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Obstructive sleep apnea and schizophrenia: A systematic review to inform clinical practice

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ABSTRACT

Background: Risk factors for obstructive sleep apnea (OSA) are common in people with schizophrenia. Identification and treatment of OSA may improve physical health in this population; however there are no guidelines to inform screening and management.
Objectives: Systematic review to determine, in people with schizophrenia and related disorders: the prevalence of OSA; the prevalence of OSA compared to general population controls; the physical and psychiatric correlates of OSA, associations between antipsychotic medications and OSA; the impact of treatment of OSA on psychiatric and physical health; and the diagnostic validity of OSA screening tools.
Data sources: Medline, EMBASE, ISI Web of Science and PsycINFO electronic databases. Cohort, case–control and cross-sectional studies and RCTs reporting on prevalence of OSA in subjects with schizophrenia and related disorders were reviewed.
Results: The prevalence of OSA varied between 1.6% and 52%. The prevalence of OSA was similar between people with schizophrenia and population controls in two studies. Diagnosis of OSA was associated with larger neck circumference, BMI > 25, male sex and age > 50 years. There were no data on physical or psychiatric outcomes following treatment of OSA. The diagnostic utility of OSA screening tools had not been investigated.
Conclusion: OSA may be prevalent and potentially under-recognized in people with schizophrenia. Further research is required to determine utility of OSA screening tools, the relationships between antipsychotic medications and OSA and any benefits of treating OSA. We propose a strategy for the identification of OSA in people with schizophrenia and related disorders.

1. Introduction

Cardiovascular disease causes a 16–18 year reduction in life-expectancy in people with schizophrenia (Laursen, 2011). Obstructive sleep apnea (OSA) may contribute to this disease burden as it is associated with heightened risk of hypertension, diabetes, stroke and heart failure (Epstein et al., 2009). High rates of obesity (Galletly et al., 2012; Mitchell et al., 2013), tobacco smoking (Myles et al., 2012), alcohol consumption (Moore et al., 2012), and sedative medication use (Al Lawati et al., 2009; Galletly et al., 2012) may increase risk of OSA in people with schizophrenia. Whilst diagnosis may go unrecognized when sleep disturbance, daytime somnolence and cognitive impairment are mistaken for negative symptoms or medication side effects. Recent reviews on OSA in schizophrenia (Alam and Chengappa, 2011; Gupta and Simpson, 2015; Kalucy et al., 2013) and physical health guidelines do not provide recommendations on screening for OSA in schizophrenia.

2. Methods

A systematic review was undertaken of English language publications in peer-reviewed journals. We searched Medline, EMBASE, PsycINFO, and ISI Web of Science using: (psychosis or schizophrenia) and (obstructive sleep apnea or obstructive sleep apnea or sleep disordered breathing). 148 papers were identified and examined; five original articles reporting applicable data were identified (see Table 1).

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Table 1
Studies reporting prevalence of OSA in populations of patients with schizophrenia.

Study	Population	Diagnostic measure	OSA criteria	Prevalence
Anderson et al. (2012)	52 outpatients with major mental illness, of which 25 (48%) had a diagnosis of schizophrenia or schizoaffective disorder	Polysomnography	Severity based on AHI Mild — AHI 5–15 Moderate — AHI 15–30 Severe — >30	52% prevalence 32% mild 14% moderate 6% severe
Sharafkhaneh et al. (2005)	4,060,504 outpatients identified through retrospective review of case notes in the Veteran's Health Database, patients with psychosis compared to general population	Previous diagnosis of OSA documented in database, diagnostic measures not specified	ICD-10 codes, AHI cut-off not defined	1.6% prevalence
Winkelman (2001)	46 inpatients with schizophrenia or schizoaffective disorder considered at high risk of OSA referred to sleep disorders clinic	Polysomnography	RDI > 10	57.1% in males 46.2% in females
Ancoli-Israel et al. (1999)	52 geriatric outpatients (mean age 59.6 years) with schizophrenia or schizoaffective disorder	Modified polysomnography	RDI > 10	48% prevalence
Takahashi et al. (1998)	101 inpatients with schizophrenia	Overnight oximetry	DI	21.9% in males 13.5% in females

Abbreviations: AHI apnea–hypopnea index as defined by AASM (Kushida et al., 2005); RDI respiratory desaturation index as defined by the ASDA criteria (ASDA, 1992; Timms et al., 1988), and DI desaturation index as defined by >4% oxygen desaturations at least 5 times per hour.

Papers were included if they reported: prevalence of OSA in a psychosis cohort alone or compared to a matched general population cohort; psychiatric, physical health or anthropometric measures and quantitative assessment of how these related to a current diagnosis of OSA; prospective assessment of OSA or daytime sleepiness screening tools and; physical health or psychiatric disease measures before and after treatment of OSA.

We included studies that specified the proportion of participants with a diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder in each cohort. Overnight multichannel polysomnography (PSG) is the gold standard for diagnosis of OSA (Epstein et al., 2009), however we included broader diagnostic definitions including modified PSG, and overnight oximetry.

3. Results

3.1. Prevalence of OSA

OSA prevalence varied between 13.5% and 57.1% across four cohort studies screening subjects using overnight multichannel PSG, modified PSG or overnight oximetry. These studies varied in diagnostic criteria and no study reported on a generalizable psychosis cohort. Winkelman (2001) was prone to selection bias as subject recruitment was based on suspicion of OSA. Anderson et al. (2012) excluded subjects with previous OSA diagnosis, potentially reducing prevalence estimates. Ancoli-Israel et al. (1999) studied an older age group (mean 59.6 years), whilst low rates reported by Takahashi et al. (1998) may result from the cohorts' low mean BMI (23.9).

3.2. Relative prevalence of OSA

Takahashi et al. (1998) reported a non-significant comparison of OSA in inpatients with schizophrenia (18.8%) matched to controls recruited from hospital staff (22%). Sharafkhaneh et al. (2005) compared prevalence of OSA in subjects with schizophrenia (1.2%) to subjects without schizophrenia (1.6%) through retrospective review of 4,060,504 veteran case records, reporting an unadjusted odds ratio of 1.49 (95% CI 1.05–1.92). This study potentially under-estimates the prevalence of OSA due to opportunistic methodology, non-standardized diagnostic criteria and lack of data on non-VHA health contact.

3.3. Physical and psychiatric correlates of OSA

Anderson et al. (2012) reported that age ($r = 0.47$, $p = 0.001$) and neck circumference ($r = 0.311$, $p = 0.028$) were positively correlated with apnea–hypopnea index (AHI). Multivariate analysis revealed male sex (OR = 21.9, 95 %CI 1.3–370.3) and BMI > 25 (OR 36.1, 95% CI 1.3–990.1) as significant predictors of OSA using AHI > 5 as the dependent variable. Using multivariate analysis, Winkelman (2001) reported significant associations for male sex (OR = 5.76, 95% CI 2.08–15.27), age (OR = 1.03, 95% CI 1.00–1.06) and BMI (OR = 1.14, 95% CI 1.08–1.21) with RDI > 10 as the dependent variable.

Takahashi et al. (1998) reported no significant correlation between dose of antipsychotic medication (mg equivalent dose of haloperidol) and oxygen desaturation index (ODI), but reported a positive correlation with hypnotic medication (number of pills per day) in the subgroup of women. Winkelman (2001) demonstrated no significant association between categorical antipsychotic use and an RDI > 10 on multivariate analysis. However, the association was significant at an RDI threshold of >20 (OR = 5.02, 95% CI 1.44–17.56). Anderson et al. (2012) reported a negative correlation between quantitative measures of antipsychotic use (percentage of maximum dose) and AHI > 5 ($r = -0.382$, $p = 0.014$) on univariate analysis, but no significant interaction between categorical benzodiazepine use and AHI on multivariate analysis.

No studies report on measures of quality of life, psychiatric symptoms, cognitive function, or social and occupational function.

3.4. Utility of OSA screening tools

Anderson et al. (2012), examined measures of daytime sleepiness and sleep disturbance with the Epworth Sleepiness Score (ESS) (Johns, 1991) and the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The mean ESS was 5.6 (SD = 5.04) and the mean PSQI was 6.5 (SD = 3.5), lower than general population controls (Johns, 1991). Sensitivity and specificity were not reported.

3.5. OSA treatment

No study reported acceptability of CPAP treatment; or measures of physical health, psychopathology or social functioning before and after treatment.

4. Discussion

OSA is common in people with psychotic illness with rates in screened populations between 13.5–57.1%. This is comparatively higher than general population estimates between 2%–4% (Young et al., 2008). Variations in age, degree of obesity, patient selection and diagnostic measures however, make no single study widely generalizable to psychiatric populations. Unfortunately one large case–control study potentially underestimates both general and relative prevalence of OSA due to its opportunistic methodology given 80% of OSA remains undiagnosed despite access to healthcare (Kapur et al., 2002; Young et al., 1997) and that people with psychotic illness have reduced access

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