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CLINICAL REVIEW

Sleep disordered breathing in Parkinson's disease: A critical appraisal

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SUMMARY

Parkinson's disease (PD) is the second most common neurodegenerative disorder, characterized by resting tremor, rigidity, bradykinesia and postural instability, and is associated with non-motor features, including sleep abnormalities. The high prevalence of excessive daytime sleepiness and snoring in PD patients has led to the suggestion that sleep disordered breathing (SDB) is more common in these individuals than in normal subjects. We aimed to review the literature on SDB prevalence and its clinical repercussions in PD. A PubMed search was performed to identify controlled studies, published from January 1990 through October 2012, which addressed the prevalence of SDB diagnosed by polysomnography in idiopathic PD. From the seven studies included, five reported similar or lower prevalence of SDB in patients when compared to healthy age-matched controls. Two studies reported less oxyhemoglobin desaturation during sleep among patients. These results did not support the idea that PD patients are at increased risk of SDB and indicate that they may not present significant hypoxemia. The prevalence of obstructive sleep apnea syndrome and the long-term outcomes of disordered breathing events during sleep have not been adequately studied in PD.

Introduction

Parkinson's disease (PD), the second most common neurodegenerative disorder, affects about 1–2% of adults over 60.[1,2]Although the diagnosis still depends on the detection of motor features of resting tremor, cogwheel rigidity, bradykinesia and postural instability, non-motor manifestations are highly prevalent and often cause significant disability.[3–6] These include autonomic and neuropsychiatric symptoms, pain, fatigue and sleep abnormalities.[7]

Sleep problems are very frequent complaints of PD patients, the most common being sleep fragmentation.[8–10] REM sleep behavior disorder (RBD) and excessive daytime sleepiness (EDS) are also widely recognized as more prevalent in PD patients than controls and may even predate the onset of the motor symptoms.[11–13]

Nevertheless, the clinical significance of sleep disordered breathing (SDB) in PD remains an issue of debate. Considering that snoring was reported by up to 70% of PD patients, it would be reasonable to hypothesize that they have an increased risk of developing obstructive sleep apnea (OSA),[14,15] but studies have yielded conflicting results.[16–18] As disordered breathing events in sleep are highly prevalent in the general population, mainly among people over 60,[19] a high prevalence of SDB in PD may reflect the underlying aging process rather than the PD pathology.

A number of reasons underscore the importance of studying the interactions between OSA and PD. There is increasing evidence that OSA may negatively impact on cardiovascular health.[20,21] OSA causes cognitive dysfunction, which is another common non-motor feature of PD and significantly decreases quality of life.[22] Moreover, OSA consequences may extend beyond general health into motor performance of PD patients. Oxidative stress and inflammation, two mechanisms linking OSA and cardiovascular diseases, are also known to be involved in PD pathophysiology.[23,24] Experimental data reinforces the role of oxidative stress on alfa-synuclein aggregation and dopaminergic cell death.[25]

Our primary objective was to review studies on the prevalence of SDB in PD. Specifically, we aimed to investigate whether SDB is more prevalent in PD than in the general population. As a secondary outcome, whenever reported, we assessed if there was any difference in clinical repercussions of SDB between PD patients and healthy individuals.

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List of abbreviations

BMI	body mass index
EDS	excessive daytime sleepiness
HY	Hoehn and Yahr
OSA	obstructive sleep apnea
OxyHb	oxyhemoglobin
PD	Parkinson's disease
PSG	polysomnography
RBD	REM sleep behavior disorder
RDI	respiratory disturbance index
REM	rapid eye movement
SDB	sleep disordered breathing
UPDRS	unified Parkinson's disease rating scale

Methods

A PubMed literature search of publications between January 1990 through October 2012 was performed to identify controlled cross-sectional and longitudinal studies addressing the prevalence of SDB in idiopathic PD as the primary outcome or one of the outcome measures. We used the terms "sleep disordered breathing", "obstructive sleep apnea", "sleep apnea" and "Parkinson disease". Abstracts were reviewed to assess eligibility and reference lists were screened to find additional relevant articles. Only studies using polysomnography (PSG) were included. Papers written in languages other than English, case reports and review articles were excluded.

Results

Search results

Our search strategy identified 110 publications. Fourteen articles were screened for eligibility (Fig. 1), seven of which were included, with a cumulative total of 347 patients (Table 1).[15,26–31] Mean disease duration ranged from 6 to 8.3 years. Different measures of PD severity were used: Hoehn and Yahr (HY) score (mean from 2.00 ± 0.7 through 2.6 ± 0.8 or median 2.5)[26–28,31] and the unified Parkinson's disease rating scale (UPDRS) score (mean from 16.8 ± 10.1 through 27.6 ± 16 or categories <12: 53%; 12–22: 40% and >22: 7%).[15,29,31] In one study, authors did not report the severity of the disease in their patients.[30] All patients were on antiparkinsonian therapy, except the 26 from the study by Ferini-Strambi et al.[26]

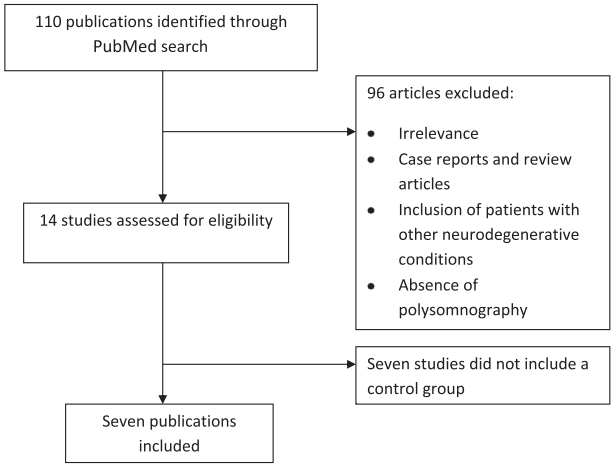

Fig. 1. Flow chart representing the process of selection of studies for inclusion in the review.

Five cross-sectional studies[32–36] and two trials[37,38] were excluded on the basis of absence of a control group of healthy subjects. (Table 2)

No longitudinal study on SDB in PD was identified.

Methodological issues

Patients and controls were matched with regard to age and gender. Body mass index (BMI) was similarly matched between the groups, except for the study by Diederich et al., in which patients and controls were matched for apnea–hypopnea index (AHI),[27] and the study by Shpirer et al.,[28] in which BMI for patients and controls were not specified. In the study by Diederich et al., controls had a greater BMI than patients (28.5 ± 6.72 vs 25.75 ± 4.34 kg/m^2, $p = 0.04$). In one paper,[30] patients were compared to previously published normative data.[39]

In one study, pulmonary function tests were performed one hour after levodopa administration.[15] Patients did not differ with regard to spirometric results when compared to controls, but presented lower maximum inspiratory and expiratory mouth pressures, indicating respiratory muscle weakness.

In two studies, the PSG criteria for respiratory events were not established.[26,31] Definition of hypopnea varied among the remainder (Table 1). Those for apnea were more similar among studies, including complete or almost complete cessation of airflow lasting 10 s or more,[15,28–30] associated with oxyhemoglobin (oxyHb) desaturation of at least four percent.[27]

A reliable blinding method to assess PSG data from patients and controls was reported only in the study by Shpirer et al.[28]

SDB prevalence

The SDB rates among PD patients are shown in Table 1. Five studies showed that PD patients have a similar or even smaller amount of obstructive apneas and hypopneas during sleep than controls.[26,27,29–31]

The study by Maria et al.[15] reported a greater median AHI for PD patients (11 vs 5.7 events/h, $p = 0.048$). Nine out of 15 patients (60%) presented moderate SDB (15 < AHI < 30 events/h), none had severe SDB (AHI > 30 events/h) and one (6%) had central sleep apnea. Shpirer et al.[28] found a greater AHI for patients when compared to controls (7.9 ± 12.5 vs 2.7 ± 3.2 events/h, $p = 0.01$), but authors did not state if patients and controls were matched for BMI. It is noteworthy that even in the PD group a low mean AHI level was found.

Four studies investigated central sleep apnea and none of them found a higher index for PD patients.[15,27,29,31]

In the study by De Cock et al.,[29] patients with increased chin muscle tone during REM sleep tended to have higher AHI than those with normal muscle atonia (18.2 ± 15.9 vs 6.8 ± 10.7 events/h, $p = 0.05$). OSA was found even during REM sleep. No study reported AHI for REM and non-REM sleep stages separately.

Relationship with motor dysfunction parameters and clinical repercussions of SDB

A significant correlation between the severity of PD and AHI was reported by Maria et al.[15] However, their study included a small sample size (15 patients) and five out of 10 patients with SDB had mild PD. De Cock et al.[29] also reported that patients with greater motor disability were more likely to have SDB. Conversely,