the sum of the number of apneas plus hypopneas per hour of sleep.

Exclusion criteria were pregnant females, chronic, severe mental disorder (Schizophrenia, Schizoaffective, and Bipolar Disorder), and history of a Substance Use Disorder (i.e. Alcohol, Marijuana, Cocaine, Opioids). Patients with medical records that were insufficient to determine a definitive date of diagnosis of insomnia, date of referral for a sleep study, and date of diagnosis of OSA were excluded from the study. In addition, patients treated at Primary Care Clinics that received a previous workshop on sleep assessment were excluded as the increased awareness of recognizing sleep disorders may have changed normal clinic practice.

Procedure

Approval for the study was obtained from the University of Florida-Jacksonville Institutional Review Board (IRB); IRB201700406. First, a Preparatory to Research query of potential participants who meet the inclusion criteria was conducted from Epic electronic health records to determine an adequate sample available for examination. Patient consent was waived by the IRB as no direct patient contact was required. The number of available medical records with both an insomnia and OSA diagnoses was 596. A majority of the records (518) were unacceptable as they either did not have a NPSG or discernable referral dates. A retrospective chart review of the remaining 78 medical records of those patients that met inclusion criteria and with complete information was performed.

The data collected included the variables age, gender, ethnic group, Body Mass Index (BMI), number of comorbidities, and whether prescribed sedative/hypnotic, antipsychotic, or antidepressant medication for sleep. The specific diagnosis of Asthma, Chronic Obstructive Pulmonary Disease (COPD), Nasal Allergies, Arterial Hypertension (HTN), Cerebrovascular Accident (CVA), Coronary Artery Disease (CAD), Gastroesophageal Reflux (GERD), Diabetes Mellitus (DM), Thyroid Disease, Seizures, Anxiety Disorder, and Depressive Disorder was noted. In addition, the date of insomnia diagnosis, date of sleep study referral, and date of OSA diagnosis was recorded. Medical information was obtained from Epic electronic health records, Epic Systems Corporation, Verona, WI.

Statistical analysis

The statistical approach used to analyze the data included first aggregating and quantifying the demographic information age, gender, and ethnic group. Statistical analysis consisted of chi-square tests to measure the frequency differences in obesity as measured by BMI, prescribed sedative/hypnotic, antipsychotic, or antidepressant medication, and comorbidity type. A Multiple Regression was performed to assess the magnitude of the relationships between the predictor variables; age, gender, ethnic group. BMI and comorbidities with the outcome variable time to diagnosis of OSA in days. The comorbidities were categorized into five groups consisting of Respiratory (i.e. Asthma, COPD, Nasal Allergies); Cardiovascular (i.e. HTN, CAD, CVA; Endocrine (i.e. DM, Thyroid Disease); Gastrointestinal (i.e. GERD); and Nervous (i.e. Anxiety Disorders, Depressive Disorders, Seizures). Significance was determined using the alpha level of 0.05. Statistical Package for the Social Sciences (SPSS) V24.0 was used to calculate all statistics.

Results

The sample consisted of 24 men (30.8%) and 54 women (69.2%). The average age of the participants was 53.9 years, SD=11.85. Forty one percent of participants identified themselves as Black, 41% identified themselves as White, 1.3% as Hispanic, and 16.7% as other. The average BMI of the participants was 36.66, SD=9.02. Forty five percent of the sample was diagnosed with a respiratory illness, 67% a cardiovascular disease, 26% an endocrine disorder, 32% a gastrointestinal disorder and 71% with a neurological disorder. The sum of comorbidites is over 100%, as many patients had more than one comorbidity. The type of medication prescribed for insomnia was significant (χ^2=39.9, df=20, p=0.001). Sedatives were the most frequently prescribed medication for sleep (45) followed by antidepressants (24) and then antipsychotics (8). While 32% of the participant were not prescribed a sleep medication, 26% were prescribed more than one medication for sleep.

The average number of days to a diagnosis of OSA was 1074. However, the normality assumption was violated as the Dependent Variable (DV) was positively skewed (Figure 1). Therefore, the average was not an accurate measure of central tendency. The median time to a diagnosis of OSA, alternatively, was 818 days. Figure 1 shows that the majority of participants received a diagnosis of OSA around 445 days after a diagnosis of insomnia. Before the regression estimates were calculated, a linear transformation of the DV was first conducted by performing a natural log transformation of the days

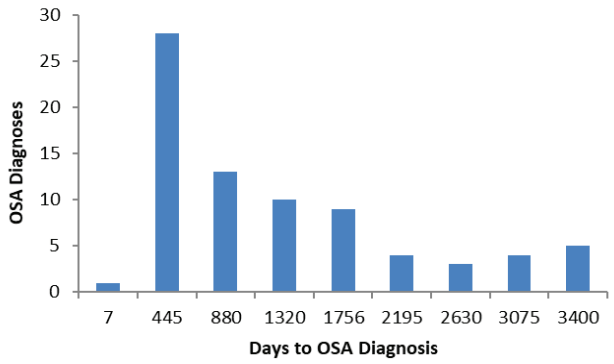

Figure 1: Distribution of Days to OSA Diagnosis.

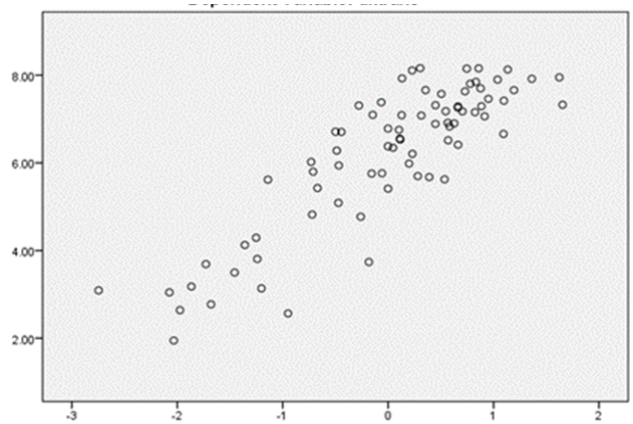

Figure 2: Plot of the transformed DV standardized residuals. DV=Dependent Variable (Days to OSA Diagnosis)

from diagnosis of insomnia to diagnosis of OSA. Next, to evaluate the linearity assumption after transforming the DV, a residual analysis was performed by plotting the standardized residuals of the regression against the observed y-values. Figure 2 shows this improved the distribution of observed y-values and that there was no apparent violation in the equal variance assumption as well.

The test for the overall model fit was statistically significant (F=2.678, p=0.01). Table 1 shows the regression coefficients for the predicted change in the DV per unit change for each IV, holding constant the effect of the other variables (Table 1). For each unit increase in BMI, the predicted value in the dependent variable was estimated to decrease by -0.065 units which was statistically significance (t=-2.701, p=0.009). For the variable Respiratory, for each unit increase in number of comorbidities, the dependent variable was estimated to decrease by -0.091 that was not significant. For the variable Cardiovascular, for each unit increase in number of comorbidities, the predicted value of the dependent variable was estimated to decrease by -0.254 which was not significant.

For each unit increase in number of Endocrine comorbidities, the dependent variable was estimated to increase by 0.712 units which was statistically significance (t=2.124, p=0.037). There is evidence of a linear relationship between number of endocrine comorbidities and number of days to diagnosis of OSA. For the variable Gastrointestinal, for each unit increase in number of comorbidities, the predicted value of the dependent variable was estimated to increase by 0.101 that was not significant. Finally, for the variable Nervous, for each unit increase in number of comorbidities, the predicted value of the dependent variable was estimated to increase by 0.294 which was not significant.

Discussion

The purpose of the present research was to investigate whether the specific type of co-morbidity would delay the referral for a sleep study to evaluate OSA. This study showed that in the primary care setting, for those patients who have insomnia, a delay in the diagnosis of OSA was the longest in patients being treated for endocrine disorders and shortest in those with increased BMI. There appears to be sufficient evidence of a linear relationship between an endocrine comorbidity (particularly DM) and days before OSA diagnosis after a diagnosis of insomnia. Patients diagnosed with a respiratory, cardiovascular, gastrointestinal and/or neurological/psychiatric condition were not found to be significantly associated with delaying the diagnosis of OSA. Finally, there were no referral biases based on age, gender, or race observed for this sample.

The differences in clinical presentation of insomnia and OSA further complicate the identification and diagnosis of sleep disorders. Patients seen in clinical practice and report only a few sleep symptoms may be overlooked in a busy clinic. For primary care providers seeing patients with sleep complaints, physical characteristics such as high BMI, snoring and daytime sleepiness would likely prompt the consideration of a sleep study, whilst a disease such as DM would become the focus of treatment. The link between OSA and DM is fairly robust. Pamidi S, et al. [15] reported that possibly 83% of patients with type 2 diabetes may also have untreated OSA. This study showed that BMI was associated with shorter times to diagnosis of OSA, whereas endocrine disorders had the opposite effect. These findings were consistent with prior research on groups with poorer glucose control [16]. A primary care physician may not recognize the presence and severity of a sleep disorder in pre-diabetics despite the evidence of an increased risk of OSA.

Another possible explanation is that underreporting of sleep symptoms in "minimally symptomatic" patients leads physicians to target the comorbidities rather than assessing for OSA. For patients who frequently reported disruption in the quality of their sleep (e.g. Pamidi S, et al. [15]), gastroesophageal reflux was associated with both initiating and maintaining sleep. It was suggested that those with minimal complaints of GERD may be an unidentified cause of insomnia [17]. Sateia MJ [18] suggested that many sleep disorders may also predispose an individual to both psychological distress and mental illness. Thus, the presence of psychiatric illness may further complicate the diagnosis and treatment of sleep disorders.

The type of medication prescribed for insomnia in this study was similar to previous research that showed patients with Sleep-disordered Breathing (SDB) plus symptoms of insomnia and poor sleep quality reported greater use of sedative and psychotropic medications [19]. When compared to patients with only SDB, more patients who reported significantly worse insomnia symptomology received prescription sleeping aids and psychotropic medications. Similarly, the frequency of hypnotic use was found to be significantly higher in patients experiencing insomnia-related symptoms as opposed to those with minimal symptoms or daytime sleepiness [7]. In this study, 68% of the participants were prescribed one or more sleep medications which may mask a more serious sleep disorder.

The limitations of the present study were the retrospective review of the research which limited the size of the sample to only those

Table 1: Regressions of Days to Diagnosis of OSA.

	Coefficients	Standard Error	t Stat	P-value
Age	0.021	0.016	1.255	0.214
Gender	0.460	0.442	1.041	0.301
Ethnic	-0.131	0.109	-1.206	0.232
BMI	-0.065	0.024	-2.701	0.009
Respiratory	-0.091	0.298	-0.307	0.760
Cardiovascular	-0.254	0.267	-0.951	0.345
Endocrine	0.712	0.335	2.124	0.037
Gastrointestinal	0.101	0.396	0.255	0.800
Nervous	0.294	0.226	1.300	0.199

Dependent Variable: Transformed days to diagnosis of OSA
BMI=Body Mass Index

existing medical records available for review. The sample may not have been powered sufficiently to find significance among the remaining comorbidities examined. Individuals with lung disease and untreated conditions such as asthma may cause sleep disruption with poor quality sleep due to coughing or dyspnea [9]. Mysliwiec V, et al. [20] found that military personnel with comorbid insomnia and OSA showed the highest rates of depression, mild traumatic brain injury, and posttraumatic stress disorder. Comorbid insomnia and OSA was a frequent diagnosis in military personnel referred for evaluation of sleep disturbances. More alarming was that higher degrees of insomnia were associated with a greater intensity of suicidal thinking [21].

Although insomnia and OSA commonly co-occur, a strategy to adequately treat both insomnia and OSA remains elusive [11]. Future research should focus on the most effective means by which OSA symptoms are identified in patients who have insomnia and underlying co-morbid diseases. This can be achieved through a prospective study conducted at sleep disorders clinics, sufficiently powered to detect interrelated factors which can then drive clinical decisions. In addition, further research is needed in the combined treatment of both sleep and mental disorders for all patients. Woznica AA, et al. [22] showed that investigations of suicidal thoughts and insomnia were found to be inconsistent across studies. Thus, more research into the relationship between suicide and insomnia seems essential.

Conclusions

This study is the first to look at potential referral bias for sleep studies amongst patients with insomnia and co-existing diseases in the primary care setting. Depending on the co-morbidities, time to referral and diagnosis varied. Prompt diagnosis and treatment of OSA in patients can improve quality of life metrics, decrease motor vehicle accidents and potentially stabilize co-existing diseases. This study highlights areas where greater awareness regarding the recognition of OSA symptoms is needed in patients who have insomnia and underlying co-morbid diseases. The thinking might conclude that as long as the DM is well controlled, then there is no need to look for OSA. However, given the metabolic and cardiovascular risks associated with OSA, inquire about OSA should become routine. Furthermore, as Sateia MJ [18] recommended, the treatment of both sleep disturbance and mental disorders should occur simultaneously. The strong link between DM and OSA reflects a need for better education and practice reforms on the part of primary care and lead to a standard of care that most successfully addresses the needs of all patients.

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Declarations of Interest

None.

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