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Review article

Obstructive sleep apnoea and schizophrenia: a primer for psychiatrists

Alam A, Chengappa KNR. Obstructive sleep apnoea and schizophrenia: a primer for psychiatrists

Objective: The main objective of this review is to improve psychiatric clinician awareness of obstructive sleep apnoea (OSA) and its potential consequences in patients with schizophrenia. This article will also discuss the diagnosis and treatment options for OSA while considering the significant role psychiatrists can play in facilitating the diagnosis and treatment of OSA.
Data sources: Ovid, Medline and PsychInfo databases were searched for articles between 1960 and 2010. Search terms used were *Sleep apnoea* or *apnoea* and *schizophrenia* or *psychosis*. The number of articles retrieved was 38. Articles were carefully reviewed for any data pertinent to OSA in patients with schizophrenia.
Conclusions: OSA is a common disorder that is frequently unrecognised. As a chronic breathing condition, OSA is associated with adverse health outcomes and high mortality. OSA may co-occur with schizophrenia or evolve over time, especially with weight gain. The diagnosis should be considered whenever a patient presents with risk factors or clinical manifestations that are highly suggestive of OSA. Those who report snoring, daytime sleepiness and are obese or have a large neck circumference should be considered for an OSA diagnosis. Appropriate diagnosis and treatment of OSA can reduce daytime sleepiness, improve cardiovascular and other medical conditions, as well as reduce mortality. Psychiatrists can play very important role in suspecting OSA in their patients and making the initial referral. Furthermore, behavioural management, especially promoting weight loss and smoking cessation, are effective components of OSA treatment that psychiatrists are positioned to facilitate with their patients.

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Summations

- We hypothesis that Obstructive sleep apnoea (OSA) is mostly underdiagnosed in patients with serious mental illness (SMI).
- OSA should be considered in a patient who snores, shows signs of daytime sleepiness, and obese or have large neck circumferences.
- OSA is associated with increased morbidity and mortality. Treatment is challenging; psychiatrists can play a very important role with referrals, counselling and advocating behavioural changes.

Considerations and limitations

- Data on OSA in patients with SMI remains scant and requires more definitive studies.
- Modifiable risk factors such as weight loss and acceptance of referrals to sleep studies, are difficult in the general population and will likely be the case in patients with SMI.
- Even after successful diagnosis of OSA, it is unclear how many SMI patients will accept, or be compliant with treatment.

Introduction

Obstructive sleep apnoea (OSA) is a common and chronic breathing disorder. When untreated, OSA has been recognised as an independent risk factor for several disorders including systemic hypertension (1), mild pulmonary hypertension, cardiovascular morbidities (2), stroke and abnormal glucose metabolism (3). Patients with severe OSA [apnoea–hypopnoea index (AHI) >30 events per hour] appear to be at increased risk for all-cause mortality (4). Furthermore, by impairing vigilance and increasing daytime sleepiness, OSA increases driving and work-related accidents and impairs concentration, memory and performance (5). The risks and costs of undiagnosed or untreated OSA have been estimated at $11.1 billion per year in indirect costs (e.g. motor vehicle accidents) and $3.1 billion in direct costs for screening and treatment (6,7).

OSA is defined by recurrent episodes of obstructive apnoeas and hypopnoeas caused by repetitive partial or complete airway obstruction during sleep. An apnoea is defined as a decrease in airflow of greater than 70% of the preceding airflow measurement that lasts at least 10 s. A hypopnoea is a 30–70% decrement in airflow from the preceding baseline for at least 10 s with an associated fall in oxyhaemoglobin desaturation (8). Such apnoeas and hypopnoeas are invariably related to full arousals, which disrupt sleep and often lead to daytime drowsiness. The more events a patient experiences during sleep, the more severe the disorder.

OSA is common in older patients with schizophrenia (9). It is more common in patients with schizophrenia compared to patients with other psychiatric disorders (10). The diagnosis may be more challenging in this population as many patients do not report snoring or they may not have a bed partner who complains about patient's snoring. Furthermore, both disorders can share some clinical features. For example, daytime sleepiness and poor cognitive performance may be misattributed as negative symptoms or medication side effects when it is possibly related to undiagnosed OSA. Subsequently, OSA may remain largely undiagnosed in people with schizophrenia.

Prevalence of OSA in the general population

It is estimated that 26% of adults are at high risk for OSA (11). According to the Sleep Heart Health Study, the largest epidemiological study in this field to date, 24% of men and 9% of women (30–60 years old) are affected by OSA (12). They estimated that 2% of women and 4% of men in the middle-aged work force meet the minimal diagnostic criteria for the sleep apnoea syndrome, which was defined as an (AHI) of 5 or higher accompanied symptom of daytime hypersomnolence (12).

It is remarkable that despite all the recent increased attention OSA has received, the majority (70–80%) of those affected remain undiagnosed (11,13,14). It is estimated that about 1 in 20 (5%) of adults in Western countries have undiagnosed OSA (15). With the increased incidence of obesity, the number of undiagnosed OSA may be even higher than previously reported.

Prevalence of OSA in patients with schizophrenia

OSA appears to occur more commonly in psychiatric conditions than with other medical conditions (16,17). Focusing only on schizophrenia, we reviewed four studies that looked into OSA in patients with schizophrenia. The largest one by Winkelman (10) retrospectively evaluated 364 inpatients from Mclean Psychiatric Hospital (Belmont, MA, USA) referred for a sleep study. He reported that schizophrenia or schizoaffective disorder was the most common diagnosis among patients who were diagnosed with OSA (odds ratio = 6.22, $p < 0.001$) (10). Also, when patients with schizophrenia were found to have OSA, it was more severe compared to patients with other psychiatric disorders. Takahashi et al. studied the prevalence of OSA in inpatients schizophrenic (64 men and 37 women) from two psychiatric hospitals in Japan (18). They reported a rate of 19% of OSA in those patients. One issue with that study is that it used overnight oximetry, a technique that lacks sensitivity and specificity in the diagnosis of OSA (18). Another study by Ancoli-Israel et al. (9) looked at the prevalence of sleep-disordered breathing (SDB) and periodic limb movements in older patients (mean age = 59.6 years) with schizophrenia. They found that 48% of these patients had at least 10 respiratory events per hour of sleep. When compared to an age-matched subsample of healthy elderly from a previous study, there was no significant difference in prevalence of SDB. However, similar to younger patients with schizophrenia, these older schizophrenia patients also had a higher prevalence of severe SDB than the subsample of healthy elderly.

The prevalence of psychiatric comorbid diagnoses in patients with OSA was studied by Sharafkhaneh et al. (19) in US veterans. They found that depression was the most common comorbid disorder at 21.8% and psychosis was noted in 5.1% of the patients (19). The authors concluded that patients with OSA when compared to patients without OSA had significantly higher prevalence of a diagnosed psychiatric disorder, including psychosis.

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Antipsychotics and OSA

It has been estimated that patients receiving antipsychotic medication for more than 6 months may gain between 15 and 75 pounds during treatment (20). This significant weight gain can increase the likelihood of developing OSA. Wirshing et al. (21) reported two cases of sleep apnoea associated with antipsychotic-induced obesity. Winkelman (10) found that the use of antipsychotic medications was an independent risk factor for OSA and concluded that the use of antipsychotics with resultant weight gain could lead to the emergence of OSA (10). Another recent study by Rishi et al. looked at the association between atypical antipsychotic (AA) medications with severe OSA. They concluded that taking AA may increase the risk of more severe OSA independent of body weight and neck circumference. Perhaps, AA tranquilizing effects independently contribute to risk of OSA, by a reduction in activity of hypoglossal or recurrent activity of laryngeal nerve on the upper motor airway musculature (22).

OSA risk factors

There are several risk factors that increase the probability of developing OSA (Table 1).

Obesity. The most significant risk factor for the development of OSA (23–25). Seventy per cent of patients with OSA are obese (26). Conversely, significant OSA is found in approximately 40% of obese individuals (26). Longitudinally, there is an association between change in weight and OSA. A person who experiences a 10% weight gain is expected to have an approximate 32% increase in AHI and to have six times the odds of being newly diagnosed as having moderate-to-severe OSA at follow-up (27). On the other hand, a 10% weight loss predicted a 26% decrease in the AHI (27). OSA correlates more specifically with an increased neck size or waist circumference than general obesity (28,29). It is predominantly common among men with a collar size >17 inches and in women with collar size >16 inches (30).

Table 1. Risk factors for OSA

Obesity
Craniofacial and upper airway mechanics
Age
African-American race
Smoking
Alcohol
Treatment refractory hypertension
Diabetes mellitus
History of stroke or CHF

CHF, congestive heart failure.

Craniofacial and upper airway features. Abnormal maxillary or short mandibular size, wide craniofacial base, an enlarged tongue or soft palate or tonsillar and adenoid hypertrophy are all anatomic risk factors for OSA (32). Nasal congestion increases the prevalence of OSA about two-fold compared to controls, regardless of the cause (33).

Age. The prevalence of OSA increases from age 20 to 45, with a plateau occurring between ages 55 and 65. Then there is two- to three-fold higher prevalence of OSA among those who are 65 years and older, compared to those who are 30–64 years old (33).

Gender. OSA is about twice as common in males compared to females. About 4% of women have OSA compared to 6–9% of men (12).

Race. Independent of body weight, OSA is more common among African-Americans who are younger than 35 years, compared to Caucasians of the same age group (33).

Smokers. Studies show that current smoking is associated with a higher prevalence of snoring and OSA (34–36). Even exposure to second-hand smoking has been independently linked with habitual snoring (37).

Alcohol. It can induce apnoeic activity in normal or asymptomatic individuals (38–40). Alcohol can also prolong apnoea duration and worsen the severity of associated hypoxemia (38,41).

Diabetes. OSA is nearly three times more prevalent in patients with diabetes or insulin resistance compared with the general population (42).

OSA risk factors in patients with schizophrenia

We were unable to locate any article that specifically examined the prevalence of OSA risk factors in patients with schizophrenia. However, the major risk factors associated with OSA noted above are more common in patients with schizophrenia compared to the general population. For example, the prevalence of obesity in the United States is 27% of the general population, but 42% of patients with schizophrenia have a body mass index (BMI) of ≥27 (43). Of the general population, about 25% are current smokers compared to about 79% among patients with schizophrenia (44). Diabetes mellitus prevalence ranges from 10 to 15% in this population (45), which is also higher than the general population with an estimated rate around 7.5% (46). On the basis of these data, we can predicate that OSA risk factors are more prevalent in patients with schizophrenia. Considering these associations, psychiatrists and other mental health clinicians may be uniquely positioned to screen their psychiatric

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Table 2. OSA symptoms

Snoring
Daytime sleepiness
No restorative sleep
Awakening with choking
Nocturnal restlessness
Insomnia with frequent awakenings
Depression
Decreased concentration and memory loss
Decreased libido and impotence
Nocturia

Table 3. Clinical features that might be seen with OSA

Obesity (BMI $\geq$ 30 kg/m^2)
Large neck circumference
Narrow or 'crowded' airway
Systemic hypertension
Hypercapnia
Pulmonary hypertension
Polycythemia
Cardiac arrhythmias
Possibility of night-time cardiac mortality

patients for OSA risk factors and refer those at risk of undiagnosed OSA for further evaluation.

Clinical presentation

Snoring and daytime sleepiness. These are the most common clinical features related to OSA. Most patients come to clinical attention because of the complaint of snoring by the patient or bed partner. Daytime sleepiness is also a common feature, and its presence is key in deciding which patients should undergo diagnostic testing for OSA.

Other features include awakening with a sensation of choking or gasping for air, insomnia or restless sleep, depression, lack of concentration, morning headaches, nocturia, decreased libido and impotence (Tables 2 and 3). It is also important to note that OSA can present with atypical symptoms such as irritability, cognitive deficits and concentration lapses, all of which are commonly seen in patients with schizophrenia with or without OSA. The prompt recognition of the signs and symptoms of OSA should trigger referral to a sleep disorder specialist.

Medical complications

Patients with untreated severe OSA appear to have a three- to six-fold increased risk of all-cause mortality compared to individuals without OSA (4,47).

Cognitive impairments. OSA induces daytime sleepiness, inattention and fatigue, each of which impairs daily function. OSA also induces or exacerbates cognitive deficits and increases the likelihood of errors and accidents (7).

Cardiovascular diseases. Clinical and epidemiological data suggest an independent association among OSA and systemic hypertension, pulmonary hypertension, and other cardiovascular disorders such as coronary artery disease, cardiac arrhythmias, heart failure, and sudden cardiac death (2). Patients with OSA may also have a higher propensity for night-time cardiac mortality (48). Cardiac dysrhythmia, bradycardia, and asystole during sleep are the most prominent and significant rhythm disturbances associated with OSA (49–51). OSA may contribute directly to the development of cardiac systolic and diastolic dysfunction. A study with echocardiography has shown that diastolic dysfunction occurred in 36.8% of patients with OSA (52).

Metabolic syndrome and diabetes mellitus. Comparing OSA patients to subjects without OSA, metabolic syndrome was 9.1 times more likely to be present in subjects with OSA (53). Independent of obesity, age, smoking and alcohol consumption, OSA was associated with increased systolic and diastolic blood pressure, higher fasting insulin and triglyceride concentrations and lower high-density lipoprotein cholesterol (53). OSA was associated with impaired glucose tolerance and insulin resistance independent of obesity (54). Severe OSA is accompanied by a five-fold increase in the risk of diabetes mellitus (55). Because of this risk, the International Diabetes Federation Taskforce on Epidemiology and Prevention has recently recommended that health professionals working with both diabetes mellitus and OSA should ensure that a patient presenting with one condition is considered for having the other (56).

OSA and mortality in patients with schizophrenia

Patients with schizophrenia have up to a 20% shorter life span than the general population, with the leading cause of death being cardiovascular disease (57). A recent review noted that there may be a 15-year decrease in life expectancy in patients who have schizophrenia compared with the general population (58). Patients who have schizophrenia face barriers to receiving prompt and appropriate medical health care (59).

The impact of OSA on mortality in patients with schizophrenia has yet to be studied in detail; nonetheless, we found two case reports on this issue. Fleischman et al. (60) reported a case of unexplained death at the psychiatric emergency room, likely linked to undiagnosed OSA. Pompeo (61) reported a case of sudden death by sleep apnoea syndrome associated with myxoedema in a patient with schizophrenia.

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Table 4. Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you.			
Use the following scale to choose the most appropriate number in each situation:			
0 = Would never dose	1 = Slight chance of dozing	2 = Moderate chance of dozing	3 = High chance of dozing
Situation:			Chance of dozing:
1. Sitting and reading			
2. Watching TV			
3. Sitting inactive in a public place (e.g. theatre or meeting)			
4. Passenger in a car for an hour without a break			
5. Laying down to rest in the afternoon when circumstances permit			
6. Sitting and talking to someone			
7. Sitting quietly after lunch without alcohol			
8. In a car while stopped for a few minutes in traffic			
Range of scores is 0–24. Normal total score is <10. A total score ≥10 suggests daytime sleepiness.			Total score:

Adapted with permission from Johns (63) (www.EpworthSleepinessScale.com).

OSA can and possibly poses an additional risk for all-cause mortality if undiagnosed and untreated in patients with schizophrenia. Therefore, early identification and referral is a very important goal, in which psychiatrists can play a significant role through being aware of OSA and facilitating referrals for diagnosis and treatment.

Diagnosis of OSA

Diagnostic testing is essential to confirm or exclude OSA, since the clinical features of OSA are nonspecific and the diagnostic accuracy of clinicians' subjective impression is low.

Polysomnography (PSG). It is considered the gold standard for diagnosis of OSA. PSG is a comprehensive recording of the biophysiological changes that occur during sleep and requires a full night stay at a sleep laboratory.

Portable monitoring. This may be used to diagnose OSA via in-home unattended monitoring. Many devices have been validated against standard PSG, but according to clinical practice guidelines, it maybe used as an alternative to PSG only in patients with a high pretest probability of moderate-to-severe OSA (62).

Who to refer for diagnosis. Diagnostic testing for OSA is advised for any patient who snores and has excessive daytime sleepiness. In the absence of excessive daytime sleepiness, diagnostic testing is recommended if the patient snores and has two or more of the features shown in (Table 2).

Patients might not complain about daytime sleepiness, but it can be noticed during group or individual therapy sessions. In such instances, further questions about other symptoms and signs of OSA should be explored. Also, a simple questionnaire, the Epworth Sleepiness Scale, is a rapid screen to reveal excessive daytime sleepiness (63) (Table 4).

OSA management

Pharmamacologic and oxygen therapy. First and important part of the treatment. Should include a discussion of risk factors, clinical consequences and treatment options (Table 5). Also, the benefits of weight loss, alcohol avoidance, and medication side effects, which can be part of a routine psychiatric clinic visit.

Behavioural modifications. Mostly related to risk factors modification (Table 6).

Weight loss. Should be recommended and frequently encouraged for all overweight or obese OSA patients. Successful weight loss, ideally to a BMI of 25 kg/m^2 or less, decreases the apnoea–hypopnoea index, improves quality of life and possibly decreases daytime sleepiness (64,65). After substantial weight

Table 5. Components of patient education for OSA

Disease signs and symptoms
Risk factors
Risk factor modification
Counselling regarding driving while drowsy
Associated disorders
Treatment options
What to expect from treatment
Patient's role in treatment
Consequences of untreated disease

Table 6. Behavioural approaches

Weight loss and exercise
Supine preclusion
Avoidance of alcohol
Avoidance of sedating drugs
Smoking cessation

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loss (i.e. 10% or more of body weight), a follow-up PSG is indicated to ascertain whether positive airway pressure (PAP) therapy is still needed (66).

Sleep position. Sleeping in a non-supine position, lateral recumbent, may correct or improve OSA and should be encouraged. However, it should not be used as the primary therapy unless normalisation of the AHI when sleeping in a non-supine position has been confirmed by PSG (30). A number of devices have been developed to reduce the likelihood of sleeping in the supine position including posture alarms, special pillows, tennis ball backpack and modified nightshirts.

Alcohol avoidance. All patients with OSA should avoid alcohol, even during the daytime, because it can exacerbate OSA, worsen sleepiness and promote weight gain.

Medication selection. In patients with OSA, medications that inhibit the central nervous system, such as benzodiazepines, barbiturates, other antiepileptic drugs, some antidepressants, antihistamines and opiates should be avoided if reasonable alternatives exist. When these medications are necessary, despite the patient's OSA, their use should be monitored. Avoidance of medications with weight gain potential should seriously be considered.

Pharmamacologic and oxygen therapy

Multiple pharmacologic agents have been investigated as primary therapies, but no agent has been identified that prevents or overcomes upper airway obstruction enough to justify pharmacologic therapy as a primary therapy. Selective serotonergic uptake inhibitors, protriptyline, methylxanthine derivatives and oestrogen therapy have been studied but are not recommended for the treatment of OSA (67). Pharmacologic therapy may be useful to treat excessive daytime sleepiness. Modafinil is recommended for the treatment of residual excessive daytime sleepiness in OSA patients who continue to experience sleepiness despite effective PAP treatment and those subjects who are lacking any other identifiable causes for their sleepiness (67). Oxygen supplementation is not recommended as a primary treatment for OSA (67).

OSA-specific therapies

PAP. First described by Sullivan (68), PAP is considered the first-line therapy for OSA. PAP provides pneumatic splinting of the upper airway and is effective in reducing the AHI (69). There is good evidence that PAP therapy reduces the frequency of respiratory events during sleep, decreases daytime sleepiness and improves quality of life (69–71). Favourable outcomes likely depend on adherence to PAP therapy. However, it is estimated that 20–40% of patients do not use their PAP device and many others do not use it all night or every night (72). Especially during the first few weeks of PAP use, close follow-up for PAP usage and problems is important to establish effective utilisation and remedy problems (73). Psychiatrists can play a major role in supporting patient's adherence with OSA treatment.

Oral appliances. Custom-made oral appliances may improve upper airway patency during sleep by enlarging the upper airway or by decreasing upper airway collapsibility (74).

Surgery. A large variety of surgical options exist. Upper airway surgery may improve OSA, if patients are appropriately chosen and treated (75).

Bariatric surgery. Bariatric surgery may be used as adjunctive treatment in obese patients with OSA (68). It is indicated in individuals with a BMI $\geq$ 40 kg/m^2 or those with a BMI $\geq$ 35 kg/m^2 with high-risk medical comorbidities and among those persons where dietary attempts at weight control were ineffective (76).

Treatment OSA in patients with schizophrenia

To our knowledge, no article has specifically examined the treatment of OSA in patients with schizophrenia. However, we found several case reports that describe improvement in psychotic or other symptoms with OSA treatment. Karanti and Landen (77) reported a case of refractory psychosis, which remitted with CPAP treatment. Boufidis et al. (78) reported significant improvement of symptoms of schizophrenia and depression in a patient with schizophrenia and OSA who was treated with nasal CPAP. Dennis and Crisham (79) reported a case of chronic assaultive behaviour that improved with sleep apnoea treatment. Berrettini (80) reported a case of paranoid psychosis with violent outbursts in a patient with sleep apnoea syndrome; weight loss and use of an oropharyngeal airway when sleeping led to improvement of that condition. Martin and Lefebvre (81) reported a case of a 13-year-old boy who presented with psychosis and found to have OSA. Surgical treatment was indicated and his psychosis cleared immediately after mandible reconstruction surgery.

Conversely, Chiner et al. (82) reported a case of acute psychosis 5 days after CPAP treatment in a patient with schizophrenia and sleep apnoea syndrome. The psychosis was controlled after stopping CPAP and starting an antipsychotic medicine. Ramos et al. (83) studied the changes in psychopathological symptoms after treatment with nasal continuous PAP

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(NCPAP). They concluded that severe OSA is associated with psychosocial impairment that improves gradually with NCPAP.

These very limited data suggest the need for a more systematic investigation about treatment of OSA in patients with schizophrenia.

Concluding remarks

OSA is a common chronic breathing disorder in the general population and in patients with schizophrenia. Although public awareness of OSA has steadily increased, the majority of those affected remain undiagnosed. In light of the serious consequences of OSA and the high cost to the patient and society it is essential that this disorder be recognised promptly and managed appropriately.

Patients with schizophrenia have about a 20% reduced life expectancy compared with the general population (58). Around three quarters of all deaths in people with serious mental illness are related to physical illness, of which cardiovascular disease is the most common cause (84). To what extent OSA contributes to this lost lifespan in people with schizophrenia is not yet known but is clearly worth studying.

Psychiatrists and mental health care clinicians are uniquely positioned to identify those who are possibly affected by OSA and facilitate making the appropriate diagnostic referral. Psychiatrists can also play a significant role in patient education and be part of the treatment by encouraging behavioural modification treatments. Many of the risk factors associated with OSA are currently part of the psychiatric treatment efforts, for example, weight reduction, smoking cessation, dietary counselling, exercise or switching to psychotropic medications with a minimal potential for weight gain.

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