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ORIGINAL PAPER

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Sleep Disorders in Acute Stroke

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ABSTRACT

Background: Stroke patients have sleep-wake disorders, mostly in form of insomnia, excessive daytime sleepiness/fatigue, or hypersomnia (increased sleep needs). **Objective:** The aim of this study was to analyze types of sleep disorder (SD) and their frequency in patients with sleep apnea and acute stroke in relation to the type of stroke and side of lesion. **Methods:** The study analyzed 110 patients with sleep apnea and acute stroke hospitalized in the Clinic of Neurology, University Clinical Centre Tuzla. Acute stroke has been verified either by computerized tomography or magnetic resonance imaging of the brain. SD was verified according to the Berlin Questionnaire Test, The Epworth Sleepiness Scale, The Stanford Sleepiness Scale and the General sleep questionnaire. Strokes were divided by: a) type, into hemorrhagic and ischemic, and b) the localization of the stroke, to right and left cerebral hemispheres. **Results:** Of the total number of respondents, all had some sleep disorder. 20% of respondents had severe level of SD, 35.4% moderate, 37.3% moderate-severe and 7.3% mild problems. There were no statistically significant differences in the frequency of SD among patients with ischemic and hemorrhagic stroke ($p = 0.58$). In relation to the side of lesion, there was more patient with SD and stroke in the both sides, but there were no statistically significant differences ($X^2=1.98, p=0.161$). According Epworth Sleepiness Scale, Stanford Sleepiness Scale and Berlin Questionnaire test snoring was present in 81% and daytime sleepiness in all patients. **Conclusion:** SD as a neuropsychological disorder has a significant incidence in the acute phase of stroke in patients with sleep apnea. Sleep disorder is more common in ischemic stroke and stroke in the both hemisphere, but it is not statistically significant difference. Daytime sleepiness, fatigue and snoring are the most common sleep problems in patients with acute stroke and apnea, but it is not statistically significant.

Keywords: Stroke, Sleep Apnea, Sleep Disorders.

1. BACKGROUND

Sleep apnea (SA) affects about 10% to 20% of middle to older aged adults (1), is characterized by the repeated obstruction of the upper airway during sleep that leads to complete cessation (apnea) or reduction (hyperpnea) of airflow, occurring irrespective of continued ventilatory effort. Before termination, these events lead to a decrease in blood oxygen saturation and an associated increase in carbon dioxide levels during longer events. The termination of the apnea is often preceded by an arousal, which leads to sleep fragmentation and activation of the sympathetic nervous system. The former is hypothesized to be involved in the neurocognitive sequelae, whereas the latter leads to cardiovascular dysfunction. This process is identified as the possible cause for the daytime sleepiness and cardiovascular health and functioning problems witnessed in these individuals (2, 3). Severe obstructive sleep apnea (OSA) has been linked to a 4- to 6-fold increased risk of mortality, irrespective of factors such as age, diabetes, or high cholesterol (4, 5). Finally, rate of insomnia vary as a function of OSA severity. Supratentorial strokes have been linked to decreases in NREM sleep time, and to a lower sleep efficiency (6).

2. OBJECTIVE

The aim of this study was to analyze types of sleep disorder (SD) and their frequency in patients with sleep apnea and acute stroke in relation to the type of stroke and side of lesion.

3. PATIENTS AND METHODS

This prospective study was conducted at the Clinic of Neurology of the University Clinical Center in Tuzla. The examined group of 110 pa-

tients in the acute phase of stroke with SA was evaluated. The average age was 65.13 ± 9.27 years. Among them, it was 65 (59%) men. The study group included patients who meet the following criteria: confirmation of a diagnosis of ischemic stroke (IS) or a hemorrhagic stroke (HS) by computed tomography (CT) and/or magnetic resonance imaging (MR) of the brain, neuropsychiatric assessment of SA performed within seven days after stroke, Mini Mental test (MMT) > 23, Glasgow coma scale (GCS) > 8, written consent for participation in the research by the patients or a member of the patients immediate family. Patients with a GCS <8 on the day of neuropsychiatric examination were excluded from the study, as well as patients with epileptic seizures at the onset of stroke, with aphasia, with MMT < 23, with verified previous dementia/cognitive impairment (based on hetero anamnesis data from patients relatives, data from previous medical findings). Neurological tests were performed in all patients at five different periods: the first test—in the acute phase of stroke (first week of stroke), second test—one month after the stroke, third test—three months after stroke, fourth test—six months after stroke and fifth test—twelve months after stroke. In these periods, all patients were evaluated by: the Mini Mental Test (7), the Berlin Questionnaire Test (8), the Epworth Sleepiness Scale (9), the Stanford Sleepiness Scale (10) and the General Sleep questionnaire (11). The findings of CT of the brain and MR of the brain were interpreted by a radiologist who was not familiar with the goals and hypotheses of the research. Based on these interpretations, there were established: type of stroke, localization of the lesion, and lesion size. The study included also the data of the following socio-demographic characteristics: gender and age.

4. METHODS / INSTRUMENTS

Berlin Questionnaire Test

The Berlin Questionnaire included 10 questions on risk factors for SA, including body weight, snoring, breathing pauses, drowsiness on walking or during the day and hypertension. The ranking of the answers is gradual: 0 = never or almost never, 1 = 1 to 2 times a month, 2 = 1 to 2 times a week, 3 = 3 times a week and 4 = almost every day.

Epworth Sleepiness Scale

It consists of 4 parts that analyze drowsiness, sleep apnea/snoring, narcolepsy and other disorders. Scoring and analysis were performed according to the attached key. The ranking of the answers is gradual: 1 = rarely or never, 2 = sometimes, 3 = often, 4 = mostly.

Stanford Sleepiness Scale

The Stanford Sleepiness Scale is designed to self fatigue and measure drowsiness. It consists of 7 levels that describe the degree of drowsiness. If the patients score is above 3, he has serious sleep problems.

General Sleep Questionnaire

This questionnaire contains the following data: socio-demographic (name, age, gender, and occupation), sleep pattern data, daytime sleepiness, chronic somatic diseases, and health data. The questionnaire has a total of 46 questions.

Statistical analysis

When testing the statistical significance of main differences, the standard Student T-test was used. Descriptive

statistics were processed using the X^2 (Hi-square test) and the proportional test. All calculations were performed using the Arcus Quickstadt Biomedical statistical data processing program as well as the long rank test with $p < 0.05$ considered significant. The research was approved by the Committee of the University Clinical Center Tuzla.

5. RESULTS

The study analyzed 500 patients with acute stroke (AS), and of those 110 (22%) were verified SA, with mean age 65.13 ± 9.27 years, and the majority were men 65 (59%). No statistically significant difference was found in the age of patients in either men or women ($t = -0.16$, $p = 0.88$). The largest number of patients with SA had an ischemic stroke (92 / 83.6%), while 18 (16.4%) had a HS, of whom 56 (86.2%) were men and 36 (80%) were women with IS and 9 (13.8%) men and 9 (20%) women with HS. Of the patients with IS 92 (83.6%) had sleep disorders. According to the severity of the problem, 38 of them (41.3%) stated that they had a moderate-severe sleep problem, 34 (37%) moderate, 16 (17.4%) severe and 4 (4.34%) did not have a serious sleep problem. In patients with HS, 18 (16.4%) had sleep disturbance. According to the severity of the problem, 6 (33.3%) patients had severe sleep problem, 5 (27.7%) moderate, 3 (16.7%) moderate severe and 4 (22.3%) did not have a serious sleep problem. The X^2 (Chi-square test) found that the presence of sleep disorders did not depend on the type of MU ($X^2 = 0.31$, $p = 0.58$). According to the ratio of sleep disorders, the incidence of sleep disorders is 1.41 times more common in the case of hemorrhagic stroke (95%, CI: 0.55-4.11), but the chances of sleep disorders in these two types of stroke do not differ statistically significantly (Tables 1).

The severity of sleep problems	Ischemic stroke N=92	Percentage Hemorrhagic stroke Percentage % N=18 %
Mild	4	4.3 4 22.3
Moderate	38	41.3 3 16.7
Moderate-severe	34	37.0 5 27.7
Severe	16	17.4 6 33.3

Table 1. The severity of sleep problems in patients with ischemic and haemorrhagic stroke. Ischemic-hemorrhagic stroke $X^2 = 0.31$, $p = 0.58$.

The severity of sleep problems	Left N=26 %	Right Both sides N=34 % N=50 %
Mild	3 12.0	2 6.0 3 6.0
Moderate	7 27.0	16 47.0 18 36.0
Moderate-severe	12 46.0	10 29.0 17 34.0
Severe	4 15.0	6 18.0 12 24.0

Table 2. The severity of sleep problems in relation to the side of the stroke. Left-right-both sides $X^2 = 1.98$, $p = 0.161$

Out of 50 (45.4.6%) patients had lesions in both hemispheres. Of these, 18 (36%) had moderate sleep problems, 17 (34%) moderate severe, 12 (24%) severe and 3 (6%) had no serious sleep problems. Of the 34 (31%) patients with right hemisphere stroke, 16 (47%) had moderate sleep problems, 10 (29%) had moderate-severe problems, 6 (18%) had severe problems, and 2 (6%) had no serious sleep problems.

Duration months	Number of respondents N=110	Percentage %
≤24	12	10.91
25-36	14	12.73
37-48	12	10.91
49-60	41	37.27
61-72	15	13.64
>72	16	14.55

Table 3. Distribution of patients with sleep apnea in relation to the duration of sleep problems. Descriptive statistics: X med= 61.6 months; SD=28.6 months; X min=12 months; X max=120 months

Frequency of snoring	Number of respondents N=110	Percentage %
Never	21	19.09
(1-2) times per month	5	4.55
(1-2) times a week	8	7.27
(3-4) times a week	25	22.73
Almost every day	51	46.36

Table 4. Distribution of patients with sleep apnea in relation to the frequency of snoring

Lesions in the left hemisphere had 26 (23.6%) patients, of whom 12 (46%) had a moderately severe problem, 7 (27%) had a moderate problem, 4 (15%) had a severe problem and 3 (12%) had no serious sleep problem. Chi-square test found that the frequency of sleep problems in patients with stroke did not depend on the side of the lesion ($X^2 = 1.98$, $p = 0.161$) (Table 2).

When examining the presence of sleep disorders according to the general questionnaire, sleep patterns were analyzed. In sleep patterns, the average time to go to sleep and the duration of sleep were analyzed. It was determined that the average time to go to sleep is 22h 34' ± 1h 52', and the length of sleep is 6h 23' ± 38'. According to the length of sleep disorders in patients with SA, the average duration of the disorder was 28.6 months (12 to 120). The largest number of patients, 41 (37%), had sleep disturbances of 49-60 months, followed by 16 (15%) who had more than 72 months, 15 (14%) who had 61-72 months, 14 (13%) who had 25-36 months, 12 (11%) who had from 37-48 months and 12 (11%) who had less than 24 months (Table 3).

According to the severity of sleep problems, the largest number of patients with SA had a moderate problem 41 (37%) patients, 39 (35%) had a moderately severe problem, 22 (20%) severe problem and 8 (7.27%) not serious problem.

According to the Berlin Questionnaire, 89 (80.9%) patients reported snoring during sleep, and 21 (19%) denied snoring. Almost every day 51 (46.36%) patients snore, 25 (22.73%) snore 3-4 times a week, 8 (7.27%) snore 1-2 times a week and 5 (4.55%) snore 1-2 times a month (Table 4).

In the group of patients with stroke, 31 (28.18%) patients had SA almost every day, 39 (35.45%) 3-4 times a week, 40 (36.36%) 1-2 times a week and 1 (0.90%) 1-2 times a month (Table 5).

Sleep fatigue was present in all patients with SA and stroke. Almost every day, 31 (28.18%) of patients had fa-

Frequency of pauses in breathing	Number of respondents N=110	Percentage %
Never	0	0.00
(1-2) times per month	4	3.64
(1-2) times a week	44	40.00
(3-4) times a week	39	35.45
Almost every day	23	28.0

Table 5. Distribution of patients with sleep apnea in relation to the frequency of respiratory pauses $p=0.082$

Incidence of fatigue after sleep	Number of respondents N=110	Percentage %
Never	0.0	0.00
(1-2) times per month	1	0.91
(1-2) times a week	40	36.36
(3-4) times a week	38	34.55
Almost every day	31	28.18

Table 6. Distribution of patients with sleep apnea in relation to the incidence of fatigue after sleep, $p=0.082$

Sleepiness after sleep	Number of respondents N=110	Percentage %
Never	0.0	0.00
Moderate	69	62.7
Moderate-severe	21	19.1
Severe	20	18.2

Table 7. Distribution of patients in relation to sleep disorders according to the Stanford scale

tigue, 38 (34.55%) 3-4 times a week, 40 (36.36%) 1-2 times a week and 1 (1%) 1-2 times a month. There is no statistically significant difference ($p = 0.082$) between fatigue and sleep disturbances in patients with SA (Table 6).

Analyzing sleep disorders according to the Epworth Sleepiness Scale, the results showed that the most common disorder was daytime sleepiness present in 110 (100%) patients of the study group, of which 75 (68.18%) had moderate sleepiness. 40 (36.36%) patients had moderate SA and 48 (43.6%) patients had moderate SA. Narcolepsy was not present in any patient. Other sleep disorders, which included periodic limb movements, restless legs syndrome, gnashing of teeth, walking, or speech during sleep, had 11 (10%) respondents.

According to the Stanford Sleepiness Scale, the results showed that daytime drowsiness was present in 110 (100%) patients, of which 69 (62.7%) had moderate drowsiness, 21 (19.1%) moderate severe and 20 (18.2%) patients severe drowsiness (Table 7).

6. DISCUSSION

Patients with stroke, primarily ischemic, may suffer from several types of sleep disorders, and their manifestation may depend on the severity of the neurological deficit (12). In this study, the presence of sleep problems was noted in all patients with stroke and SA. The majority of subjects 37% had a moderate degree, 35.4% moderately severe, 20% severe, and 7.3% of patients reported mild sleep disturbance. These results indicate that there is a high incidence of sleep

disorders in patients with stroke. The largest number of surveyed patients with SA had an IS of 83.6% and all of them stated that they had more or less sleep problems, and the largest number of 41.3% had a moderately severe degree of sleep disorders. 16.4% of patients had HS, and the largest number, 33.3%, had a very serious sleep problem. The differences are not statistically significant. According to a prospective study conducted on 152 patients with acute IS, Bassetti et al. (13) confirmed that patients with acute IS have a high incidence of SD, it was 72%, and in a large number of cases SD precede stroke, including transient ischemic attack. In this study, relative to the lesion side, the largest number of patients had a stroke of 45.4% in both hemispheres. A chi-square test found that the frequency of sleep problems in patients with stroke did not depend on the side of the lesion, which supports the results of other studies. Wierzbick et al. (14) analyzed the influence of a foreign lesion on SD in 43 patients with stroke. Out of those, lesions were reported in one hemisphere for 35 patients, of whom 19 had lesions in the left and 16 in the right hemisphere, while other patients had lesions in both hemispheres. The results of this study also indicated that the side of the stroke lesion was not associated with SD. In this study in the SA group, the mean duration of sleep disorders was 61.6 ± 28.6 (range 12–120) months. The largest number of patients had sleep disturbances of 4–60 months (37%), followed by more than 72 months (14.5%). All patients had increased daytime sleepiness and difficulty sleeping at night. In the Pasic study, sleep problems were reported in 78% of patients with stroke and, for the most part, the problem was very severe, while 22% of patients denied sleep problems (15). The results of our study indicate that there is a high incidence of SD in patients with stroke and SA. According to a study with 190 patients with SA and stroke increased drowsiness was found in 47% of patients, which is lower than in this study (16). According to the Berlin Questionnaire, 81% of patients stated that they snore during sleep, and 19% denied snoring. Almost every day 46.4% snore and 22.7% snore 3–4 times a week. Similar results were found in the Pasic study that was conducted in 200 patients with stroke and sleep disturbances where it was stated that 82.5% snore during sleep, which is identical to our study (15). Similar results are reported by Dunai et al. (17), in a study conducted on 12,643 patients, where snoring was registered in 58% of cases almost every day, and confirmed that patients who snore have a 67% higher risk of stroke compared to patients who do not snore. According to other studies, there is a significant association between snoring and stroke (18). Snoring is significantly more common in patients who have suffered stroke (47.4%), and SA is present in 60% of patients with stroke and snoring in the post-acute period (19). Similar results as in our study were obtained by Sprigs et al. (20) in a study conducted in 400 patients with stroke and 400 control groups, adjusted by age and sex. Snoring was verified in 81.5% patients with stroke and 86.2% patients in the control group. The risk ratio for patients with stroke is 3.2 times higher for regular snorers, as opposed to those who did not snore regularly. Palomaki (21) states that the probability ratio of snoring as a risk factor for IS was greatly increased if snoring is accompanied by excessive daytime

sleepiness and obesity, probably due to a higher incidence of SA in among snorers compared to non-snorers. In this study in the group of patients with stroke and SA, 28.18% had SA almost every day and 35.45% of patients 3–4 times a week. The Pasic study stated that the largest number of patients, 23.5%, have SA almost every day, and 15% of patients 3–4 times a week (15). Many researchers have shown that the association between stroke and SA is quite high, somewhere between 30%–90% in surviving patients (22, 23), which is supported by our study. In our study, sleep fatigue was present in almost every day in 28.18% and in 34.55% patients 3–4 times a week. There was no statistically significant difference ($p = 0.082$) between fatigue and sleep disturbances. Colei et al. (24) claim that 37% of patients with stroke and SA experience sleep fatigue. Thurnheer et al. (16) reported energy deficiency in 62% and fatigue in 57% of patients with stroke and SA. According to the Epworth scale, the presence of daytime sleepiness was found in all patients with SA. Moderate daily drowsiness was present in 68% of patients, of whom 30% had severe drowsiness and 1.8% had moderate drowsiness. According to Guilleminault et al. (25) daytime sleepiness ranged from 30%–40% in patients with SA. Similar results were obtained in his study by Jha et al. (26) who reported a prevalence rate of excessive daytime sleepiness of 11% to 53% in patients with SA. The Epworth scale for daytime sleepiness was used, which confirmed the presence of this problem in 47% of milder patients, while 9% of patients had a more severe degree of daytime sleepiness. This study also indicates that the risk of stroke is 4.5 times higher in those patients who have a more severe degree of daytime sleepiness, while this risk is significantly reduced, to 2.6 times, in patients who have mild forms of the problem. Narcolepsy, as a form of sleep disorder, occurs in 20%–40% of patients after stroke; however in this study it was not observed in any patient with SA. Patients with a milder form of this disease often remain undiagnosed (27). According to the Stanford Sleepiness Scale, the results showed that daytime drowsiness was recorded in all patient patients with SA, of whom 62.7% had moderate drowsiness, 19.1% moderate severe and 18.2% had severe. According to Happe, excessive daytime sleepiness (EDS) occurs in 30% of the elderly and is defined by a subjective feeling of much-needed sleep at unusual times and in unusual places (28). It occurs far more frequently in stroke and primary sleep disorders such as SA, narcolepsy, and periodic limb movements during sleep (PLMS) (29–31). In the study of 190 patients with SA and stroke, lack of energy was found in 62%, fatigue in 57% and drowsiness in 47% of patients. When asked to choose the most significant symptom, 40% of patients said it was a loss of energy, and 22% said they were drowsy (16).

7. CONCLUSION

Sleep disturbance has a significant incidence in the acute phase of stroke in patients with sleep apnea. Sleep disorder is more common in ischemic stroke and stroke in the both hemisphere. Daytime sleepiness, fatigue and snoring are the most common sleep problems in patients with acute stroke and apnea.

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