Obstructive Sleep Apnea and Psychiatry Disorders

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ABSTRACT

The prevalence of Obstructive Sleep Apnea (OSA) has increased remarkably during last twenty years, 60.6% of men and 36.9% of women from 50-70 years old have been diagnosed with OSA, the relevance of this pathology remains in the comorbidities associated with it, one that has not been studied deeply is psychiatric disorders, that have negatively affected the life of patients with OSA. Five main disorders were reviewed according to latest data from 1983 to 2016 on Bipolar Disorder, Dementia, Insomnia, Psychosis, and Attention deficit hyperactivity disorder. For some of this illness the symptomatology is very similar to the ones experienced in OSA, such as sleep deprivation, daytime sleepiness and cognitive impairment and their treatment is difficult due to poor compliance. Recent studies have shown that treatment of OSA with CPAP or surgery has a positive impact in decreasing psychiatric symptoms, four out of the five pathologies reviewed had remarkable improvement of psychiatric symptomatology, ADHD, Insomnia, Psychosis and Dementia. In bipolar disorder the results are not conclusive because there are some reports that stated that CPAP actually increased the risk of mania episodes, however in this particular illness the risk factors in common with OSA are less that the rest of psychiatric disorders reviewed.

Core tip: OSA prevalence has been increasing along with the aging population, and the comorbidity with psychiatric disorders needs to be evaluated in order to have a complete approach with better outcomes. The symptomatology on this pathologies may overlap, but the treatment in four out of the five disorders reviewed have a positive outcome in psychiatric symptoms after treatment with CPAP or surgery. OSA may be undiagnosed in this population and this results show the importance of early diagnosis, to improve quality of life in this patients.

Keyword: Obstructive Sleep Apnea; Insomnia; Bipolar Disorder; Dementia; Psychosis; Attention deficit hyperactivity disorder.

Introduction

Obstructive sleep apnea (OSA) is a condition characterized by repetitive partial (hypopnea) or complete (apnea) upper airway obstruction during sleep [1]. During the last twenty years there is data that suggested there has been an increase in psychological conditions among individuals with OSA [2,3]. The importance of these pathologies are based in their fast increase rate, the prevalence of OSA in the general population in 1993 was estimated at 3 to 7% of adult men and 2 to 5% of adult women, twenty years later is around 36.1% in men and 14% in women between 30-49 years and up to 60.6% and 36.9% respectively in people from 50-70 years [2,3]. The comorbidity of psychiatric disorders has reported to negatively affect the quality of life of OSA patients, and the prevalence of OSA in serious mental disorders has been reported to be 25.7%, of those, the most frequent was major depressive disorder 36.3% followed by bipolar disorder 24.5% [4,5].

In this review we evaluate the effect of OSA treatment in psychiatric conditions such as Bipolar Disorder, Dementia, Insomnia, Psychosis, and Attention deficit hyperactivity disorder (ADHD).

Bipolar disorder (BD) is a debilitating condition and is characterized by episodes of mania, hypomania and major depression [6]. The prevalence of BD is highly variable depending on the inclusion criteria and definition use by every author, Hattori reported 69% meanwhile Levine reported just
2.9% [3,7]. From a Quality Improvement project done in 2012, 69% of the patients with severe mental illness were at high risk for OSA, and among this group 14% had a diagnosis of bipolar disorder [8].

ADHD is a neurocognitive disorder characterized by a persistent pattern of either inattention or hyperactivity-impulsivity that interferes with functioning or development [9]. ADHD world prevalence in children is 5.29%, while OSA prevalence in children is around 2.9%, and 20%-30% of children with ADHD have OSA, while in adults there was one study that reported prevalence of 7.4% [10-12]. One of the mechanisms by the one OSA may increase the symptomatology in ADHD patients is that the episodes of hypoxia/hypercapnia along with sleep interruption might have a negative impact in brain development affecting cognitive function and leading to inattention, another one will be that this children have elevated levels of C-reactive protein and interleukin-6 which may also contribute to this poor cognitive function [10]. Children with ADHD which symptoms persists in adulthood have bad outcomes in their work [13].

Insomnia is a lack of sleep due to insufficient sleep quality or quantity, and it can have symptom comprising sleep specific complaints (difficulty falling asleep, difficulty staying asleep, early awakenings, unrefreshing or nonrestorative sleep) [14]. Depending on the definition use, the prevalence reported goes from 4.4% to 48%, and the prevalence of insomnia in OSA patients has been reported around 39%-42%[15,16].

Psychotic disorder has as primary symptoms delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, and negative symptoms [9].

In 2016, Stubbs reported prevalence of OSA in schizophrenia to be 15.4%, which is even lower than in general population [19], but we need to consider that the diagnosis of OSA in this population may be unrecognized due to the overlapping symptomatology, mainly daytime sleepiness and cognitive impairment that are usually attributable to use of psychotropic drugs or as negative symptoms [17]. In some studies the prevalence has been reported on 1.6% in veteran patients, while retrospective case series show 46.2% in males and 57.1% in females, although this remarkable differences may be due to bias by sample selection [18].

Alzheimer’s disease is the most common type of dementia, that causes progressive cognitive decline, presents with memory impairment and alteration on executive function, aphasia and apraxia, and complain of insomnia, nocturnal agitation, and nocturnal wandering, AD prevalence by 2000 in USA was 4.5 million, with expected 14 million by 2050 [42-44]. It represents one of the most expensive diseases, by 2010 the amount expend on it was $172 billion [42]. 44.8% women with SDB developed mild cognitive impairment or dementia compared to 31.1% without SDB [45]. In patients with dementia the incidence of SDB is 71% and SDB is more frequent in AD up to 48%, and its severity correlates with cognitive impairment [46]. Moderate to severe OSA is a risk factor for White Matter change and its early recognition and treatment could reduce this risk [47]. OSA impairs the integrity of structures such as medial temporal lobe and hippocampus, through hypoperfusion, hypometabolism and other pathophysiological mechanisms and because some of these are reversible, its treatment may reduce or at least delay dementia symptoms [44]. The main functions affected by OSA are attention, working memory, episodic memory, and executive functions [43].

### Discussion

In 2016 Lu et al. presented a study that found that patients with sleep apnea were 1.82 to 2.07 fold greater risk of mood disorder than the patients without it, specifically in patients from 18 to 34 years, and the main disorders associated were bipolar and major depressive disorder, and as treatment of OSA with CPAP have showed reduction in respiratory disturbances and daytime sleepiness, and improvement in cognitive function, sleep quality, and quality of life, evaluation of improvement in psychiatric pathologies after treatment of OSA should be evaluated [19,20].

The sleep disturbance experienced by these patients is important because it jeopardize quality of life, and also contributes to relapse and has unfavorable outcomes for affective functioning [21]. Russo et al. in 2015 showed a study performed in 117 patients to evaluate neurocognition in bipolar disorder according to sleep quality the one reported that working memory and social cognition were directly negatively predicted by sleep disruptions, also this sleep deprivation could trigger episodes of hypomania or mania in patients with bipolar disorder, because while OSA treatment with CPAP improves daytime sleepiness, sleep quality and psychological symptoms, there are also case reports of developing mania following treatment of OSA with CPAP, for example two male subjects admitted for depressive episodes developed mania after 2-4 weeks of CPAP use, while other 2 subjects continued with long-term CPAP use [22-27]. In addition to that, it is believed that OSA can be exacerbated by the use of sedatives such as benzodiazepines and antipsychotics, although recent data has not confirmed this, there is one case reported by Weber that added 100 mg/day of topiramate to the existing drug regimen of a 50-year-old man with BD, resulting in a reduction of snoring and a decrease in apneas from 20.0/h to 6.6/h [23,28].

The main problem to analyze the studies is the variability in inclusion criteria, diagnosis criteria, and the subjectivity of clinician. Maybe we could take Soreca example to objectivize the results, in 2012 took 72 individuals with diagnosis of bipolar disorder and overweight to complete the Berlin Questionnaire finding that 54.1% were in high risk for OSA, but in 2014 presented a screening that allowed to compare subjective and objective measures for OSA in patients with bipolar I disorder; they used the ApneaLink, the Berlin Questionnaire and polysomnography [29]. Patients using the ApneaLink device had an AHI >5 in 39%, suggesting a high prevalence of OSA among patients with bipolar I disorder. This study also showed that the positive predictive value of the Berlin Questionnaire was only 47% [30].

Treatment of OSA with CPAP had positive results in all populations except bipolar disorder patients where a series
of case studies suggested that CPAP may be linked to the development of manic episodes, this opens the door to analyze that patients with BD may have different set of risk factors because they receive mood stabilizers that may elevate the risk of apnea through multiple mechanisms including decreased arousability during sleep, weight gain, and upper airway muscle dysfunction [31,32]. Although concerning the use of benzodiazepines in patients with OSA, it was thought that they should not be used because they are associated with decreased airway muscle tone, after reviewing data it seems that the use of hypnotics can be safe and even beneficial, increasing compliance to CPAP treatment [14].

Treatment of OSA in BD is still controversial due to case reports that showed increased in mania episodes after use of CPAP, but there are some strategies that can decrease the risk of this episodes that can be implemented as Krakow did in 2008, with patients with insomnia requiring CPAP, that reported history of claustrophobia in 30%, and after implementing these strategies the use of CPAP increased from 23% to 67% [33].

Concerning to ADHD, in 2016 Filho presents a study using P300 potential and polysomnography to evaluate the impact of sleep fragmentation in patients with OSA to increase the attention disorder in ADHD, and it showed that in the group of ADHD the mean AHI value was 0.44 (±0.24) but, in the group of ADHD and OSA the mean AHI value was 3.1 (±1.4) [34].

Treatment of OSA with adenotonsillectomy had showed an improvement in ADHD symptoms, even more significantly that treatment with methylphenidate, a specific medication to treat ADHD [13]. In a recent study, 529 children underwent adenotonsillectomy as treatment for OSA and ADHD symptoms were evaluated before and after the procedure, finding medium improvement of symptomatology (Hedges’ g 0.43, 95% CI = 0.3-0.55, p < 0.001) [10].

In adults, of three case reports of ADHD patients that were been treated with CPAP for OSA, two reported improvement in psychosocial functioning, and the improvement in attention was so remarkable that they did not require treatment with ADHD medication [11,12].

Base on literature review, we suggests that patients with suspicion of ADHD should assess for OSA before doing diagnosis.

In patients with insomnia and OSA it is difficult to evaluate if treatment of OSA improves insomnia symptoms and vice versa, but it is clear that treating both entities improves insomnia and OSA symptomology.

Luyster et al. performed a systematic review of comorbid insomnia and OSA in 2010 finding a high prevalence of insomnia symptoms in patients with OSA, from 39% to 55%; and prevalence of 29% to 67% of OSA in patients with insomnia [14]. The marked difference between these percentages can be attributed to inconsistencies in definitions of both OSA and insomnia. According to observational studies the prevalence of insomnia symptoms were higher in women than in men, but in 2014 Li et al. collected data from 860 patients with wide range of ages from 18 to 81, and 409 men, finding that men had greater prevalence than women prior to 55 years of age, but not at greater ages [35]. As we mention previously when this pathologies overlap it is difficult the diagnosis and sometimes the treatment of either one can lead to bad outcomes, for example in an analysis done by Choi in 2015 reported that OSA patients without treatment had 20.5% of suicidal ideation (SI) while in general population is just 2%, this study also found a strong relation between insomnia and suicidal ideation, the severity of insomnia was directly proportional to the risk of SI, but this was not significant after adjusting for depressive symptom severity [36,37].

In order to understand the relation between treatment of OSA and improvement of psychiatric symptoms, Krakow in 2004 performed a retrospective study and a prospective study of sleep disordered breathing treatment on two different samples of chronic insomnia patients, reporting that combination therapy with cognitive behavioral therapy and OSA treatment improved sleep quality, and achieved an outcome close to curative status and also the compliance for OSA therapy was higher [33].

In our research about psychosis we found that Muñoz et al. reported a 72 year old gentleman that woke up in the middle of the night with psychomotor agitation, temporospatial disorientation and hallucinations, and during one of the episodes he jumped out of his window, in this case the consequences were minimal but symptoms persisted until nCPAP was started [38].

One important factor that increases the risk of OSA in this population is the use of psychotropic medication, because they are orexigenic, the ones that have short term weight gain are olanzapine, clozapine, chlorpromazine, quetiapine and risperidone, they are also associated with diabetes type II, and extrapyramidal symptoms that increase risk of OSA [18,39]. In 2010, Rishi et al. reported the use of atypical antipsychotic medications increases the apnea-hypopnea index from 0.8/h to 3.5/h, with p = 0.03, but this was a small sample size [40].

Another risk factors for OSA are age, neck circumference, male sex and body mass index >25 Kg/cm², and due to the overlapping symptoms of OSA and psychosis, these factors should be taken in consideration more than daytime sleepiness, snoring and reported apneas [17].

Gupta found from 1989 to 2014, ten case reports of OSA and schizophrenia and psychosis, with improvement of psychotic symptoms and daytime sleepiness after treatment of OSA. The treatment of OSA in these patients was not only based on CPAP, but also weight lost or surgery [31]. There was only one case report where the patient had a psychotic episode after 5 days of using CPAP, probably due to increased dopaminergic activity that increase REM sleep [41].

AD patients have improve their cognition, sleep quality, and mood, after treatment with CPAP, it has been tolerated well and compliance depends a lot of caregivers [46]. studies improvement in sustained attention with CPAP, also in flexibility, and episodic memory, but other studies have not found any improvement in selective and divided memory, executive functions, motor function and recognition memory [43]. There is also report of a Randomized double blind placebo controlled trial used to evaluate CPAP treatment and its effect on cognitive function on patient with mild to moderate Alzheimer’s disease, reported significant improvement of neuropsychological tests.
scores, mainly in verbal learning, memory, cognitive flexibility and metal processing speed [43]. CPAP treatment delays progression of cognitive impairment [44].

Conclusion

Treatment of OSA in patient with psychiatric disorders have different outcomes, it is known that patients with OSA have a greater risk of mood disorders, and for most of them the treatment with CPAP or surgery reduces respiratory disturbances and daytime sleepiness, and improves cognitive function, sleep quality, and as main consequence, better quality of life. The outcome of OSA treatment in bipolar disorder is still unclear, because it has been reported that some patients may actually develop a manic episode after use of CPAP, however the physiopathology of this entity request to evaluate other risk factors that may contribute to the negative outcome. For the other four pathologies evaluated in this review the treatment of OSA have a positive impact in psychiatric symptomatology, in children with ADHD the surgery has improve symptoms even more that specific medication for ADHD and in adults their improvement was so significant that they did not needed ADHD medication anymore. In patients with insomnia and OSA the combination therapy of both achieved an outcome close to curative status. OSA and schizophrenia and psychosis, have reported improvement of psychotic symptoms and daytime sleepiness after treatment of OSA, but this was not only CPAP but also weight lost or surgery. Apparently, CPAP treatment delays progression of cognitive impairment and in patients with AD improves their cognition, sleep quality, and mood. This review have found that treatment of OSA using CPAP or surgery has improve psychiatric symptoms in patients with ADHD, Insomnia, dementia and Psychosis.

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