Clinical Significance Of Brain Lesion And Sleep Disorder In Stroke Patients

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Citation

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Abstract

Introduction: Stroke is a condition in which a person has sudden neurological deficits that is caused by a disorder to blood vessels in brain. The sleep cycle is regulated by the brain thus stroke may cause a sleep disorder due to the brain's structures that play role in sleep regulation. There are 21-77% stroke patients who have post-stroke sleep disorder. On the other hand, sleep plays role in stroke rehabilitation. Data regarding the association between sleep disorder and brain lesion in stroke patients is still limited.

Aims: To determine the association between brain lesion and sleep disorder in stroke patients which were hospitalized in the neurological ward of Dr. Hasan Sadikin Hospital, Bandung.

Methods: This is an analytical observational cross-sectional study. The study population were hospitalized stroke patients in the neurological ward of Dr. Hasan Sadikin Hospital Bandung. The inclusion criteria were patients who were compos mentis, first acute stroke, stable vital signs, and medical records completed with CT scan results. The data were collected from the result of Pittsburgh Sleep Quality Index (PSQI) and the secondary data from the CT scan results in patients' medical records. The data was analysed by chi-square with fisher's exact test.

Result: The subjects' characteristics data from 20 acute stroke patients, there were 10 male patients and 10 female patients, with the most common age range was 61-70 (7 patients), 17 patients had ischemic stroke, 14 patients had hypertension, and 3 patients had diabetes mellitus. The PSQI results showed 10 patients were interpreted as good sleepers and 10 patients as bad sleepers. Amongst 10 bad sleepers, the most common lesion was basal ganglia. The prevalence ratio of the sleep disorder in stroke patients with subcortical lesion was 6.7 more likely than in stroke patients with cortical lesion.

Conclusion: There was a significant association between brain lesion location and sleep disorder in stroke patients with p-value 0.033 ($p<0.05$). Therefore, stroke patients with subcortical lesion should be more monitored concerning their sleep.

INTRODUCTION

Stroke is a condition in which a person has sudden neurological deficits caused by disorder to brain blood vessels.[1] According to Indonesia's statistical profile published by World Health Organization (WHO) in 2015, stroke ranked first as the most life-threatening common diseases, with prevalence 21.2%,[2] meanwhile according to Riset Kesehatan Dasar (Riskesdas) 2013 conducted by the ministry of health of Indonesia, the stroke prevalence in Indonesia is 12% and in West Java is 12.1%.[3]

The sleep cycle is regulated by the brain and stroke can cause sleep disorder as the affected brain structures may play role in sleep regulation. 21-77% stroke patients had post-stroke sleep disorder. Post-stroke sleep disorder may take many forms such as sleep disordered breathing (SDB), insomnia, hypersomnia, and others. Post-stroke sleep disorder can be diagnosed using questionnaires and polymsonography (PSG). Based on the previous study that used questionnaires to acute ischemic stroke patients, it was found that 77% had a decrease in sleep quality, 44.6% had difficulty to initiate sleep, 24.8% had difficulty to stay awake, 11.9% had excessive daytime sleepiness (EDS), and 65.35% had SDB. According to a study conducted to 277 stroke patients that used questionnaires, 56.7% had insomnia, 50-71% had SDB, and 10-15% had restless legs

syndrome (RLS). The study concerning post-stroke sleep disorder is still limited although the study concerning stroke and sleep disorder has been conducted in many times. This explains why the data regarding the post-stroke sleep disorder is limited4 and there is no specific guidelines for doctors to do about sleep disorder in stroke rehabilitation that was published by UK National Institute of Clinical Excellent (NICE).[5]

The data regarding the association between sleep disorder and brain lesion in stroke patients is still limited. Some studies have analysed the association between brain lesion location and sleep disorder in stroke patients, however the studies were only done to the specific sleep disorder such as RLS, insomnia, and REM sleep behaviour disorder (RDB). An observational study concerning RLS found that subcortical lesion such as pyramidal tracts and axis of basal ganglia-brainstem, which plays role in motoric function and sleep cycle, is associated with RLS.[6] An observational study concerning insomnia found that lesion in left dorsomedial frontal is associated with insomnia.[7]

Based on the previous studies regarding post-stroke sleep disorder, it was recognized that there was an association between post-stroke sleep disorder and stroke rehabilitation. However, the study about brain lesion and post-stroke sleep disorder is still limited.[4] A previous study regarding the topic didn't indicate a significant association.[6] The study about brain lesion location and post-stroke sleep disorder in Indonesia has never been conducted before, therefore it is needed to conduct a study about the association between brain lesion location and post-stroke sleep disorders.

METHODS

This study is an analytical observational cross sectional study that analyse the association between brain lesion and sleep disorder in stroke patients which was approved by The Ethical Committee of Health Research of Medicine Faculty Universitas Padjadjaran and The Ethical Committee of RSUP Dr. Hasan Sadikin Bandung. The inclusion criteria were patients aged 20-70 years, compos mentis, had acute stroke, had stable vital signs, and had complete medical records with the CT scan results. The exclusion criteria were patients with aphasia, had sleep disorder before stroke, consumed sedative drugs and antidepressants, and had dementia.

The data collection was done with consecutive sampling technique to stroke patients that were hospitalized in RSUP Dr. Hasan Sadikin Bandung. From 68 stroke patients, 48 patients were excluded and 20 patients were included. The independent variable of the study is brain lesion location. The dependent variable of the study is sleep disorder.

The instruments used in this study were Pittsburgh Sleep Quality Index (PSQI) and CT scan results that were collected from the patients' medical records. PSQI consists of 19 questions, but only 10 questions were asked to the patients and 9 questions were asked to the patients' company. PSQI measured 7 components that are, the subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disorder, the use of sleep drugs, and dysfunction of daytime activities. The PSQI scores then were interpreted as good sleepers (score 0-5) which indicates the patient doesn't have sleep disorder and as bad sleepers (score >5) which indicates the patient has sleep disorder. The data then was analysed using SPSS 16.0 (SPSS, IBM Corporation, Somers, NY, USA) for Windows. Both of the variables were analysed using chi-square fisher because the cells didn't have expected count <5 more than 20%. $P<0.05$ was considered statistically significant.

RESULTS

Based on 20 acute stroke patients, 11 patients were men, 8 patients aged in range 61-70 years old, 17 patients had ischemic stroke, 14 patients had hypertension, 3 patients had diabetes mellitus, 3 patients had hyperlipidemia, and the most common lesion found in the study were basal ganglia, internal capsule, and pons. The demographics and clinical characteristics of the patients are shown in Table 1.

Table 1

Demographics and Clinical Characteristics of Patients

Characteristics	N
Gender	
Male	10
Female	10
Age	
20-30	1
31-40	1
41-50	6
51-60	4
61-70	8
Stroke Type	
Ischemic	17
Hemorrhagic	3
Brain Lesion	
Cortical	
Temporal	3
Parietal	2
Subcortical	
Basal Ganglia	6
Internal Capsule	4
Thalamus	1
Pons	3
Midbrain	1
Hypertension*	
Yes	14
No	6
Diabetes Mellitus*	
Yes	3
No	17
Hyperlipidemia*	
Yes	3
No	17

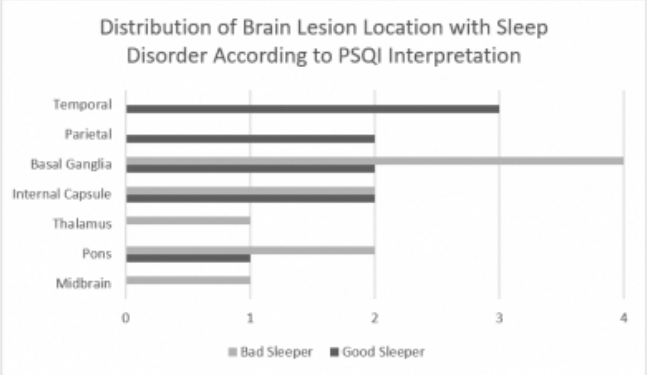
* The patients may have more than one risk factor

Based on the interview conducted to the patients, 10 patients were categorized as bad sleepers and 10 patients were categorized as good sleepers.

Distribution of the brain lesion location with sleep disorder status is shown in graphic 1, 4 of 6 patients who had lesion in basal ganglia had sleep disorder, 2 of 3 patients who had lesion in pons had sleep disorder, patient who had lesion in thalamus and midbrain had sleep disorder, 2 of 4 patients who had lesion in internal capsule had sleep disorder. All patients who had cortical lesions didn't have sleep disorder.

Graph 1

Distribution of Brain Lesion with Sleep Disorder According to PSQI Interpretation



The 20 samples were analysed using chi-square with Fisher's Exact Test. The association of the brain lesion location and sleep disorder is shown in table 2.

Table 2

Distribution of Sleep Disorder According to PSQI Interpretation With Brain Lesion

Brain Lesion ıtion	Frequency (N) *Good Sleepers* (Skor 0-5)	*Bad Sleepers* (Skor lebih dari 5)	P value
Cortical	5	0	0.033
Subcortical	6	9	
Total	11	9	

According to table 2, the stroke patients who had subcortical lesion were 6.7 times more likely to have sleep disorder than stroke patients who had cortical lesion. The p value acquired by Fisher's Exact Test was 0.033 ($p<0.05$) which means that there was a significant association between brain lesion and sleep disorder in stroke patients.

DISCUSSION

In this study, there was a significant association between brain lesion and sleep disorders in stroke patients. Stroke patients with subcortical lesion is 6.7 more prone to have sleep disorder than stroke patients with cortical lesion. However, this finding contradicts with the previous study that was conducted to 241 acute ischemic stroke patients by using PSQI. The study didn't find any significant association between brain lesion location and sleep disorder.[8,10] In addition, a cohort study that was conducted to 142 stroke patients didn't find any significant association between brain lesion and sleep disorder, specifically sleep related-breathing disorder.[9] On the other side, this study supports a prospective cohort study that was conducted to 157 stroke patients. The study found that sleep disorder, specifically restless legs syndrome, was found in 1 of 54 patients with cortical lesion,

whilst the rest of the patients had subcortical lesion.1

Based on the study, 4 of 6 patients whose lesion in basal ganglia had sleep disorder. Basal ganglia consists of 4 mayor structures, striatum, globus pallidus, subthalamic nucleus, and substantia nigra.[11] The study's finding supports a finding of an experimental study that was conducted to mice. The study found that the mice that had lesion in globus pallidus and substantia nigra were associated with an increased wake.[12] This is caused by the anatomical structure of the basal ganglia. Striatum consists of inhibitory GABAergic neurons (gamma amino butyric acid) and excitatory cholinergic neurons. Most of the neurons in striatum are GABAergic. Globus pallidus consists of internal globus pallidus and external globus pallidus. All the neurons in external globus pallidus are GABAergic and all the neurons in internal globus pallidus are glutamatergic and GABAergic. Thus, the basal ganglia has a significant role in the sleep regulation. This is also supported by the previous study's finding that the bilateral lesion in striatum and nucleus accumbens led to a significant reduction of the wake state. Therefore, the findings prove that striatum has a role in maintaining the wake state. The lesion in external globus pallidus also led to insomnia in mice with 45% increase of the wake state duration.[13] However, this study's finding may be affected by the number of patients who had lesion in basal ganglia. Stroke patients with lesion in basal ganglia is associated with hypertension while there are stroke patients with hypertension in this study.

Based on the study, 2 of 3 stroke patients whose lesion in pons had sleep disorder. Pons is believed to play role in promoting the rapid eye movement (REM) phase in sleep and in promoting wake.[14] This supports a case report that found the lesion in pons, precisely in dorsomedial pons that involves dorsal sublateral tegmental nucleus, and subcerleus nucleus is associated with sleep disorder, specifically REM sleep behaviour disorder (RDB).[15]

Based on the study, the stroke patient whose lesion in thalamus had sleep disorder. According to a study, thalamus plays important role in sleep-wake regulation because there is a direct projection to thalamus from some areas in midbrain and other structures of brain including hypothalamus that's also crucial in sleep promotion.[16] This supports another study that found the stroke patients with lesion in paramedian thalamus had cognitive and psychic disorder, and disorder in nonrapid eye movement phase (NREM) in sleep. However, not all stroke patients that had lesion in thalamus had the same sleep disorder characteristics. Therefore, sleep disorder associated with lesion in thalamus depends on the extension of the lesion.[17]

Based on the study, 2 of 4 stroke patients whose lesion in internal capsule had sleep disorder. This finding supports a study that was conducted to 87 stroke patients who had lesion in internal capsule or pons. The study found a significant association between brain lesion in internal capsule or in pons with sleep disorder, specifically sleep related disorder breathing.[18] This finding also supports a case control study that was conducted to 40 patients with primary insomnia. The study found that primary insomnia is associated with a reduced integrity of white matter in anterior internal capsule.[19]

The stroke patient whose lesion in midbrain had sleep disorder. It is hypothesized that it is because midbrain is an essential source of dopamine in basal ganglia. The dopaminergic neurons project from midbrain to striatum, external globus pallidus and internal globus pallidus. The dopaminergic neurons in that area promote sleep.[13]

The limitation of this study was less data distribution and no consideration of confounding factors. The data distribution in this study was limited due to less amount of hospitalized stroke patients in RSUP Dr. Hasan Sadikin Bandung that met the inclusion and exclusion criteria of the study. Therefore, it is recommended to conduct another research with more variable and homogenous data distribution, bigger sample size, and also, with more tools such as Epworth Sleepiness Scale (ESS) that screens excessive daytime sleepiness, Insomnia Severity Index (ISI) that screens insomnia, and other questionnaires that could detect a specific sleep disorder because each kind of sleep disorders require different treatments. In addition, it is needed to conduct a prospective cohort research to observe the changes of sleep patterns whether it gets better during post-acute stroke. The consideration of confounding factors such as the risk factors in stroke; genders, age, diabetes mellitus status, hypertension status, and other factors such as depression status is also recommended.

CONCLUSION

Based on this study's finding, there is a significant association between brain lesion location and sleep disorder in stroke patients in which stroke patients who had subcortical lesion were 6.7 more likely to have sleep disorder than stroke patients with cortical lesion. It is also concluded that stroke patients with subcortical lesion have to

be more monitored concerning their sleep. This is due to the fact that sleep has many benefits such as physical and mental functions restoration,8 memory consolidation, and increasing the learning capabilities in motoric and sensoric function. Thus, sleep plays role in stroke patients' rehabilitation.[20]

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