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The prevalence of stroke in patients with obstructive sleep apnoea

Abstract

Background: Previous population and clinical studies have confirmed the relationship between stroke and obstructive sleep apnoea (OSA). Our previous study on the epidemiology of sleep-disordered breathing among the inhabitants of Warsaw, conducted on 676 subjects aged 56.6 ± 8.2 years in whom polysomnography was performed and OSA was confirmed in 76 cases (11.3%) with the mean apnoea-hypopnoea index (AHI) of 25.3 ± 16.1, revealed a low prevalence of stroke in subjects with OSA (2 subjects [2.6%]) and in subjects without OSA (20 subjects [3.4%]). The aim of the study was to evaluate the prevalence of stroke in newly diagnosed patients with OSA qualified for continuous positive airway pressure (CPAP) treatment.

Material and methods: We investigated 342 patients (263 men and 79 women) aged 55.4 ± 10.1 years with severe disease (AHI 39.7 ± 22.5) and considerable obesity (body mass index [BMI] 35.0 ± 6.6 kg/m^2). A history of stroke was confirmed in 16 patients prior to the initiation of CPAP (4.7%; Group 1). Group 2 (subjects without a history of stroke) comprised 326 subjects (95.3%).

Results: Multiple regression analysis revealed a significant correlation between stroke and the time spent in desaturation below 90% at night (T90) during polysomnography ($b = -0.22$, $p = 0.009$), diabetes mellitus ($b = 0.16$, $p = 0.006$), Epworth sleepiness score ($b = 0.14$, $p = 0.02$), and coronary artery disease ($b = 0.14$, $p = 0.03$).

Conclusions: A correlation was demonstrated between stoke in patients with OSA (before CPAP treatment) and overnight and daytime oxygenation, diabetes mellitus, daytime sleepiness, and coronary artery disease. The incidence of stroke in the study population was low (4.7%) and similar to that observed in previous population studies.

Key words: obstructive sleep apnoea, stroke, CPAP

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Introduction

In the recent years, sleep-disordered breathing and its impact on the quality of life and the course of cardiovascular disease have attracted the interest of many specialists, mainly pulmonologists, cardiologists, and neurologists. The numerous recent publications in the international literature provide increasing evidence confirming the association of sleep-disordered breathing with hypertension, arrhythmia, coronary artery disease, pulmonary hypertension, stroke, and type 2 diabetes mellitus.

Obstructive sleep apnoea (OSA) is the main clinical problem within the category of sleep-disordered breathing. OSA is defined as brief and repeated airflow disturbances in the upper respiratory tract that take the form of apnoeas and periodic hypopnoeas during sleep. The diagnosis of OSA is based on establishing an apnoea-hypopnoea index (AHI) or respiratory disturbance index (RDI) of > 10 in polysomnography (PSG) accompanied by excessive daytime sleepiness (an Epworth sleepiness score of > 9) [1]. An apnoea is defined as a complete cessation of airflow in the

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upper respiratory tract for at least 10 seconds. A hypopnoea is defined as a reduction in airflow by at least 50% lasting more than 10 seconds and accompanied by fragmentation of sleep, an arousal from sleep, and a decrease in arterial blood oxygen saturation.

Observations of acute neurological events, such as strokes (both ischaemic and haemorrhagic strokes) or transient ischaemic attacks (TIAs), in the context of sleep-disordered breathing have revealed a close association [2–7].

The pathogenesis of stroke in OSA is quite complex. The risk factors for cerebrovascular accidents in patients with OSA include: high blood pressure, rheological abnormalities in the blood (increased platelet aggregation and increased blood coagulability), blood flow abnormalities in the central nervous system (CNS) and abnormalities of the cerebral blood flow autoregulation mechanisms, episodes of decreased oxygen saturation and hypoxia resulting from apnoeas, and coexistent or apnoea-related cardiac arrhythmias. Episodes of reduced CNS perfusion may also be associated with an excessive reduction in blood pressure, which, particularly in patients with clinically significant occlusion of the carotid or vertebral arteries, may lead to abnormalities of CNS circulation [8, 9].

The principal aim of our study was to evaluate the prevalence of stroke in a large group of unselected patients with OSA qualified for continuous positive airway pressure (CPAP) treatment.

Material and methods

342 consecutive patients with OSA qualified for CPAP treatment and hospitalised at the Institute of Tuberculosis and Lung Diseases, Warsaw, Poland between 2005 and 2006 were included in the study.

Before OSA was confirmed the subjects completed a questionnaire concerning epidemiological data (age, height, weight, co-morbidities, previous treatment, past surgeries) and information about the occurrence and severity of snoring, sleep apnoeas, daytime sleepiness, and smoking. Polysomnography was performed using the SomnoStar Alpha system (Sensormedics, USA). Detailed characteristics of these investigations have been discussed previously [10]. An AHI/RDI value exceeding 15 was adopted as a qualification criterion for OSA treatment with an auto-CPAP device. Patients were informed about the necessity to undergo treatment for their OSA by telephone or personally upon arrival to collect their polysomnography results.

During hospitalisation the subjects also underwent routine laboratory tests, a chest X-ray, ECG, spirometry and arterial blood gas analysis before treatment with an auto-CPAP (a device that automatically monitored continuous positive airway pressure). Based on the history and medical records it was established that 16 subjects (4.7%) with OSA had a history of stroke. The group of subjects in whom a history of stroke was not confirmed comprised 326 patients (95.3%).

Obesity was diagnosed if the body mass index (BMI) exceeded 30 kg/m^2. Hypertension was diagnosed if blood pressure values on repeated measurements during hospitalisation exceeded the normal values (140 mm Hg systolic and 90 mmHg diastolic), if the patient had a typical history, or if the patient was receiving antihypertensive treatment.

Ischaemic heart disease in patients qualified for the study was diagnosed on the basis of ECG findings (postinfarction scars, left bundle branch block, signs of ischaemia), previous diagnostic evaluation and medical data, a typical history, or typical treatment. Diagnosis of heart failure was not only based on previous medical records but also on physical findings (peripheral oedema), radiographic findings (signs of congestion in the pulmonary circulation, Kerley lines, enlarged cardiac silhouette), and echocardiographic findings (left ventricular ejection fraction below 50%).

Diagnosis of diabetes mellitus was based on the typical signs and symptoms, laboratory results (fasting glucose of ≥ 126 mg% on two occasions, random glucose of ≥ 200 mg% accompanied by clinical manifestations or blood glucose of ≥ 200 mg% at 120 minutes following the administration of 75 g of glucose), or on the basis of glucose-lowering medication.

Statistical analysis

The study data were analysed using the Statistica 6.0 software package. The results were summarised as means and standard deviations. Qualitative differences between the study variables were assessed using Pearson's chi-squared test or, in the case of less numerous groups, with the Fisher-Yates test. Quantitative differences between the study variables in the study subgroups were assessed using ANOVA. Multiple regression analysis was used to identify variables that were significantly associated with the occurrence of stroke.

Results

A total of 342 consecutive patients (263 men [78%] and 79 women [22%]) were included in the study. The mean age of the subjects was 55.4 ±

Table 1. Comparison of AHI/RDI index. age. Epworth score in studied groups

	Stroke (group 1) (n = 16)	No stroke (group 2) (n = 326)	p
Age (years)	59.8 ± 7	55.2 ± 10.2	NS
Sex (F/M)	2 (2.5%)/14 (5.3%)	77 (97.5%)/249 (94.7%)	NS
BMI [kg/m^2]	34 ± 6.5	35.1 ± 6.6	NS
AHI/RDI (No./h)	37.4 ± 17.6	39.8 ± 22.7	NS
Mean SaO_2 (%)	91.8 ± 4.3	90 ± 4.9	NS
T90 (%)	20.5 ± 6.8	34.7 ± 29.7	NS
ESS (points)	15.4 ± 4	12 ± 5.6	NS

NS — Other explanations of abbreviations in the text

10.1 years. Most subjects were obese (the mean BMI was 35.0 ± 6.6 kg/m^2). These subjects had moderate to severe disease and the mean AHI/RDI was 39.7 ± 22.5 episodes per hour of effective sleep during PGS. Patients spent an average of 34% ± 29.7% of the test duration in desaturation below 90% (T90), and the mean arterial blood oxygen saturation (SaO_2) was 90.1% ± 4.9%. The Epworth sleepiness score was 12.2 ± 5.6.

The prevalence of co-morbidities in the study population was as follows: 59 subjects (17%) were suffering from diabetes mellitus, 89 (26%) from ischaemic heart disease, 252 (73%) from hypertension, 45 (13%) from heart failure, and 28 (8%) from atrial fibrillation (paroxysmal or permanent).

The subjects were divided into two groups. Group 1 comprised subjects with confirmed stroke and Group 2 consisted of subjects without confirmed stroke. In 16 subjects from Group 1 (4.7% of the overall study population) a history of stroke was documented before initiation of CPAP treatment. Episodes of stroke were more often observed in men with OSA than in women (14 [5.3%] and 2 [2.5%], respectively). Group 2 consisted of 326 subjects (95.3%). Both groups were similar in terms of the percentage of men and women, age, BMI, AHI/RDI, mean SaO_2, and the Epworth sleepiness score.

Hypertension and diabetes mellitus were much more prevalent in Group 1 than in Group 2 (p = 0.02 and p = 0.01, respectively). Polysomnography results and anthropometric data are compared in Table 1. The incidence of the other diseases and habits was similar in Groups 1 and 2, as illustrated in Table 2.

Multiple regression analysis was used to evaluate the effect of such factors as AHI, BMI, age, and co-morbidities (coronary artery disease, heart failure, atrial fibrillation, hypertension, and smoking) on the occurrence of stroke. The analysis also took into account the effect of such factors as the Epworth sleepiness score, diabetes mellitus, COPD, hypercholesterolaemia, T90, and FEV_1 % predicted on the occurrence of stroke. A statistically significant correlation has been demonstrated between the incidence of stroke and T90 (β = –0.22, p = 0.009), diabetes mellitus (β = 0.16, p = 0.006), excessive daytime sleepiness (β = 0.14, p = 0.02), and coronary artery disease (β = 0.14, p = 0.03). The coefficient of regression for the entire model was: R = 0.36, R^2 = 0.13, p = 0.0009.

Discussion

In our previous population study investigating the incidence of OSA conducted at our centre on the inhabitants of Warsaw (676 subjects undergoing polysomnography; mean age 56.6 ± 8.2 years; OSA diagnosed in 76 cases (11.3%) with a mean AHI of 25.3 ± 16.1) we found a low (statistically non-significant) incidence of stroke in subjects with OSA (2 subjects [2.6%]) and in subjects without OSA (20 subjects [3.4%]) [11].

In the present study we attempted to evaluate the prevalence of stroke in patients with OSA already confirmed by polysomnography. In contrast to other publications, the prevalence of stroke in our group of OSA patients who qualified for CPAP treatment was low (only 4.7%).

The first report on the association between stroke and snoring were published in 1987 by Koskenvuo et al. [12]. Subsequently, Palomaki et al. demonstrated that snoring is an independent risk factor for stroke [13]. In 1996, Dyken et al. confirmed the presence of OSA in 77% of men and 64% of women hospitalised for recent stroke [14].

An increasing body of evidence is being published in the literature concerning the effect of OSA on the development, occurrence, and course of cardiovascular disease. In a large prospective study (the Sleep Health Heart Study) polysomno-

Table 2. Concomitant diseases and habits

	Stroke (group 1) (n = 16)	No stroke (group 2) (n = 326)	p
Coronary artery disease n (%)	8 (50)	81 (24.85)	NS
Arterial hypertension n (%)	14 (87.5)	238 (73)	p = 0.02
Heart failure n (%)	2 (12.9)	43 (13.2)	NS
Atrial fibrillation n (%)	3 (18.75)	25 (7.7)	NS
Diabetes n (%)	7 (43.8)	52 (16)	p = 0.01
Habit of smoking n (%)	4 (25)	95 (29.1)	NS

NS — Other explanations of abbreviations in the text

graphy was performed at home in 6424 subjects. A total of 1023 subjects (16%) had a history suggestive of cardiovascular disease. Coronary artery disease was confirmed in 838 subjects (13%), stroke in 232 subjects (3.6%), and heart failure in 123 subjects (2%). The risk of stroke in subjects with sleep-disordered breathing (AHI > 11) was 1.58 times higher (p = 0.03) compared to subjects without sleep-disordered breathing (AHI ≤ 1.3) [15, 16].

In two subsequent studies [3, 4] in stroke patients, OSA was diagnosed in 43–91% of the subjects, which was much more frequently than in the control group of patients without a history of stroke. In both studies it was observed that the incidence of OSA in these subjects was much higher than central apnoeas, which accounted for less than 10%. Because the number of apnoeas during sleep did not decrease over the 3 months of post-stroke follow-up, while the number of central apnoeas did, it seems that stroke predisposes to the development of central apnoeas, while OSA precedes neurological events.

A high prevalence of OSA (44–72%) in patients with confirmed stroke has also been reported elsewhere [17–19].

The prospective Wisconsin Sleep Cohort Study demonstrated that AHI values above 20 were associated with a 4-fold increase of the risk of stroke during 4 years of follow-up [20]. In the Caerphilly Cohort study a high rate of stroke (31%) during 10 years of follow-up was demonstrated in men who snored and experienced apnoeas, daytime sleepiness, and problems with falling asleep at night [21].

So what could have been the reasons for the low prevalence of stroke among the subjects with OSA in our study? It seems that multiple factors may have played a role. It appears that first of all, patients presenting to the Sleep Laboratory at the Institute of Tuberculosis and Lung Diseases were already a selected group of patients in whom the manifestations of OSA were the principal cause of reduced quality of life. Stroke in these subjects was confirmed on the basis of medical records from neurology wards several months or even years before. No data were available on the occurrence of small-extent strokes and TIAs in the subjects we investigated (the patients had not sought medical assistance for their transient symptoms or had not associated neurological events with brain ischaemia). For financial reasons no CT scans to confirm the history of stroke were ordered. Patients with suspected or confirmed OSA with a history of severe strokes did not present to our Institute because their condition prevented it or because treatment for OSA was not a priority for them due to the other accompanying illnesses.

We did, however, confirm in our subjects the close association of stroke and coronary artery disease (β = 0.14, p = 0.03) and of stroke and diabetes mellitus (β = 0.16, p = 0.006), consistent with the literature. In addition to that, the occurrence of stroke was associated with the time spent in desaturation at night (T90) (β = –0.22, p = 0.009) and the Epworth sleepiness score (β = 0.14, p = 0.02).

Conclusions

We have demonstrated an association of stroke in patients with OSA (prior to the initiation of CPAP treatment) and oxygenation during sleep and arousal, diabetes mellitus, daytime sleepiness, and coronary artery disease.

The prevalence of stroke in the study group was low (4.7%) and did not differ from that in the population study conducted on the inhabitants of Warsaw.

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