SLEEP DISORDERED BREATHING AND RECURRENCE OF CEREBROVASCULAR EVENTS, CASE-FATALITY, AND FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE OR TRANSIENT ISCHEMIC ATTACK

Ninety one patients with stroke or transient ischemic attack (TIA) were screened for sleep-disordered breathing (SDB). Case fatality, rate of recurrence of cerebrovascular events, and functional outcome were analyzed during a 2-year follow-up. The patients were stratified into groups: without (AHI ≤ 5) and with SDB (AHI > 5). SDB was present in 61 (67.7%) patients with stroke or TIA. The rate of recurrence of TIA or stroke in patients with SDB was significantly higher (12 patients, OR=1.52, P<0.05) as compared with patients without SDB (3 patients) within two years of observation. Case-fatality rates were not significantly different (4 patients with SDB and 2 patients without SDB). Our data show that SDB significantly increases the incidence of recurrent cerebrovascular events in patients with TIA or stroke in a two-year follow-up. SDB in patient with stroke or TIA did not influence functional outcome of stroke during the long-term observation.

Key words: AHI, ischemic stroke, NIHSS, sleep-disordered breathing, transient ischemic attack

INTRODUCTION

Sleep-disordered breathing (SDB) is defined as cessation or reduction of airflow in the airways associated with a consecutive decrease of blood oxygenation. The first SDB described was the crescendo-decrescendo pattern of breathing followed by cessation of airflow reported by Cheyne and Stokes (1, 2) in the 19th
In the 1956 Burwell *et al* (3) described a Pickwickian syndrome (3). Following years gave tremendous development of the knowledge in the field of sleep-disordered breathing. Palomaki *et al* (4, 5) have shown that snoring, a manifestation of SDB, is the risk factor for cardiovascular events and ischemic stroke. These results were further confirmed by other authors in subsequent studies (6, 7). The most prevalent SDB is the obstructive sleep apnea syndrome (OSAS) caused by an obstruction along the upper airway (8, 9). Another example of SDB is the central sleep apnea syndrome (CSAS), where apnea is secondary to the lack of respiratory drive and followed by lack of inspiratory muscle contraction (10). Mixed apneas are a combination of both apnea types. Overlapping syndromes are a frequent occurrence in clinical practice. The prevalence of OSAS is at least 2% in women and 4% in men in the general population (9). According to some authors, in selected populations, e.g., in men aged 30-60, the prevalence of OSAS exceeds 10% or even 20% (11-15).

Ischemic stroke is the third leading cause of death worldwide (15). There are many convincing results from large cohort studies showing that SDB, especially obstructive sleep apneas, are associated with increased risk of stroke and are regarded as a risk factor independent of other cardiovascular risk factors (12-16).

The aim of the present study was to assess the long-term influence of the sleep-disordered breathing on health status of patients with ischemic stroke or transient ischemic attacks. Our previous studies have shown that the incidence of SDB, especially obstructive sleep apneas, is quite high in the population of Polish patients with stroke or transient ischemic attacks (17, 18). We also found a correlation between the severity of the neurological deficit on admission and discharge from the hospital and the severity of sleep-disordered breathing and desaturation events (18). The present study was focused on the long-term consequences of sleep-disordered breathing in patients with cerebrovascular events, especially on the recurrence of the cerebrovascular event and case fatality.

**MATERIAL AND METHODS**

**Patients**

Patients recruited to the study were admitted to the First Department of Neurology at the Institute of Psychiatry and Neurology in Warsaw, Poland, with the diagnosis of the first-ever ischemic stroke or transient ischemic attack within the years 2004-2007. The diagnosis was determined by neurologists on the basis of clinical symptoms according to the guidelines of the American Academy of Neurology. CT brain scan was performed within the first 6 hours after admission. Patients with significant reduction of consciousness (Glasgow Coma Scale, GCS<10), symptoms of severe neurological deficit (NIHSS score >20), aphasia, history of significant heart failure (NYHA >3), or dementia were not included into the study. Patients with transient ischemic attacks were included into the study only if they presented hemispheric symptoms. All of the patients were informed about the protocol and gave written consent to participate in the study. The
study was approved by a local Ethics Committee and was conducted according to the Helsinki Declaration for Human Research.

Clinical assessment

The neurological deficit was assessed with the National Institute of Health Stroke Scale (NIHSS) (19) on the day of admission. Functional disability was assessed using the Rankin and Barthel scales also on the day of admission. The functional outcome during a 2-year follow-up after the stroke or TIA was assessed with the same scales during a telephone interview with patients, caregiver, or family member.

Risk factors for cardiovascular events such as increased body mass index (BMI), smoking, hypertension, diabetes mellitus, cardiac arrhythmias, and hypercholesterolemia were assessed in all patients on admission.

Sleep-disordered breathing evaluation

All patients included to the study underwent an 8-h nocturnal (between 10 p.m. to 6 a.m.) screening for SDB with a portable 8 channel recorder (Embletta, Medcare, Iceland). The examination took place within 7 days after the onset of stroke or TIA symptoms. The recorded variables were: nasal flow, abdominal and thoracic efforts, pulse oximetry, body position, and snoring. Breathing parameters were automatically analyzed with Somnologica Software (Medcare, Iceland) and were visually corrected by a researcher.

The Apnea-Hypopnea Index (AHI) was estimated according to the American Academy of Sleep Medicine Task Force guidelines and definitions (19). The patients with stroke or TIA were stratified according to AHI into groups: without SDB (AHI ≤5) and with SDB (AHI >5).

Statistical comparisons were done with a t-test or one-way ANOVA followed by Tukey’s test after the normal distributions of data had been established. The rate of recurrence and case fatality were assessed with Fischer’s exact tests. Results are shown as means ±SD

The follow-up analysis

We followed 72 patients after ischemic stroke or TIA for 24 months. The points of interest were the rate of recurrence of cerebrovascular events (transient ischemic attack or recurrent ischemic stroke), case fatality, and functional outcome. The rate of recurrence of TIA or stroke and case fatality were assessed from an analysis of the medical Solmed database system with subsequent phone interviews with the patient, caregiver, or family member. Functional outcome was analyzed with the Barthel and Rankin scales during similar phone interviews.

RESULTS

 Ninety one patients (mean age 65.2 ± 10.3; 79 males 12 females, 69 patients with stroke and 22 patients with TIA), without previously diagnosed SDB, were included into the study. According to the AHI score, the patients were stratified into two groups: without SDB (AHI ≤5, 30 patients) and with SDB (AHI >5, 61 patients). The mean age and BMI of the patients with SDB did not differ statistically from those of the patients without SDB (66.9 ± 9.7 and 62.1 ± 9.7 years and 27.7 ± 4.1 and 25.1 ± 4.0 kg/m², respectively). The cardiovascular
risk factors for stroke were distributed similarly in both groups. Hypertension was present in 75.4% and 73.4% patients with and without SDB, respectively; P>0.05. Nicotinism was present in 65.5% and in 66.6% patients with and without SDB, respectively; P>0.05. There were no statistical differences between the respective groups of patient with and without SDB concerning the incidence of heart ischemic disease (40.9% vs. 43.3%), cardiac arrhythmias (26.2% vs. 23.3%), diabetes mellitus (18.0% vs. 18.5%), and hypercholesterolemia (72.3% vs. 76.6%) (P>0.05 for all). The clinical neurological status assessed with the NIH stroke scale was slightly, but not significantly, worse in the patients with SDB than in those without SDB (NIHSS 5.7 ± 2.2 and 4.4 ± 1.9 respectively; P>0.05) (Fig. 1).

Sleep-disordered breathing (AHI >5) (20) was present in 61 (67.7%) patients with stroke or TIA. The mean AHI in patients with SDB was 20.8 ±15.8 compared with the 1.75 ± 1.4 in patients without SDB (P<0.05). Thirty seven patients with SDB (60.7%) had mild-to-moderate SDB (AHI <20) and 24 patients (39.3%) had severe SDB (AHI >20). In patients with SDB, apneas predominated and made up 57.2 ± 21.6% of all hypopneic/apneic events. Among the apneic events, the obstructive apneas were significantly more frequent (P<0.01) as they

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**Fig. 1.** A - Demographic data, B - respiratory and clinical parameters, C - risk factors. Abbreviations: BMI - Body Mass Index, SDB – Sleep Disordered Breathing, AHI – Apnea Hypopnea Index, NIH - National Institute of Health Stroke Scale.
made up 75.2 ± 12.6% of all apneic events. Central apneas in patients with stroke and TIA were responsible for 12.2 ± 9.6% of all apneic events.

DISCUSSION

Most of the papers published so far have focused on the issue of the sleep-disordered breathing as a risk factor for ischemic stroke. There are many convincing results from large cohort studies that sleep-disordered breathing, especially obstructive sleep apneas, are independent risk factors for stroke (4, 5, 7, 10, 12, 13, 15). It has also been demonstrated that the severity of sleep apneas contributes to the functional outcome after stroke and significantly increases the risk of death (21, 22). Less is known about the recurrence of the cerebrovascular event in patients with the history of stroke or TIA and SDB. The recent study from Germany shows that the incidence of sleep apnea is much more frequent in patients with recurring stroke than in those with the first ever stroke (23). These data are consistent with our results which clearly show that patients with ischemic stroke or TIA and sleep-disordered breathing have a higher risk of consecutive cerebrovascular event within the next 2 years than those with stroke and TIA but without SDB (Odds Ratio 1.52; 95% Confidence Interval 1.06-2.14). Our patients with, or without SDB, did not differ with respect to age, BMI, or other cardiovascular risk factors. It is noteworthy that they did not have significantly increased BMI (mean BMI: 27.7 ± 4.1) and their initial NIH score was not statistically different between the patients with and without SDB and relatively low, (mean NIH value 5.7 ± 2.2). These data have important practical implications.
Firstly, since it is possible to effectively treat the sleep-disordered breathing, all patients with stroke and SDB should undergo non-invasive or invasive treatment of SDB. It would be advisable to refer all of them (despite mild or moderate SDB) to sleep research centers or pulmonologists. Secondly, it should be recommended to perform a routine sleep-apnea screening in all patients having suffered an ischemic stroke or transient ischemic attack.

Although we did not find significant differences between patients with or without SDB in functional parameters after a 2-year follow-up, which may be caused by the strict inclusion criteria to the study, and relatively mild neurological deficit in majority of patients, we think that the patient after ischemic stroke or TIA with SDB should be under careful supervision of the neurologist, caregiver, and neurorehabilitant.

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REFERENCES


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