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Assessment of Sleep Quality of Patients with Pre-ischemic Stroke the Relationship Between Ischemic Stroke and Sleep

İskemik İnme Öncesi Hastaların Uyku Kalitesinin Değerlendirilmesi-İskemik İnme ve Uyku İlişkisi

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ABSTRACT Objective: Research on the effects of sleep on health and quality of life is ongoing. As part of this study, we aim to evaluate the role of sleep disorders associated with modifiable or non-modifiable risk factors in stroke aetiology. **Material and Methods:** A total of 137 individuals participated in the study. After an ischemic stroke, we compared the patients' sleep quality and duration in the last month with a control group that had not had a stroke with similar classical risk factors. For this, we used simple sleep questionnaires. **Results:** The total scores of the participants on the Epworth Sleepiness and Pittsburgh Sleep Quality Scale were statistically different between the groups. The total score of the Berlin Questionnaire (BQ) and the rates of the Stanford Sleepiness Scale were statistically different between the patient and control groups. According to the total scores of the BQ, 40.0% (n=28) of the patient group and 16.4% (n=11) of the control group were found to be at high risk for obstructive sleep apnea (OSA). Our study supports that poor sleep quality, short sleep duration, and increased risk of OSA play a directly proportional role in the development of ischemic stroke. Furthermore, our patients' high frequency of OSA was associated with short sleep duration. **Conclusion:** With this study, we would like to remind you again that the importance of sleep disorders in the etiology of stroke and its treatment should not be forgotten.

Keywords: Sleep; ischemic stroke; sleep disorders

ÖZET Amaç: Uykunun sağlık ve yaşam kalitesi üzerindeki etkileri üzerine araştırmalar devam etmektedir. Bu çalışma ile, inme etiyolojisinde değiştirilebilen veya değiştirilemeyen risk faktörleri ile ilişkili uyku bozukluklarının rolünü değerlendirmeyi amaçlıyoruz. **Gereç ve Yöntemler:** Çalışmaya toplam 137 kişi katıldı. İskemik inme sonrası, hastaların son bir aydaki uyku kalitesini ve süresini benzer klasik risk faktörlerine sahip inme geçirmemiş kontrol grubu ile karşılaştırdık. Bunun için basit uyku anketleri kullandık. **Bulgular:** Katılımcıların Epworth Uykululuk ve Pittsburgh Uyku Kalitesi Ölçeği toplam puanları gruplar arasında istatistiksel olarak farklıydı. Berlin Anketi Berlin Questionnaire (BQ) toplam puanı ve Stanford Uykululuk Ölçeği oranları hasta ve kontrol grupları arasında istatistiksel olarak farklıydı. BQ toplam puanlarına göre hasta grubunun %40,0'ı (n=28) ve kontrol grubunun %16,4'ü (n=11) obstrüktif uyku apnesi (OUA) açısından yüksek risk altında bulundu. Çalışmamız, kötü uyku kalitesi, kısa uyku süresi ve artmış OUA riskinin iskemik inme gelişiminde doğru orantılı rol oynadığını desteklemektedir. Ayrıca hastalarımızın yüksek OUA sıklığı, kısa uyku süreleri ile ilişkilendirilmiştir. **Sonuç:** Bu çalışma ile inme etiyolojisinde uyku bozukluklarının önemini ve tedavisinin unutulmaması gerektiğini tekrar hatırlatmak isteriz.

Anahtar Kelimeler: Uyku; iskemik inme; uyku bozuklukları

There is no doubt that sleep accounts for about a third of our lives. The effects of variations in sleep duration and/or rhythm in adults can adversely affect their health in the long run. A considerable amount of research has been conducted to determine the impact of inadequate sleep on health and quality of life. A sleep disorder can be associated with various health conditions that affect the cycle and/or duration of the sleep cycle, which can have serious complications if left untreated. Using simple questionnaires, we examined the sleep problems of patients with ischemic strokes over the past month. This article aims to provide a brief review of the role of sleep disorders in stroke aetiology and emphasize their importance as a

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contributing factor. During our literature review, we came across articles that attempted to explain the relationship between stroke and sleep based on research findings. There is no doubt that there are many links between strokes and sleep, regardless of the different results obtained from different studies.[1,2]

MATERIAL AND METHODS

This study was approved by the Ethics Committee of the Hitit University School of Medicine (date: November 11, 2020, no: 347). The study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants before the study was conducted.

We conducted the study with patients with ischemic stroke aged 45-70 years who were hospitalized with ischemic stroke and had classical risk factors. These patients were conscious, cooperative, and oriented during the study. As part of the study, cases with dementia, chronic obstructive pulmonary disease, infectious conditions on chest X-rays, and morbidly obese people were excluded. We selected patients based on exclusion and inclusion criteria, and questionnaires were administered to them from the second day after they had suffered an ischemic stroke. The sleep quality, daytime sleepiness, obstructive sleep apnea (OSA) screening, and the level of daytime sleepiness of the patients and the control group were evaluated by a single neurologist using simple questionnaires.[2-5]

STATISTICAL METHOD

For the analysis of the data in this study, SPSS package program was used (version 22.0, SPSS Inc. Chicago, IL, USA. Hitit University Licensed). In descriptive statistics, continuous data with a normally distributed mean have been expressed as the mean±standard deviation, non-normally distributed continuous data have been expressed as the median (minimum-maximum), and variables with ordinal data have been expressed as numbers and percentages (%). The Kolmogorov-Smirnov test was used to determine the normality of the distribution. The Mann-Whitney U test was used for continuous variables whose mean comparisons did not show a normal distribution. In order to examine the relationships between categorical variables, either a chi-square test or Fisher's Exact test was used. According to the statistical significance level, it was evaluated as p=0.05.

RESULTS

There were 137 participants in the study. There were 67 (48.9%) patients in the control group, while 51.1% (n=70) were in the patient group. A total of 42.3% (n=58) of the participants were females, while 57.7% (n=79) were males. In accordance with Table 1, a comparison was made between the patients and control groups with regards to sociodemographic characteristics, diabetes mellitus, hyperlipidemia, atrial fibrillation, smoking, and alcohol use based on socio-demographic characteristics (p=0.572, p=0.714, p=0.793, p=0.731, p=0.45, p=0.622, p=0.304, p=0.234, p=1.000, respectively).

Statistically, there was no significant difference in the age of the patient group compared to the control group (p=0.995).

As for the total scores for the Epworth Sleepiness Scale and Pittsburgh Sleep Quality Scales, there was a statistically significant difference between the 2 groups (p<0.001, p<0.001, respectively) (Table 2, Figure 1). There was a statistically signbificant difference between groups with regard to Berlin Questionnaire (BQ) total score and the Stanford Sleepiness Scale (SSS) ratios (p=0.002, p=0.021, respectively) (Table 3). It was determined that a patient group with a total score of 60.0% (n=42) could be classified as low-risk, while a patient group with a total score of 40.0% (n=28) could be classified as high-risk. There were 83.6% of those in the control group (n=56) who had a low risk of OSA and 16.4% (n=11) who had a high risk for the condition. Among the patients (n=32) who completed the SSS, 45.7% reported feeling active and alert, while 68.7% (n=46) of the control participants reported feeling the same way. During the course of our study, we found that short sleep duration and poor sleep quality were associated with an increased risk of ischemic stroke. There is an association between short sleep duration and ischemic strokes. It has been found that short sleep du-

TABLE 1: The socio-demographic characteristics of the participants and the relationships between patient and control groups with regard to DM, HT, CAD, HL, AF, smoking, and alcohol use.

			Patient	Control	Total	p value
Gender	Female	n	28	30	58	0.572[a]
		%	40.0%	44.8%	42.3%	
	Male	n	42	37	79	
		%	60.0%	55.2%	57.7%	
Education	Uneducated	n	15	18	33	0.714[a]
		%	21.4%	26.9%	24.1%	
	Educated	n	12	13	25	
		%	17.1%	19.4%	18.2%	
	Primary school	n	20	15	35	
		%	28.6%	22.4%	25.5%	
	Secondary scholl	n	11	7	18	
		%	15.7%	10.4%	13.1%	
	High school	n	9	8	17	
		%	12.9%	11.9%	12.4%	
	University	n	3	6	9	
		%	4.3%	9.0%	6.6%	
DM	No	n	53	52	105	0.793[a]
		%	75.7%	77.6%	76.6%	
	Yes	n	17	15	32	
		%	24.3%	22.4%	23.4%	
HT	No	n	11	12	23	0.731[a]
		%	15.7%	17.9%	16.8%	
	Yes	n	59	55	114	
		%	84.3%	82.1%	83.2%	
CAD	No	n	55	56	111	0.455[a]
		%	78.6%	83.6%	81.0%	
	Yes	n	15	11	26	
		%	21.4%	16.4%	19.0%	
HL	No	n	41	42	83	0.622[a]
		%	58.6%	62.7%	60.6%	
	Yes	n	29	25	54	
		%	41.4%	37.3%	39.4%	
AF	No	n	56	58	114	0.304[a]
		%	80.0%	86.6%	83.2%	
	Yes	n	14	9	23	
		%	20.0%	13.4%	16.8%	
Smoking	No	n	48	52	100	0.234[a]
		%	68.6%	77.6%	73.0%	
	Yes	n	22	15	37	
		%	31.4%	22.4%	27.0%	
Alcohol	No	n	68	66	134	1.000[b]
		%	97.1%	98.5%	97.8%	
	Yes	n	2	1	3	
		%	2.9%	1.5%	2.2%	
Total		n	70	67	137	
		%	100.0%	100.0%	100.0%	

[a]Chi-square test: [b]Fisher exact test; DM: Diabetes mellitus; HT: Hypertension; CAD: Coronary artery disease; HL: Hyperlipidemia; AF: Atrial fibrillation.

TABLE 2: Comparison of age, BMI, Epworth Sleepiness Scale and Pitsburg Sleep Quality Scale total scores among the research groups.

	Group	n	Mean	Std. deviation	Median	Minimum	Maximum	p value
Age	Patient	70	65,7857	12,45618	66,0000	29	88	0.995
	Control	67	66,0746	10,54760	68,0000	35	88	
BMI	Patient	70	25,9271	1,96991	26,1500	22.50	29.7	0.477
	Control	67	25,7313	1,73731	25,7000	22.50	29.2	
Epworth Sleepiness Scale total scores	Patient	70	3,6429	4,06482	2,0000	0	14	**<0.001**
	Control	67	1,3881	2,25600	,0000	0	10	
Pitsburg Sleep Quality Index total score	Patient	70	5,0286	4,46556	3,5000	0	14	**<0.001**
	Control	67	1,9701	2,77963	1,0000	0	14	

Mann-Whitney U test; BMI: Body mass index.

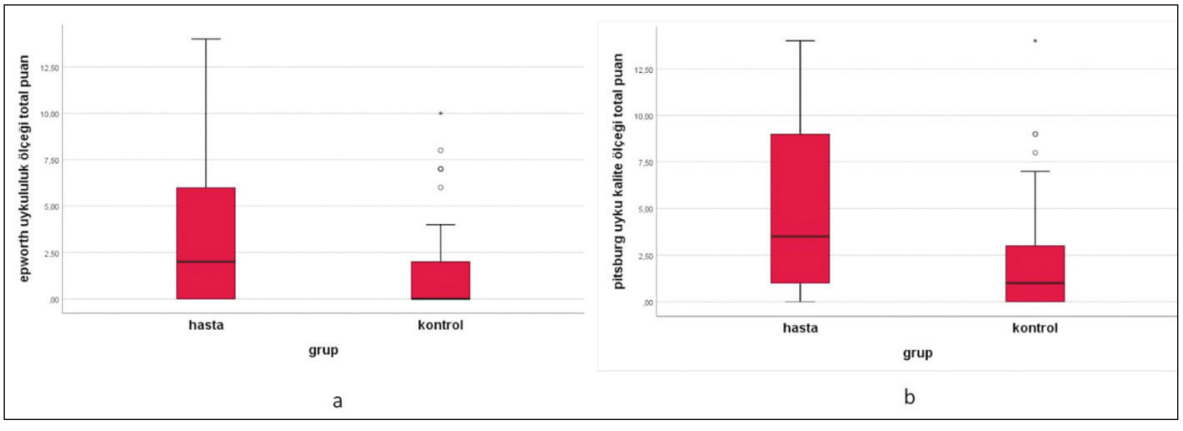

FIGURE 1: Box-plot plot of the distribution of Epworth Sleepiness Scale and Pitsburg Sleep Quality Scale total scores among the research groups of the participants.

TABLE 3: Comparison of the ratio of the Berlin Survey total score and the Stanford Sleepiness Scale according to the research groups.

			Group			
			Patient	Control	Total	p value
Berlin Questionnaire	Low risk	n	42	56	98	**0.002**[a]
		%	60.0%	83.6%	71.5%	
	High risk	n	28	11	39	
		%	40.0%	16.4%	28.5%	
Stanford Sleepiness Scale	Feeling active, vital or wide awake	n	32	46	78	**0.021**[a]
		%	45.7%	68.7%	56.9%	
	Functionig at high levels, but not at peak;	n	17	13	30	
	able to concentrate	%	24.3%	19.4%	21.9%	
	Awake but relaxed;responsive but not fully alert	n	11	7	18	
		%	15.7%	10.4%	13.1%	
	Somewhat foggy, let down	n	5	1	6	
		%	7.1%	1.5%	4.4%	
	Confused and slowed in movements	n	5	0	5	
		%	7.1%	0.0%	3.6%	
Total		n	70	67	137	
		%	100.0%	100.0%	100.0%	

[a]Chi-square test

ration is associated with a high frequency of OSA in our patients. As a result of this, we believe that this group of patients with ischemic stroke has a short sleep duration.

DISCUSSION

Millions of people suffer from strokes every year around the world. Identifying stroke risk factors is one of the most important steps in reducing the morbidity associated with cerebrovascular diseases (CVD).[6,7] It is important to understand that sleep disorders play a significant role in the etiology and recurrence of strokes, in addition to unanswered questions.

The purpose of this study was to evaluate the sleep quality of patients in the last month before they suffered an ischemic stroke by using simple questionnaires in order to determine how they felt about their sleep. A sleep-wake cycle disorder, a sleep-disorder, sleep breathing disorder (SBD) are evaluated in this study.

There have been numerous studies and meta-analyses that have examined the relationship between sleep duration and stroke risk. Yet, despite these studies being conducted up to this point, their results have been contradictory. Several studies in the literature indicate that both long and short periods of sleep are associated with an increased risk of stroke, presenting a U-shaped relationship.[8,9]

A study examining the relationship between sleep duration and stroke found that sleep for more than nine hours was associated with an increased risk of both total stroke and ischemic stroke. An increased risk of intracerebral haemorrhage is associated with less than seven hours of sleep per night.[10]

A bidirectional relationship between sleep and stroke has been found to be quite complex.[11] Sleep-related physiological changes and circadian variations are believed to play a significant role in both the aetiology and the onset of strokes due to the changes occurring in the cardiovascular system due to sleep. In fact, it has been shown in the literature that certain sleep disorders may increase the risk of cardiovascular disease; for example, OSA and sleep duration have been considered modifiable risk factors for strokes.[12] It has been shown that OSA can increase blood pressure fluctuations that are made worse by sleep splitting. This can increase stroke risk through its effects on traditional stroke risk factors, especially hypertension, due to increased sympathetic activity.[13,14] A variety of mechanisms may explain these relationships between strokes and sleep apnea. It has been found that OSA patients have increased sympathetic outflow cycles and oxygen desaturations throughout the night due to their recurrent decreases in ventilation, which can lead to sustained nocturnal hypoxia as well as chronic hypoxia during the day. As a result of carbon dioxide partial pressure changes observed in OSA, cerebral circulation is affected. During periods of apnea and hyperpnea, cerebral circulation is affected by vasoconstriction and vasodilation. Besides affecting endothelial dysfunction, OSA may also affect inflammation-related vasodilators and vasoconstrictor substances, which are thought to contribute to the development of atherogenic and prothrombotic conditions associated with OSA.[15-18]

Various mechanisms have also been identified as predisposing OSA to the development of atrial fibrillation (AF).[19] There was a significant difference between the control and patient groups in terms of the results of the BQ in our study. According to this simple questionnaire, the patient group was likely to be at risk of OSA than those in the control group.

According to a study published in 2015, it has been shown that long sleep duration is associated with a higher risk of hemorrhagic stroke, while short sleep duration is associated with a higher risk of ischemic stroke.[20] According to Eguchi et al., short sleep duration was an independent risk factor for stroke among hypertensive patients.[21] In our study, as in many studies in the literature, the duration of sleep was shortened in our patients in the pre-stroke period, similar to what has been found in many studies. It has been shown in another study that in individuals with ischemic and hemorrhagic stroke, the frequency of both stroke subgroups increases if they sleep less than 6 hours or more than 9 hours per night.[22]

The results of the studies that investigated the putative effect of habitual sleep on cerebrovascular risk have indicated that sleep duration is associated with stroke incidence in a J-shaped pattern. It has been found that an increase of one hour in sleep time is associated with an increase of 10-15% in stroke risk. It is estimated that individuals who sleep more than 8 hours a night are more likely to have a stroke by about 50% than individuals who sleep a normal amount of time during the night for 10 years.[23] This study aims to demonstrate that sleep disorders play a significant role in the aetiology of strokes and that this can be demonstrated even by simple tests. There is no doubt that sleep disorders play a significant role in the aetiology of stroke, and it is important to keep this in mind as well.

There are a number of traditional risk factors for stroke, including AF, age greater than 65, heart disease, carotid artery stenosis, smoking, diabetes mellitus, and dyslipidemia. There is an association between sleep duration and traditional stroke risk factors. One of the first studies to propose that short and long sleep are risk factors for high blood pressure can be found in the sleep heart health study.[24] Short and long sleep durations have been found to be associated with diabetes, obesity, heart disease, and low levels of serum high-density lipoprotein cholesterol, which are all diseases associated with a lack of sleep.[25,26] It has also been shown that long sleep duration is also associated with the development of AF.[27] As a result of classical risk factors that can also be associated with short sleep duration, we found a statistically significant short sleep duration in the aetiology of ischemic stroke in the patient group.

There is also evidence that poor sleep quality plays a role in the etiopathogenesis of stroke. For example, REM sleep behaviour disorder (RBD) independently increases the risk of stroke by a factor of 1.5.[28] As a result of RBD, the stroke mechanism can be summed up as increased sympathetic activity and changes in blood pressure in conjunction with a deterioration in sleep quality.[29] The ultrasound measurement of carotid intima-media thickness (IMT) is a non-invasive method of determining the extent of atherogenic damage to the arteries of the carotid artery.[30] Based on the literature review, it is evident that there are many different results that have been obtained between IMT and sleep duration.[31,32]

There is conflicting evidence regarding the relationship between sleep duration and stroke risk. Several studies have shown that short sleep durations are associated with an increased stroke risk, while long sleep durations are associated with an increased stroke risk.[33,34] Depending on the type of stroke, sleep duration can be either long or short, but the reasons for this are unclear. Stroke risk is largely unknown regarding the mechanism behind long or short sleep durations. Although many mechanisms continue to be investigated today, long sleep duration has been associated with increased levels of inflammatory biomarkers, which is one important biological pathway.[35,36] While sleep disorders before stroke are considered risk factors, sleep disorders may also occur in the post-stroke period. According to recent studies, identifying sleep disorders is crucial to stroke prevention. For a deeper understanding of this issue and an evaluation of the pathophysiological causes of these possible associations, longitudinal prospective studies with more participants with each stroke subtype are required.[37]

In preventing stroke, sleep is becoming increasingly recognized as an important lifestyle factor. SBD therapy can potentially improve stroke prevention and post-stroke outcomes in future long-term and comprehensive clinical trials. Although many studies have revealed the importance of sleep disorders, we still believe that clinicians have not shown the necessary sensitivity to sleep disorders in the etiology of stroke. Sleep disorders are bidirectionally related to stroke. This demonstrates the importance of establishing greater collaboration between clinicians interested in sleep and stroke in order to improve prevention and treatment of these disorders. We are sure that more comprehensive and prospective studies in which people with sleep disorders are followed for a long period in terms of stroke will clarify this paradoxical situation between stroke and sleep. The study's limitations included not examining the carotid IMT values and the patients' daily activity levels. There is statistically significant evidence that sleep plays an important role in stroke development, even in this small sample.

CONCLUSION

Sleep quality and duration were associated with an increased risk of ischemic stroke in our study. Poor sleep quality and sleep loss due to various causes are common health problems often overlooked by physicians and are associated with serious medical conditions such as diabetes, hypertension, obesity, depression, and anxiety. The presence of these comorbidities increases the risk of stroke for the individual. Sleep disorders are associated with CVD and stroke, as they represent both a risk factor and a consequence.

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